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What's New and Important in Pediatric Ophthalmology and Strabismus for 2019

Senior Instructor: Darron A Bacal MD
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What's New and Important in Pediatric Ophthalmology and Strabismus for 2019

The Complete and Unabridged handout

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October 14, 2019

Presented by the

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1.AMBLYOPIA

Microvascular changes in amblyopic eyes detected by optical coherence tomography angiography.

Karabulut M, Karabulut S, Sül S, Karalezli A. *JAAPOS* 2019 June; 23 (3): 155.e1-155.e4

The available evidence of direct retinal changes in amblyopic eyes is inconclusive. The aim of this prospective cross-sectional study was to investigate retinal microvascular findings detected by optical coherence tomography angiography (OCT-A) in amblyopic eyes compared with normal eyes. A total of 23 amblyopic (strabismic, ametropic, anisometropic, and meridional amblyopia) and 22 normal eyes were included. All patients underwent complete ophthalmological examination and OCT-A imaging. Vessel density (VD) percentage in the superficial and deep retinal vessel plexus, foveal avascular zone (FAZ) area, flow area in the outer retina and choriocapillaris, and retinal thickness in μm in a 6.00 × 6.00 mm scan size were measured and compared between groups. Mean FAZ area was smaller in the amblyopic group; however, the difference was not statistically significant (P = 0.145). The outer retina flow area was significantly wider in the amblyopic group (P = 0.03). The fovea was thicker in the amblyopic group (P = 0.02). In addition, VD in both the superficial and deep retinal plexus was significantly lower in amblyopic eyes in all quadrants except the fovea. In amblyopic subgroups, VD of anisometropic amblyopic eyes was significantly higher than other subgroups in both superficial and deep retinal plexuses at all regions except the fovea. Other measures were similar in between groups. The study demonstrated some differences between amblyopic eyes and normal eyes on the OCT-A. Nonetheless, the study has several limitations, including its small sample size. Of note, the documented changes in FAZ size may be related to the axial length of the eye and not to the presence of amblyopia. The clinical significance of the OCT-A findings in amblyopia remains to be clarified.

Binocular amblyopia treatment with contrast-rebalanced movies.

Birch EE, Jost RM, De La Cruz A, Kelly KR, et al. *JAAPOS* 2019 June; 23(3): 160.e1-160.e5

Binocular amblyopia treatments promote visual acuity recovery and binocularity by rebalancing the signal strength of dichoptic images. Most require active participation by the amblyopic child to play a game or perform a repetitive visual task. The purpose of this prospective non-randomized study was to investigate a *passive* form of binocular treatment with contrast-rebalanced dichoptic movies. A total of 27 amblyopic children (4-10 years of age) wore polarized glasses to watch

six contrast-rebalanced dichoptic movies on a passive 3D display during a 2-week period. Amblyopic eye contrast was 100%; fellow eye contrast was initially set to a lower level (20%-60%), which allowed the child to overcome suppression and use binocular vision. Fellow eye contrast was incremented by 10% for each subsequent movie. Best-corrected visual acuity, random dot stereoacuity, and interocular suppression were measured at baseline and at 2 weeks. Amblyopic eye best-corrected visual acuity improved from 0.57 ± 0.22 at baseline to 0.42 ± 0.23 logMAR (t_{26} = 8.09; P < 0.0001; 95% CI for improvement, 0.11-0.19 logMAR). Children aged 3-6 years had more improvement (0.21 ± 0.11 logMAR) than children aged 7-10 years (0.11 ± 0.06 logMAR; t_{25} = 3.05; P = 0.005). Children with severe amblyopia (≥0.7 logMAR) at baseline experienced greater improvement (0.24 ± 0.12 logMAR) than children with moderate amblyopia at baseline (0.12 ± 0.06 logMAR; t_{25} = 3.49; P = 0.002). The authors conclude that in this cohort, passive viewing of contrast-rebalanced dichoptic movies effectively improved visual acuity in amblyopic subjects. The degree of improvement observed was similar to that previously reported for 2 weeks of binocular games treatment and with 3-4 months of occlusion therapy. Several limitations are acknowledged by the authors. The study did not have a randomized comparison to patching or other amblyopia treatments. To address these limitations, the authors state that they are currently conducting a randomized trial of at-home dichoptic movies versus patching for the treatment of amblyopia (NCT03825107).

Self-perception in Children Aged 3 to 7 Years With Amblyopia and Its Association With Deficits in Vision and Fine Motor Skills

Birch EE, Castañeda YS, Cheng-Patel CS et al. *JAMA Ophthalmology*. May 2019;137(5):499-506.

This was a cross-sectional study at a pediatric vision laboratory from 2016 to 2018 in healthy children aged 3 to 7 years. Included were 60 children with amblyopia; 30 children without amblyopia but previously treated for strabismus, anisometropia, or both; and 20 control children. In addition to assessment of visual acuity and stereopsis, children completed the Pictorial Scale of Perceived Competence and Social Acceptance for Young Children, which includes the specific domains: (1) cognitive competence, (2) peer acceptance, (3) physical competence, and (4) maternal acceptance. Fine motor skills were evaluated with the Manual Dexterity and Aiming and Catching scales of the Movement Assessment Battery for Children, second edition.
Results found that children with amblyopia had significantly lower mean peer acceptance and physical competence scores compared with the control children (*P* = .04 and *P* = .009, respectively). In the children with amblyopia, self-perception of physical competence was significantly correlated with aiming and catching skills (*P* = .001) and stereoacuity (*P* = .02). In addition, the authors found that children treated for strabismus or anisometropia, but without amblyopia, had significantly lower mean physical competence scores compared with control children

($P = .03$). In summary, the authors suggest that in children with altered visual development, lower self-perception of peer acceptance and physical competence are part of the broader effects of amblyopia, anisometropia, and/or strabismus in everyday life.

Self-Perception of School-aged Children with Amblyopia and Its Association with Reading Speed and Motor Skills

Birch EE, Castañeda YS, Cheng-Patel CS BS; et al. *JAMA Ophthalmology*. February 2019;137(2):167-174.

The authors of this study performed a cross-sectional analysis from January 2016 to June 2017 at the Pediatric Vision Laboratory of the Retina Foundation of the Southwest to determine if reading and eye-hand coordination deficits in children with amblyopia could impact their scholastic, social, and athletic competence. The study included 81 children in third to eighth grade: 50 children with amblyopia, 13 children without amblyopia with strabismus, anisometropia, or both; and 18 control children. Of the participants, 62% were girls and the mean age was 10.6 years. Study findings indicated that children with amblyopia had significantly lower scores than control children for scholastic ($P = .004$), social ($P < .001$), and athletic ($P = .001$) competence. Among the children with amblyopia, a lower self-perception of scholastic competence was associated with a slower reading speed ($P = .002$) and a lower self-perception of scholastic, social, and athletic competence was associated with worse performance of aiming and catching (scholastic $P = .007$; social $P < .001$; athletic $P = .003$). No differences in the self-perception of physical appearance, conduct, or global self-worth were found between the amblyopic and control groups of children. Study findings suggest that lower self-perception is associated with slower reading speed and worse motor skills in children with amblyopia. While this study of < 100 children has imitations, the authors highlight the wide-ranging effects of altered visual development for children in their everyday lives.

Impaired Spatial Hearing in Amblyopia: Evidence for Calibration of Auditory Maps by Retinocollicular Input in Humans

Michael D Richards, Herbert C Goltz, Agnes MF Wong *Invest Ophthalmol Vis Sci*. March 2019;60:944-953.

This study evaluates the correlation between amblyopia and the auditory neural pathways; whether alteration in visual neural pathways also caused an alteration in auditory neural pathways. Ten subjects with and ten subjects without amblyopia were examined for minimal audible angle as well as accuracy in localization of the sound. The subjects had either strabismus or anisometropic amblyopia with the

poorer seeing eye being 20/30, at best. Patients with amblyopia performed poorer on both examinations than their non-amblyopic counterparts. This study shows the potential effects on non-visual pathways during the development of amblyopia. Further studies are needed to be able to stratify the density of the amblyopia as well as together with neurological testing such as electroencephalography.

Amblyopia Elimination Project: Pediatric Medical Home Based Community Vision Screening.

Howard Freedman, MD; Adam Fundora, RN, MPH, CPH; John Baker, MD; J. Timothy Diegel, MD *J Ped Ophth & Strabismus*,2019;56(3):146-150

The purpose of this study was to examine whether facilitating access to instrument-based screening equipment will increase the total number of high-quality, age-appropriate vision screenings provided to the preschool aged population. The goal of the Naples Lions Amblyopia Elimination Project was to place a SPOT Vision Screener (Welch Allyn, Skaneateles Falls, NY) in every pediatric medical home using philanthropic dollars. Participating medical homes agreed to provide data on the number of children screened, number of referrals made, criteria for referral, and follow-up notes regarding examination outcomes. The study showed that in 2012, only 4 of the 23 pediatric medical homes in Collier County were using instrument-based vision screening equipment. By 2017, 19 of the 25 pediatric medical homes (76%) used SPOT Vision Screeners. In 2017, 6,052 preschool children were screened in these 19 pediatric medial homes. The authors conclude that the concept for this community-based philanthropic effort is original in its design and implementation and is a significant step forward in the goal to eliminate preventable permanent vision loss in children.

A Randomized Trial of Binocular Dig Rush Game Treatment for Amblyopia in Children Aged 7 to 12 Years

Pediatric Eye Disease Investigator Group: Jonathan M Holmes, Ruth E Manny, Elizabeth L Lazer, Eileen E Birch, et al *Ophthalmology*. March 2019;126(3): 456-466.

The purpose was to compare visual acuity (VA) improvement in children aged 7 to 12 years with amblyopia treated with binocular iPad game (Dig Rush) plus spectacle correction vs spectacle correction alone. It is a multi-center randomized clinical trial with 138 participants with amblyopia from strabismus, anisometropia, or both. Participants were required to have at least 16 weeks of optical treatment in spectacles if needed or demonstrate no improvement in amblyopic-eye visual acuity (VA) for at least 8 weeks prior to enrollment. Participants were randomized to Dig Rush (1 hour per day 5 days per week) plus spectacle wear as needed or continued spectacle wear. The main outcome measure was change in amblyopic eye VA from baseline to 4 weeks. There was no greater im-

provement in the amblyopic eye VA in the Dig Rush plus spectacle group compared to spectacle only group. Although adherence with Dig Rush was suboptimal it was better than that reported in other studies making it unlikely that decreased adherence was the cause of the poor response. The authors note that previous studies have suggested that the failure to find any dose-response relationship between duration of play, or increment of contrast, and improvement in VA casts doubt on the efficacy of binocular treatments such as Dig Rush per se. Although there is no apparent benefit of Dig Rush treatment over a 4 to 8- week period for 7 to 12-year old children, there is evidence that is may be beneficial in younger children. This is being evaluated in an ongoing PEDIG trial enrolling children age 4 to 6 years.

Bagolini filter bars: an analysis of light transmittance and their use in a pediatric population.

England LC, Davis H. *Strabismus*. 2019 Jun;27(2):78-87.

The density of suppression can be used to guide occlusion therapy, however there is limited data outside of a single, small, retrospective study that investigates its use. Previously the density of suppression was measured with a Bagolini Filter bar by Sbisa Ophthalmic Instruments, but production of this instrument was stopped in 2008. The aim of this article is to compare the results of the new Sbisa bar and Bagolini filter for measuring single binocular vision in children in a prospective, cross-sectional, repeated measures study. Thirty-three patient from 5-12 years old with unilateral strabismus were enrolled. The authors found that the Sbisa bars are limited by their lack of comparability or repeatability as filter readings differ when comparing between Sbisa bars or between a Sbisa bar with a Bagolini filter. This study identified the need for bars with consistent, reproducible reduction of light transmittance in order to obtain accurate clinical information regarding suppression.

Amblyopia treatment and quality of life: the child's perspective on atropine versus patching.

Steel DA, Codina CJ, Arblaster GE. *Strabismus*. 2019 Jul 22:1-9.

Amblyopia treatment has the potential to affect a child’s psychosocial well-being. In this prospective study, the authors aimed to compare the impact of patching and atropine treatment on the quality of life questionnaires (CAT-QoL and the PedsQL HRQoL) in 5-7 year old children with amblyopia. They enrolled 46 patients with similar ages and demographics (patching n = 30, mean age 69.7 months; atropine n = 16, mean age 69.3 months) and assessed the quality of life prior to treatment and after four weeks of treatment. Parents/patients were not randomized but rather were allowed to select their preferred treatment option. Results showed that there was no statistically significant difference in the quality of life scores between the patching and atropine groups (patch median = 6.3, Atropine median = 5.6, U = 199, p = .341, 95% CI of the median difference of -2.3

to 0.9). Future studies of larger, equally sized, randomized groups of patients receiving amblyopia treatment for the first time and during the entire course of their amblyopia treatment would help address some of the limitations of this study, particularly over a longer time period.

Refinement of the Child Amblyopia Treatment Questionnaire (CAT-QoL) using Rasch analysis.

Carlton J. *Strabismus*. 2019 Apr 23:1-12.

The Child Amblyopia Treatment Questionnaire is designed for children 4-7 years old. The authors aimed to refine the questionnaire and validate this refinement. They included 331 patient, however 11 were excluded due to incomplete data and an additional 41 were excluded due to extreme responses. After performing Rasch analysis, the updated instrument consisted of 8 times each with a 3 level response. They found the refined scale has good range and coverage. The authors provide a link to the instrument and indicate it may be useful in providing an objective measure of quality of life in amblyopia treatment from a child's perspective. Further research is required to examine reliability and validity.

Comparison of the CAT-QoL and PedsQLTM instruments in measuring quality of life in amblyopia treatment: preliminary results.

Carlton J. *Strabismus*. 2019 May 23:1-7.

The aim of this study was to compare the amblyopia-specific quality of life surgery with the generic pediatric quality of life inventory. Using the same population from the prior month's publication, the author found that both instruments had good reliability and that there was a moderate correlation between them. The amblyopia instrument was not able to discriminate between severity groups. The authors conclude that the CAT-QoL can be used by other groups/populations to assess the reliability, validity and responsiveness of the instrument. If subsequent studies confirm its reliability, it could be useful clinical and research tool.

Retinal Microvasculature in Amblyopic Children and the Quantitative Relationship Between Retinal Perfusion and Thickness

Wuhe Chen, Jiangtao Lou, Frank Thom, Yingjie Mao, et al *Invest Ophthalmol Vis Sci*. March 2019;60:1185–1191.

This study evaluated retinal vessel density in both amblyopic and non-amblyopic eyes using OCT-Angiography. They compared 85 amblyopic patients with bilateral, anisometropic, or strabismic amblyopia to 66 age-controlled participants. Foveal, parafoveal, and sectoral quadrants in both the superficial capillary plexus (SCP) and deep capillary plexus were examined. No significant differences in retinal vas-

cular density were noted in the deep capillary plexus. There was a decreased capillary density in amblyopic eyes when compared to control eyes. This was shown to be the case only in anisometropic amblyopic eyes. This difference was also seen in the fellow eyes of the amblyopic eyes when compared to the control eyes. As stated by the authors, there is relevant differences of capillary density when comparing amblyopic to control eyes, though the significance and and causality of this difference is yet to be defined.

The Effects of Anisometropic Amblyopia on the FNS and TNO Stereotest Thresholds in Four- to Eight-Year-Olds

Ateiza, Aishat; Davis, Helen *Br Ir Orthopt* J 2019; 15(1): 72-81

The purpose of the study was to compare stereoacuity measured by random dot stereogram TNO Randot Stereotest (TNO) and real depth stereogram Frisby Near Stereotest (FNS) in patients with anisometropic amblyopia versus controls. The study showed that all patients performed better on FNS compared to TNO and that control subjects achieved better stereoacuity on both TNO and FNS compared to patients with anisometropic amblyopia. There was no statistically significant difference between the level of spherical anisometropia, visual acuity, and intraocular acuity difference (IAD) and their FNS stereoacuity. TNO stereoacuity did correlate with the level of visual acuity in the amblyopic eye, the IAD, and degree of anisometropia.

Visual Search in Amblyopia: Abnormal Fixational Eye Movements and Suboptimal Sampling Strategies

Chen D, Otero-Millan J, Kumar P, Shaikh AG, et al. *Invest Ophthalmol Vis Sci*. Sept 2018;59:4506-17.

Microsaccades shift the image on the fovea and counteract visual fading. They are also thought to serve as an optimal sampling strategy while viewing complex visual scenes. This study assessed visual search in amblyopic children. Twenty-one amblyopic children with varying severity of amblyopia and 10 healthy controls were recruited. Eye movements were recorded using infrared video-oculography during amblyopic and fellow eye viewing while the subjects performed (1) visual fixation, (2) exploration of a blank scene, and (3) visual search task (spot the difference between two images). The number of correctly identified picture differences and reaction time were recorded. Microsaccades, saccades, and intersaccadic drifts were analyzed in patients without latent nystagmus (LN). Slow phase velocities were computed for patients with LN. Both patients with and without LN were able to spot the same number of differences but took longer during fellow eye viewing compared to controls. The ability to identify differences was diminished during amblyopic eye viewing particularly in those with LN and severe amblyopia. Reduced frequencies of microsaccades and saccades were found in both amblyopic and fellow eyes during fixation and visual search but not during exploration of blank scene. Across all tasks, amblyopes with LN had increased

intersaccadic drifts. These findings suggest that deficient microsaccade and saccadic activity contributes to poorer sampling strategy in amblyopia, which is seen in both amblyopic and fellow eye. These deficits are more notable among subjects who experienced binocular decorrelation earlier in life, with subsequent development of LN. The results of this study are in agreement with other studies demonstrating slower reading in amblyopes related to fellow eye fixation instability. Future research should be directed at determining the influence of attentional deficits on decreased microsaccades frequencies in amblyopes.

Comparison of effect of Cycloplegia on Astigmatism Measurements in a Pediatric Amblyopic Population: A Prospective Study

Ped Ophthalm Sunali Goyal, Paul H.Phillips, Mallikarjuna Rettinganti, Jeffrey M.Gossett et al. *J Ped Ophthal & Strabismus*.2018;55(5):293-298

The purpose of this article was to study the effect of cycloplegia on astigmatism measurements in pediatric patients with amblyopia. This was a prospective comparative clinical study. Participants 4 to 17 years old were recruited from the patient population after informed consent was obtained. Autorefractor measurements were used to obtain values of refractive error in amblyopic and non-amblyopic patients before and after cycloplegia. The groups were subdivided into myopia and hyperopia and with and without underlying amblyopia. The refractive error was expressed as sphere, cylinder, axis of astigmatism, and spherical equivalent. The treatment effect was summarized as the mean difference (95% confidence interval) for each outcome. The study showed that there was no statistically significant difference on the axis and power of astigmatism before and after cycloplegia in patients with amblyopia (p=.28 and .99, respectively). The authors conclude that non-cycloplegic autorefraction measurements may be considered safe for refining astigmatism power and axis in pediatric patients with amblyopia. The information provided by the current study would benefit pediatric patients by facilitating more accurate spectacle prescriptions with the least amount of diagnostic testing. The study has the obvious limitations of a small sample size and patients not classified according to age or accommodative amplitude. The authors believe further multi-center studies in this area may be beneficial for further utilization of this information with more confidence.

Analysis of Macular Vessel Density and Foveal Avascular Zone Using Spectral-Domain Optical Coherence Tomography Angiography in Children with Amblyopia.

Bengi Demirayak, Asli Vural, Ismail Umut Onur, Fatma Selin Kaya et al. *J Ped Ophthal & Strabismus*.2019;56(1):55-59.

The purpose of this study is to quantify the foveal avascular zone and the whole, parafoveal, and foveal vessel density of superficial and deep capillary plexus in amblyopic eyes and age-matched controls and to compare the measurements.

This cross-sectional study involved 49 eyes from 17 patients with amblyopia and 21 healthy children (aged 6 to 16 years). Optical coherence tomography angiography was performed for all participants and superficial capillary plexus, deep capillary plexus, and foveal avascular zone were evaluated. Data from amblyopic eyes, fellow eyes with unilateral amblyopia, and control eyes were compared using the Mann–Whitney *U* test. The mean patient age was 8.6 ± 2.5 years in the amblyopia group and 9.6 ± 2.9 years in the control group. The mean foveal avascular zone measurements were 0.251 ± 0.1 mm^2 in the amblyopia group and 0.291 ± 0.1 mm^2 in the control group. The whole, foveal, and parafoveal vessel densities of superficial capillary plexus were 48.8% ± 3.7%, 23.8% ± 8.8%, and 50.9% ± 4.6% in the amblyopia group and 48.4% ± 2.5%, 19.3% ± 5.4%, and 51.3% ± 2.7% in the control group. The whole, foveal, and parafoveal vessel densities of deep capillary plexus were 51.8% ± 4.3%, 37.6% ± 5.8%, and 54.8% ± 4.2% in the amblyopia group and 54.4% ± 3.2%, 34.9% ± 7.4%, and 56.8% ± 3.2% in the control group. No statistically significant difference was detected in all measurements. The study concludes that amblyopic eyes and normal eyes have similar retinal capillary plexus densities and foveal avascular zone. Small subgroup analysis showed there was no difference between amblyopic eyes and fellow eyes. Based on these results, the authors hypothesize that the amblyopic process does not involve retinal microvasculature because animal models could not detect such evidence. Different levels of the visual pathways might or might not be affected in amblyopia. Also, these alterations might be structural or functional. Studies including histological sections are required to respond to these questions. This study is limited by the relatively small sample size. It is unclear whether our findings would be generalizable to a larger group of patients. However, it is novel that amblyopic eyes and control eyes have analogous retinal microvasculature. Further studies using a larger sample size will clarify our findings.

The positive predictive value of Smartphone Photoscreening in Pediatric Practices

Robert W. Arnold, Andrew W. Arnold, Taryn T.Hunt-Smith, Robin L.Grendahl et al *J of Ped Ophthal & Strabismus*.2018;55(6):393-396

The purpose of this study is to compare smartphone photoscreening with other commercial objective screeners for amblyopia screening for young children. Ten pediatricians in four practices employed Nokia 1020 smartphones (Espoo, Finland) with single-axis Gobiquity software (Scottsdale, AZ) during well-child visits. Outcomes of confirmatory pediatric ophthalmology examinations were prospectively compared using American Association for Pediatric Ophthalmology and Strabismus uniform standards. The study showed that five percent of 6,310 in-office screenings were referred: 25% for high anisometropia, 31% for hyperopia, and 15% for myopia. The positive predictive value (PPV) in 217 follow-up examinations was 68% (95% confidence interval: 62% to 74%) by 2013 age-stratified

standards and 77% (confidence interval: 71% to 83%) by 2003 American Association for Pediatric Ophthalmology and Strabismus standards. The follow-up rate was 65%.

Evaluation of retinal structure in unilateral amblyopia using spectral domain optical coherence tomography.

Lekskul A, Wuthisiri W, Padungkiatsagul T. *J AAPOS*. Oct 2018; 22(5): 386-389.

This cross-sectional study investigated the potential differences in the retinal nerve fiber layer (RNFL) thickness, macular thickness and foveal thickness between amblyopic eyes and normal fellow eyes on spectral domain optical coherence tomography (SD-OCT). The study included patients ≥10 years of age with unilateral amblyopia resulting from anisometropia, strabismus or deprivation. Comprehensive ophthalmic examination was completed and the retinal structures of both eyes were measured using SD-OCT. Twenty-six unilateral amblyopia patients with a mean age of 29.92 ± 14.19 years old participated in the study, of which 17 (65.4%) were classified as anisometropic amblyopia, 7 (26.9%) as strabismic amblyopia, and 2 (7.7%) as deprivation amblyopia. For the amblyopic eye and fellow normal eye, respectively, the mean RNFL thickness was 95.87 ± 14.56 μm and 97.87 ± 14.56 μm (P = 0.628), the mean macular thickness was 270.87 ± 14.43 μm and 275.60 ± 14.43 μm (P = 0.251) and the mean foveal thickness was 250.59 ± 27.82 μm and 242.91 ± 27.82 μm (P = 0.332). SD-OCT assessments revealed no statistically significant differences between both eyes. The authors concluded that there were no significant changes in the retinal structure of amblyopic eyes on the SD-OCT; Therefore, amblyopia does not seem to have a profound structural effect on the retinal nerve fiber layer, the macula, or the fovea. However, the study has several limitations, including the small sample size and diverse group of patients, including a wide age range (12-59 years) and different types of amblyopia. It seems that deprivation amblyopia wouldn't affect the visual pathways in a similar way as anisometropic amblyopia would.

Increased choriocapillaris vessel density in amblyopic children: a case-control study.

Borrelli E, Lonngi M, Balasubramanian S, Tepelus TC, et al. *J AAPOS.* Oct 2018; 22(5):366-70.

In this prospective case-control study the choriocapillaris in children with amblyopia, and age-matched controls was investigated using optical coherence tomography angiography (OCT-A). On OCT-A, the choriocapillaris measures 30 μm starting 31 μm posterior to the retinal pigment epithelium. The section of choriocapillaris under superficial retinal vessels was excluded from analysis to avoid shadowing or projection artifacts. The main outcome measure was choriocapil-

laris vessel density. Secondary outcome measures were foveal macular thickness and parafoveal macular thickness. A total of 20 eyes of 16 patients with amblyopia and 25 eyes of 25 controls were included. Mean age of amblyopic subjects was 7.6 ± 3.6 years; of controls, 9.3 ± 2.2 years (P = 0.10). Mean refractive error of subjects was 4.3 ± 6.2 D; of controls, 0.0 ± 1.6 D (P = 0.004). Mean choriocapillaris vessel density was 74.8 ± 5.8 in the amblyopic group and 71.1 ± 3.6 in the control group, which was significant even after adjusting for age and refractive error (P = 0.012). There was no difference between groups in foveal macular thickness or parafoveal macular thickness; however, outer parafoveal macular thickness (the inner boundary of the inner nuclear layer to the retinal pigment epithelium outer boundary) was significantly greater in amblyopic eyes than in control eyes, even after adjustment for age and refractive error (203 ± 11 μm and 189 ± 12 μm, resp. [P = 0.014]). The authors concluded that in their cohort, amblyopic eyes were found to have increased choriocapillaris vessel density as well as a greater outer parafoveal macular thickness, which may be due to alterations in outer retinal maturation. Some possible explanations for this finding are offered in the discussion. OCT-A is an exciting new imaging modality; however, its clinical relevance is still under inspection.

OCT angiography findings in children with amblyopia

Sobral I, Rodigues TM, Soares M, Seara M, et al. *JAAPOS*. Aug 2018;22(4):286-289.e2.

The purpose of this paper is to compare the microstructure and vascularity of amblyopic eyes in children with their contralateral eye and with eyes from control children using optical coherence tomography angiography (OCT-A). The authors conducted a prospective, cross-sectional evaluation of macular and optic disk vascular density and flow area using OCT-A (Avanti RTVue XR, Optovue Inc, Fremont, CA). Parameters were calculated using automated software. A total of 52 children were included: 26 subjects with amblyopia and 26 nonamblyopic controls. In this study, the amblyopic eye of subjects showed a statistically significant decrease in macular vascular density (P = 0.0171) of the superficial capillary plexus (SCP), in the optic disk flow area (P = 0.0195) and in the average retinal nerve fiber layer thickness (P = 0.0194) as well as a marginally statistically significant decrease in the macular flow area of the SCP (P = 0.0305) and in the optic density (P = 0.0279). Compared with randomly selected eyes of controls, amblyopic eyes showed a statistically significant decrease in the macular flow area of the SCP (P = 0.005) and of the deep capillary plexus (DCP; P = 0.002), in the macula vascular density of the SCP (P = 0.022), in the optic disk flow area (P = 0.004), and a marginally statistical significant increase in the area of foveal avascular zone of the DCP (P = 0.038). The authors also found that the contralateral eyes of amblyopic eyes did not have completely normal vascularization. In this study cohort amblyopic eyes manifested significant differences in macular and optic disk vascularization. The clinical significance of these findings warrants further research. It remains to be determined if the vascularization defect is the

cause of amblyopia or the consequence of it, however the findings may provide information for future studies.

A pilot study using electronic reminders for amblyopia treatment.

Vagge A, Gunton KB, Schnall B. *Strabismus.* 2018 Oct 16:1-7.

Compliance with patching therapy for amblyopia therapy is limited, thought to be as low as 33-58%. In addition, accurately assessing compliance is difficult. The authors performed a prospective pilot study in 3-7 year old patients with a new diagnosis of amblyopia who were randomized to receive the standard compliance instructions or use the RemindmeRx app. Twenty-four of the 27 enrolled patients completed the study, with 12 in each group. The mean age, gender distributions, socioeconomic characteristics, amblyopia type or mean follow up duration were similar between the groups. The percentage compliance was high and similar in both groups (93 vs 94%), and there were no statistically significant differences in the outcome. The authors address the limitations of the study, which include small sample size, short follow up (6 weeks), and self-reported compliance. Future studies in larger groups and over longer time periods may be helpful in determining the benefit.

Is microtropia a reliable indicator of the presence of amblyopia in anisometropic patients?

Lysons D, Tapley J. *Strabismus*. 2018 Sep;26(3):118-121.

It is thought that the type of refractive error and degree of anisometropia are not reliable indicators of the presence or severity of amblyopia. The authors performed a retrospective case series over a 10 year period of 4-5 year old children with unequal visual acuity and no manifest strabismus who were prescribed glasses to correct anisometropic refractive errors. Of the 532 children included in the study, 190 achieved equal vision after 2 months of glasses wear, 134 achieved equal vision after 4-6 months of glasses wear, and 208 persisted with unequal vision after 6 months of glasses wear. In the first two groups, none of the children had a microtropia. Of the 208 with unequal vision that persisted after 6 months of glasses wear, all presented with a microtropia. Of these patients, 30 had unequal vision after 6 months with glasses but the vision in the amblyopic eyes was above the threshold for patching. The remaining 178 children had unequal vision after glasses wear for 6 months and required patching. The authors conclude that the presence of a microtropia appears to be a reliable indicator of amblyopia and possible need for occlusion therapy.

Multiple-Choice Answer Form Completion Time in Children With Amblyopia and Strabismus

KR Kelly, RM Jost, A DeLaCruz, EE Birch. *JAMA Ophthalmol*. August 2018 136(8):938-41.

In this cross-sectional study completed between 2014 and 2017 at a nonprofit eye research institute to assess for a time difference in academic tasks in children with amblyopia and/or strabismus. At the research institute, there were enrollment of 47 children with amblyopia treated for strabismus, anisometropia, or both, 18 children with non-amblyopic strabismus, and 20 normal controls. In particular, children were asked to transfer the correct answers from a standardized reading achievement test booklet to a multiple-choice answer form as quickly as possible without making mistakes or reading the text. Of the 85 included children, 40 (47%) were female, the mean (SD) age was 10.09 (0.91) years, and the last mean (SD) grade completed was 3.42 (0.92). Compared with children in the control group (mean [SD] time to completion, 230 [63] seconds), children with amblyopia (mean [SD] time to completion, 297 [97] seconds; difference, 63 seconds; 95% CI, 24-102; P = .001) and children with non-amblyopic strabismus (mean [SD] time to completion, 293 [53] seconds; difference, 68 seconds; 95% CI, 21-115; P = .002) required approximately 28% (95% CI, 20-37) more time to fill out a multiple-choice answer form. Completion time was not associated with etiology, visual acuity, or stereoacuity. In summary, this study found that longer completion time in children with amblyopia or strabismus may affect a child's performance on tests using multiple-choice answer forms and may hinder academic success.

Assesment of an Advanced Vision Screener in the Detection of Amblyopia in the Nebraska Pediatric Population.

Mary Haschke, Hannah Kinberg,Linda Morgan, Donny W. Suh *J of Ped Ophth and Strabismus*.2018; 55(3): 189-193

The purpose of this cross-sectional study is to determine the validity of the OPTEC 5500 vision screener (Stereo Optical Co., Inc., Chicago, IL) in assessing visual acuity and amblyopia in pediatric patients between the ages of 3 and 17 years by comparing it statistically to gold standard comprehensive ophthalmic examinations. Sixty four patients between the ages of 3 and 17 years underwent a vision screening test at a pediatric ophthalmology office using the OPTEC 5500 vision screener, followed by traditional visual acuity testing via the Snellen or Lea optotypes. After data were collected, the results of the OPTEC 5500 vision screener were compared to the Snellen and Lea visual acuity tests and statistical analysis was subsequently performed for the right and left eyes separately. Patients were considered to have risk factors for amblyopia based on the American Association for Pediatric Ophthalmology and Strabismus referral criteria guidelines.The results of the OPTEC 5500 vision screener for the right eye of participants of all ages were a sensitivity of 77.4%, specificity of 100.0%, positive predictive value of 100.0%, negative predictive value of 50.0%, and accuracy of 81.5%. Results for the left eye were a sensitivity of 81.0%, specificity of 87.0%, positive predictive value of 91.9%, negative predictive value of 71.4%, and accuracy of 83.1%.

Although the specificity and positive predictive value were acceptable, the sensitivity and negative predictive value of the OPTEC 5500 vision screener were below average when compared to other available devices, exhibiting some of the weaknesses of the device. Additional studies of the OPTEC 5500 vision screener with a larger population are necessary to assess the device in the general pediatric population, such as in general pediatric clinics and public schools. Additionally, other options for pediatric vision screening devices should be explored.

Practice Patterns in the Management of Amblyopia: A Survey Study

Jacquelyn Laplant, Aldo Vagge, Leonard B.Nelson *J of Ped Ophth & Strabismus*.2018; 55(2): 100-106

The purpose of this study is to investigate the practice preferences of pediatric ophthalmologists in the management of amblyopia and whether these are influenced by demographic variables. A 10-question survey was distributed to all pediatric ophthalmologists and fellows attending the Annual Joseph H. Calhoun Pediatric Ophthalmology Forum at Wills Eye Hospital in 2016. The questionnaire consisted of demographic information and clinical management of amblyopia using clinical scenarios commonly encountered in pediatric ophthalmology practice. Of the 133 pediatric ophthalmologists who attended, 74 completed the survey, all of which were included in the data analysis. Seventy-six percent of respondents prescribed refractive correction to a 3 year old with untreated anisometropic amblyopia prior to initiating occlusion therapy. For a child with coexisting exotropia, 57% recommended refractive and occlusion therapy until significant visual improvement, then surgery; however, 30% would perform surgery earlier. Fifty-seven percent stopped occlusion therapy at 10 years of age or older. Sixty-four percent estimated a patient patching compliance rate of 50% to 75%. There was no significant relationship ($P < .05$) between any of the demographic variables, indicating that no group was more or less likely to respond to the question in any way. This study highlights the lack of a united approach to certain aspects of amblyopia management. Physician-related demographic variables did not significantly affected clinical decision-making; however, variation did exist among respondents, a finding that warrants further investigation. Limitations of our study include a small sample size and failure to identify other factors that may play a role in practice patterns (eg, sex or geographic location). In conclusion, this study emphasizes the need to not only identify practice pattern variations among pediatric ophthalmologists in the treatment of amblyopia, but also the need for well-designed prospective randomized controlled trials to establish treatment guidelines and determine whether practice approaches standards of care.

Amblyopia in High Accommodative Convergence / Accommodation Ratio Accommodative Esotropia. Influence on Bifocals on Treatment Outcome.

Tejedor J and Gutierrez-Carmona FJ *Am J Ophthalmol.* 2018; 191: 124-128.

This is a retrospective comparative case series of 61 children with high ac/a accommodative esotropia between 2011 and 2016. All patients were in single vision glasses for 2 months and were evaluated at that time as a baseline exam. At that time, 46 patients were changed to bifocals. There were 27 patients who had amblyopia at diagnosis, 21 of those still had amblyopia at the 2 month baseline exam in single vision hyperopic spectacles. 13 of amblyopic patients were placed in bifocals. Overall, the decision to add the bifocal was based on the clinician and the family. Most clinicians were in favor of the bifocals, but parents were given opportunity to opt out of the bifocal after recent studies suggested that this practice was controversial since it is unclear if this provided long term benefit. No patient required surgery for decompensated esotropia during this study. The authors demonstrated that there was faster short term improvement in amblyopia in the group of patients who used the bifocal, but that the acuities in the two groups were similar at 1 year. Similar to previous studies, the patients in the bifocal group of this study did not demonstrate improved stereoacuity compared to the non bifocal group. The conclusion of this paper is that bifocals can provide a transient advantage in the rate of improvement in vision of amblyopic eyes in patients with high ac/a accommodative esotropia. The authors point out that this difference could be due to hypoaccommodation in amblyopic eyes and not because of the alignment at near in these glasses.

The Need for a Unified Protocol for Termination of Amblyopia Treatment

Nassar, MM. and Mitchell, FC *Br Ir Orthopt* J 2018; 14(1): 20-24

The protocols for cessation of amblyopia treatment and duration of post-treatment follow-up remains arbitrary despite the extensive investigation and evidence-based approach on diagnosis and treatment of amblyopia. The studies purpose is to evaluate the stability of visual outcome after amblyopia treatment. 39 patients were included, 72% treated with patching alone and 28% patching and atropine. 92% of patients had improved visual acuity with amblyopia treatment. 80% of patients had tapering of treatment and 20% had abrupt cessation of amblyopia treatment. No patient had a significant recurrence of amblyopia after treatment ended, however 8 patients had an insignificant reduction in their visual acuity. There was no correlation between timing of cessation of treatment or method of cessation in this small retrospective case study. The authors conclude that an end of treatment protocol needs standardization and future research.

2.VISION SCREENING

Evaluation of the Spot Vision Screener for children with limited access to ocular health care.

Barugel R, Touhami S, Samama S, Landre C, et al *JAAPOS* 2019 June; 23 (3): 153.e1-153.e5

The aim of this cross-sectional prospective study was to compare the sensitivity, specificity, and referral rate of the Spot Vision Screener (Welch Allyn Inc, Skaneateles Falls, NY) with the gold standard cycloplegic measurements acquired using the Retinomax in a population of underprivileged children and teenagers with limited access to medical care. A total of 41 children (19 males, age range 48-246 months) were recruited for the study by social workers in the vicinity of Robert Debre Hospital, Paris, France. Refractive errors (hyperopia of ≥ +2.00 D spherical equivalent [SE]; myopia of ≤ -0.50 D SE; astigmatism of ≥1.00 D between the two main meridians; anisometropia of ≥1.00 D SE difference between eyes) were assessed using the Spot Vision Screener and the Retinomax. Sensitivity (true positive rate), specificity (true negative rate), and referral rate of the Spot Vision screening program were evaluated. The sensitivity of the Spot Vision Screener for the detection of refractive errors was 82.35%; specificity was 91.67%. The sensitivity of the Spot Vision Screener to detect hyperopia, myopia, astigmatism, and anisometropia was 27.27%, 84.61%, 78.57%, and 66.67%, respectively. Its specificity to detect hyperopia, myopia, astigmatism, and anisometropia was 100%, 98.55%, 89.71% and 94.29%, respectively. The authors conclude that the specificity of the Spot Vision Screener to detect refractive errors was found to be relatively high (>90%). However, its low sensitivity for hyperopia seems to remain a major limitation of the device, because hyperopia is particularly important to detect in children given its high prevalence and possible adverse consequences. Several reasons for this finding were raised including, the fact that accommodation might have influenced the results or that there is an intrinsic technical weakness of the Spot Vision Screener for the detection of hyperopia. The study has several limitations, including its small sample size, wide range of ages (young subjects with amblyopia risk factors and older subjects beyond the critical period for amblyopia development). The criteria that were chosen by the authors for referral were much lower than the AAPOS 2013 criteria for automated preschool vision screening and this may have increased the referral rate.

Performance of a quick Screening version of the Nintendo 3DS PDI check game in patients with ocular suppression.

Kyle A.Smith, AndrewW.Arnold, Jacob H.Sprano, StephanieL.Arnold et al.

J of Ped Ophthal & Strabismus 2019;56(4):234-237

Visual acuity screening, especially in children, is recommended as a distance chart with the untested eye patched and approved optotypes crowded or surrounded to select for amblyopia. Current guidelines propose age-based referral cut-offs of 20/50 for age 3 years, 20/40 for pre-kindergarten, and 20/32 for older children.[6] The PDI Check is a near test with a unique method of ensuring monocular testing. The purpose of this study is to evaluate the ability of the PDI Check(PDI Check LLC,Anchorage, AK) near vision screening game to assess monocular acuity, streopsis, suppression and color. Instead of a 20/40 cut-off for near, the authors aimed for the low-vision classification of 20/70, but because that is not logarithm of the minimum angle of resolution, the authors chose the next

smallest size of 20/63. Children and adults consented to perform the PDI Check Quick Screening game following conventional near testing of patched Rosenbaum acuity, Titmus Fly stereo, Worth 4-dot, and Ishihara color. Time to complete each test and preferred method were recorded. A total of 77 patients (5 to 63 years old) attempted all tests. There was a positive correlation between the PDI Check and conventional tests for all visual tasks. Using previously determined instrument referral criteria, sensitivity/specificity was determined for right acuity (67%/91%), left acuity (55%/94%), stereopsis (87%/95%), red-green color (80%/99%), and ocular suppression (58%/98%). Screening time was 202 ± 96 versus 99 ± 42 seconds for the PDI Check and the game was preferred by 87%. The authors concluded that the dynamic Quick Screening version of the PDI Check video game correlates with conventional static clinical tests for monocular visual acuity, suppression, stereopsis, and color, but it is substantially quicker. Limitations of this study included a relatively small sample size of normal participants despite an ample number of patients with prior strabismus or ocular suppression. Only six patients with color deficiency were included. The same technician who presented and timed the conventional tests also presented the PDI Check game. The screen presentation-to-clinical correlation functions for this and former PDI Check version calibrations have been derived from just over 300 clinical cases, so further testing with high pre-screening probability cohorts is needed to better refine clinical data ranges. Further work with this near vision testing format also needs to be done in more patients with different age ranges with nystagmus, patients with aversion to patching or goggles, and those with developmental delays such as autism spectrum disorder. Finally, because the visual acuity test on the PDI Check is not directly comparable to static chart optotype identification/matching, but rather a dynamic, enlarging forced-choice process, it is not sure whether the PDI Check near task is better or worse in comparison with distance vision; further testing should be performed.

Evaluation of a free public smartphone application to detect Leukocoria in High risk children aged 1 to 6 years.

Aldo Vagge, Nutsuchar Wangtiraumnuay, Marco Pellegrini, Riccardo Scotto et al. *J of Ped Ophthal & Strabismus*.2019;56(4):229-232

The purpose of this study is to determine whether a white-eye detector smartphone application (app) can be used as a screening tool to detect early signs of leukocoria in a clinical practice. In this prospective, single-visit study a complete pediatric Ophthalmologic examination was performed. All children who met the enrollment criteria (n=122, 244 eyes) were screened by an orthoptist with the CRADLE (Computer Assisted Detector of Leukocoria) smartphone app for an iPhone operating system (iOS) (iPhone 7; Apple, Cupertino, CA). Cycloplegic retinoscopy and fundus examination were performed 30 minutes after one to two drops of a pediatric combination drop, comprising tropicamide 1% and phenylephrine 2.5%, were instilled. A comparison between the two methods yielded

sensitivity, specificity, and negative likelihood ratio values. The study showed that nine eyes of 244 (3.6%) had leukocoria evaluable by penlight caused by amblyogenic cataract, 1 (0.4%) patient had retinopathy of prematurity stage 5, and 3 (1.2%) patients had retinoblastoma. The sensitivity of the white-eye detector app was 15.38% (95% confidence interval [CI]: 1.92% to 45.45%), the specificity was 100% (95% CI: 98.48% to 100.00%), and the negative likelihood ratio was 0.85 (95% CI: 0.67 to 1.07). The CRADLE app produces algorithms that can learn from examples to automatically detect when a photograph or video contains a white eye. Although the specificity of this app was 100%, the authors observed that the sensitivity was only 15.38%. The app was not able to recognize 11 eyes with leukocoria that were evaluable by penlight or ophthalmoscope. The reason for this was the lack of similar sample images in the experimental database. Additionally, cataract may produce a darker rather than a whiter fundus reflex. The authors also conclude that although high specificity (100% in this study) may reduce the over-referral, it can also result in missing at risk children due to low sensitivity. The imbalance in sensitivity and specificity constitutes the greatest limitation of the CRADLE app. In conclusion , using smart-phone photoscreening apps to detect leukocoria may be valuable support for children's parents and relatives, unless they cause decreased vigilance in the case of a normal result. However, the authors believe that the CRADLE app cannot be considered an alterative to the ophthalmoscope for children aged 1 to 6 years. Further improvements in the app, such as an expansion of the pathological samples database, are required before it can be recommended as an effective screening tool. Therefore, pediatricians and volunteers on community health projects in under-developed countries should be trained to perform the red reflex eye test. Further studies with larger simple sizes are needed to confirm the role of this tool in the detection of leukocoria.

Comparative analysis of the Lang Stereopad in a non-clinic population.

Rowe FJ, Hepworth LR, Howard C, Chean CS, et al. *Strabismus*. 2019 Jul 22:1-9.

The Lang Stereopad is a newly developed test of stereopsis consisting of a lenticular surface and random dot patterns that allows a larger range of testing. In this prospective cross-sectional study, the authors compared the Lang Stereopad stereopsis in patients over 18 years old without strabismus to other previously established tests (Lang II, Frisby and TNO). They enrolled 98 patients with a mean age of 33.5 years (SD 14.1). They found that the Lang Stereopad has poor agreement with TNO and Frisby, but similar values to the Lang II test. The benefits of the Stereopad are that it allows greater testing range and it is easy to administer as it does not require glasses. There was no significant differences for retest values for any of the stereopsis tests. Future testing in patients with abnormal stereopsis may help elucidate which of the stereopsis tests is the most accurate assessment of stereopsis.

The Repeatability of Values Measured Using the Spot Vision screener in healthy Children and Children with Refractive Errors

Satou, Tsukasa; Niida, Takahiro; et al. *Journal of Binocular Vision and Ocular Motility*, 2019; 69:2, 82-86

Autorefractors are becoming increasingly more valuable in detecting amblyopia in vision screenings. Many of the instruments used induce myopia therefore the refractive value is inaccurate. The Spot vision screener device is a hand-held autorefractor that measures refraction with photorefraction. The patient gazes at a target 1m away on the instrument and it takes approximately 1 second to measure binocular refraction. These factors reduce the effect of accommodation therefore induced myopia. The purpose of the study is to determine the repeatability of refractive values measured using the Spot vision screener in healthy children and children with refractive errors. The examiners performed 3 consecutive tests on normal and spectacle wearing glasses at time of vision screen. The spherical equivalent, cylindrical value, and amount of anisometropia were obtained and analyzed using intra-class correlation coefficients (ICCs). The ICCs of the spherical equivalent values and anisometropia were higher in the spectacles group without their spectacles than those in the normal group. Also, the ICCs were lower in the spectacles group with their glasses compared to the spectacle group without their glasses, likely secondary to the lenses affected on irradiated light and retinal reflection. The authors conclude that the Spot vision screener can ensure stable, better than moderate reliability of refractive values with and without spectacles.

A comparison of Three Different Photoscreeners in Children.

Kuddusi Teberik, Mehmet Tahir Eski, Murat Kaya, Handan Ankarali. *J Ped Ophthal & Strabismus*.2018;55(5):306-311

The purpose of this study is to compare the results obtained from three non-cycloplegic handheld photorefractometers with cycloplegic autorefractometry (Topcon KR-8100; Topcon Corporation, Tokyo, Japan) measurement in children. The refractive status of 238 eyes in 119 healthy children was assessed. The values acquired using photorefraction with the non-cycloplegic PlusoptiX A12 (Plusoptix GmbH, Nuremberg, Germany), Retinomax K-plus 3 (Righton, Tokyo, Japan), and Spot Vision Screener (Welch Allyn, Skaneateles Falls, NY) devices were compared with those obtained from the cycloplegic Topcon KR-8100. The agreement between the measurements was assessed using the intraclass correlation coefficient. The mean age was 10.1 ± 3.2 years (range: 6 to 17 years). The mean spherical value for the right eyes was 0.38 diopters (D) (range: −4.50 to 6.25 D) for the Plusoptix A12; 0.45 D (range: −4.50 to 6.25 D) for the Spot Vision Screener; −1.15 D (range: −8.75 to 6.50 D) for the Retinomax K-plus 3; and 0.62 (range: −4.50 to 6.00) for the Topcon KR-8100. The mean spherical equivalent value for the right eyes was 0.41 D (range: −4.50 to 7.90 D) for the Plusoptix

A12; 0.18 D (range: −4.75 to 6.13 D) for the Spot Vision Screener; −1.30 D (range: −10.50 to 6.38 D) for the Retinomax K-plus 3; and 0.67 D (range: −4.00 to 6.00 D) for the Topcon KR-8100 (for the right eyes. The authors conclude that the photorefractometer method was found to be beneficial in the measurement of refractive errors of school-aged children. However, its disadvantages are a limited measurable refractive error range and being affected by mydriatic pupils. The PlusoptiX A12 photorefractometer may eliminate the need for cycloplegia in the detection of refractive errors in children. Further studies examining more cases with an extreme range of refractive errors may be needed to confirm the outcomes of this study.

Overestimation of hyperopia with autorefraction compared with retinoscopy under cycloplegia in school-age children

Hashemi H, Khabazkhoob M, Asharlous A, Yekta A, et al. *Br J Ophthalmol*. December 2018;102:1717-1722.

This was a cross-sectional study to compare refraction values using retinoscopy and autorefraction in Iranian children. The Nidek ARK-510A autorefracokeratometer was used. Cycloplegic refraction was performed with the autorefracter and retinoscopy. 5620 children were included with mean age of 9.2 years and 52.5% boys. The results showed that mean sphere and spherical equivalent refraction were significantly higher with autorefraction compared with retinoscopy. Looking at total study population numbers, the mean spherical equivalent by autorefraction was +1.067 compared to +0.994 with retinoscopy. Autorefraction tended to over plus hyperopic and under minus myopic cases. Although the differences obtained were statistically significant, the actual difference was felt to be clinically insignificant (because they were <0.25D), concluding that autorefraction is a suitable substitute for retinoscopy.

Implementing enhanced education to improve the UCLA Preschool Vision Program

Mehravaran S, Quan A, Hendler K, Yu F, et al. *JAAPOS*. Dec 2018;22(6):441-444.

The purpose of this paper is to examine whether educational pamphlets and videos for adults can increase follow-up rates for eye examinations among preschool children. The target population was 3- to 5-year-olds attending 144 preschools within Los Angeles County and receiving services from the UCLA Preschool Vision Program (UPVP). Preschools were randomly assigned to standard and enhanced-education groups. The same procedures were followed in each group, except that preschool personnel and parents of children referred for eye examinations in the enhanced-education group received education materials and watched a 3-minute informational video on the screening day. The outcome measure was the follow-up rate for comprehensive examinations performed by

the UPVP on a second date. The follow-up rate for receiving a complete eye examination was 75.3% (438/582) in the enhanced-education group and 65.1% (430/661) in the standard group (P < 0.0001 [Fisher exact test]; OR = 1.63; 95% CI, 1.28-2.09). The authors conclude that educating adults during the screening session can increase follow-up rates. Further studies are recommended to understand barriers to seeking eye care for children and to devise initiatives to help increase targeted awareness.

Efficacy and outcomes of a summer-based pediatric vision screening program

Hark LA, Shiuey E, Yu M, Tran E, et al. *JAAPOS.* Aug 2018;22(4):309.e1-309.e7.

This study sought to investigate the prevalence of decreased visual acuity and uncorrected refractive error in school-aged children participating in summer programs. During the summers of 2014-2016, Wills Eye Hospital collaborated with summer programs in Philadelphia to provide vision screenings for underserved children. Fail criteria included children in grades K-1 (ages 5-6) with visual acuity worse than 20/40 in either eye, children in grades 2-6 (ages 7-13) with visual acuity worse than 20/30 in either eye, or children with ≥2 lines of interocular difference. If decreased visual acuity was correctable to ≥20/30 by the onsite optometrist, two pairs of free eyeglasses were provided. Children with other ocular abnormalities were referred to pediatric ophthalmology. Of 1,627 children screened, 360 children (22.1%) did not pass vision screening, and 64 (3.9%) were referred for further evaluation. The prevalence of decreased distance visual was 34.1% in this group of patients. Younger children were more likely to have worse visual acuity than older children (OR = 0.943; P = 0.023; 95% CI, 0.896-0.992). The incidence of refractive error in the group of 303 patients who underwent manifest refraction was: myopia (73%), astigmatism (56.8%), hyperopia (15.5%), spherical anisometropia (12.5%), and cylindrical anisometropia (11.9%). Myopia increased with age (OR = 0.818; P = 0.001; 95% CI, 0.724-0.922), whereas astigmatism decreased (OR = 0.817; P < 0.001; 95% CI, 0.728-0.913) with age. Two pairs of glasses were provided to 301 children. The authors feel that partnership with summer programs and other community initiatives to provide vision screenings facilitates access to eye care ultimately aimed at improving social functioning and academic performance. This vision screening technique yielded a successful and high number of patients who required further evaluation.

Clinical Assessment of an Ocular Photoscreener

Thomas Williams, Linda A. Morgan, Robin High, Donny W. Suh *J of Ped Ophthalmology & Strabismus*.2018;55(3):194-199

The purpose of this study is to determine the accuracy of the PlusoptiX A12 photoscreener (PlusoptiX, Inc., Atlanta, GA) in detecting amblyopia or amblyogenic

risks factors in pediatric patients in Nebraska. The data were collected from pediatric patients seen at a single pediatric ophthalmology practice. Each patient was screened using the device and also received a comprehensive ophthalmic examination. The results of the PlusoptiX A12 photoscreener were compared to the gold standard, comprehensive ophthalmic examination findings. The assessment of amblyopia or amblyogenic risk factors in the patients was based on the updated American Association for Pediatric Ophthalmology and Strabismus (AAPOS) referral criteria guidelines. Two hundred nineteen consecutive pediatric patients (438 eyes) participated in this study for the 3-month period of time. Among the patients, 87 (40%) children were determined to have amblyopia or ambylogenic risk factors after the comprehensive pediatric ophthalmology examination based on the AAPOS guidelines. The study showed that the PlusoptiX A12 photoscreener had a sensitivity of 93.02%, specificity of 84.96%, false-positive rate of 9.13%, false-negative rate of 2.74%, positive predictive value of 80.00%, and negative predictive value of 94.96%. The authors concluded that the PlusoptiX A12 photoscreener is viable and comparable to various commercially available devices in the detection of refractive amblyogenic risk factors based on the Nebraska pediatric patient population. Future studies may show increased sensitivity by combining the use of the PlusoptiX A12 photoscreener with an alternate cover test.

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

Goyal P, Padhi TR, Das T, Pradhan L, Sutar S, Butola S, Behera UC, Jain L, Jalali S. *Eye* (2018) 32, 67–73

Universal newborn eye screening is an emerging concept for early intervention of many eye diseases that present at birth. The purpose was to analyze the outcome of this universal newborn eye screening with wide-field digital retinal imaging (WFDRI), assess the cost-benefit margin and compare it with few similar studies reported so far in the literature. Pupillary dilation with a mixture of 2.5% phenylephrine hydrochloride and 0.5% cyclopentolate eye drops. Assessment of red reflex with the help of the illumination from the Ret Cam 130-degree lens; imaging of the external structures of both eyes including eye lids and anterior segments of each eye and entire fundus imaging with five fundus photographs included the posterior pole, including disc and fovea, superior retina-optic disc at the inferior pole of the field of view, inferior retina-optic disc at the superior pole of the field of view, temporal-optic disc at the nasal most part of field of view and nasal retina- optic disc at the temporal most part of the field of view. In addition, the superotemporal, inferotemporal, inferonasal, superonasal quadrant retina were also imaged when required. A total of 1152 babies were examined. Average time to examination was 3.68 days (median: 3.08 days; range 0–21 days). The mean GA and BW were 39.07 weeks (SD: 1.19) and 2.88 kg (SD: 0.46) respectively. Most babies were delivered by lower segment caesarean section

(78.4%) Ocular abnormality of any kind was seen in 14.9%, Retinal hemorrhages were the major finding (13.28%); it was of varying severity- superficial, subhyaloid and vitreous hemorrhages. Most were bilateral (77%). Hemorrhages were distributed in all quadrants with varying severity with a tendency to be more around the optic nerve and along the retinal vessels Retinal hemorrhages were seen in 47.6% of babies born by normal vaginal delivery and 5.2% born by LSCS. The majority of the findings were retinal hemorrhages which usually do not require treatment and the ones that required treatment could have been detected by a routine red reflex test too.

3.REFRACTIVE ERROR

Prevalence and Risk Factors

Current Prevalence of Myopia and Association of Myopia With Environmental Factors Among Schoolchildren in Japan

Yotsukura E, Torii H, Inokuchi M et al. *JAMA Ophthalmology*. Published online August 15, 2019.

This was a cross-sectional study in Tokyo, Japan of 1416 children to determine the prevalence of myopia in children aged 6 to 14 years. The authors analyzed two schools with 726 elementary school students and 752 junior high school students with eye examinations in the Spring of 2017. Evaluation included: (1) autorefractometry with non-cycloplegic refraction and (2) ocular biometric factors. Of note, authors excluded children with previous treatment with atropine or orthokeratology. The mean age was 10.8 years old and 55.9% were male. The prevalence rates of myopia (spherical equivalent ≤−0.5 diopters [D]) were 76.5% (95% CI, 73.4%-79.7%) among the elementary school students and 94.9% (95% CI, 93.3%-96.5%) among the junior high school students. The prevalence rates of high myopia (spherical equivalent ≤−6.0 D) were 4.0% (95% CI, 2.5%-5.4%) among the elementary school students and 11.3% (95% CI, 8.8%-13.7%) among the junior high school students. The prevalence rates of high myopia classified based on axial length of 26.0 mm or longer were 1.2% (95% CI, 0.4%-2.0%) among elementary school students and 15.2% (95% CI, 12.5%-17.8%) among junior high school students. Multiple regression analysis showed that higher-order aberrations and dry eye disease were associated with refractive error in elementary school students ($P < .001$) and with axial length in junior high school students ($P < .001$). The authors noted that there is a limitation of the non-cycloplegic autorefraction with a cutoff of −0.50 D leading to overestimation of results, their findings in Japanese elementary and junior high school students suggest that the current prevalence rates of myopia are high, especially if these are findings are from two schools in < 2000 students. Further demographic analysis is

needed to address the high prevalence of myopia and its impact on visual function for this population.

Association Between Type of Educational System and Prevalence and Severity of Myopia Among Male Adolescents in Israel

Bez D, Megreli J, Bez M et al. *JAMA Ophthalmology*. August 2019;137(8):887-893.

This was a nationwide, cross-sectional study in Israel of the prevalence of myopia in male teenagers who were studying in the ultra-Orthodox, Orthodox, and secular educational systems. The authors sought to analyze the association between studying in different educational systems and the prevalence and severity of myopia among Jewish male adolescents in Israel. In 2013, there were 22, 823 male candidates for military service in Israel aged 17 to 18 years attending the military draft board who underwent a medical examination and a visual acuity assessment. Among the 22, 823 participants, there was a higher proportion of teenagers in the ultra-Orthodox educational system with myopia (1871 of 2276 [82.2%]) compared with adolescents in the Orthodox educational system (1604 of 3189 [50.3%]) and those in the secular educational system (5155 of 17 358 [29.7%]). Compared with teens in the secular educational system, those in the Orthodox educational system were more likely to have myopia ($P < .001$), as were those in the ultra-Orthodox educational system ($P < .001$). The multivariable analysis for high myopia (refractive error of at least −6.0 diopters) was 4.6 ($P < .001$) for teens in the Orthodox educational system and 38.5 ($P < .001$) for teens in the ultra-Orthodox educational system compared with teens in the secular educational system. The authors of this study provides evidence of the independent association between educational systems and the prevalence and severity of myopia. In particular, male teenagers in the ultra-Orthodox educational system have higher odds of having myopia and high myopia. Furthermore, these authors suggest that study styles that involve intensive reading and other near-work activities warrant consideration of further prevention strategies.

Myopia growth Chart Based on a Population-Based Survey (KNHANES IV-V):a NOVEL prediction model OF myopic progression in Childhood.

Dae Hee Kim, Hyun Taek Lim.*J of Ped Ophthal & Strabismus*.2019;56(2):73-77

The purpose of this study is to introduce a novel myopia growth chart based on a population-based survey for the prediction of myopic progression. The study included 7,695 Korean participants aged 5 to 20 years from a population-based health survey (Korean National Health and Nutrition Examination Survey IV–V). The authors collected spherical equivalent (SE) data converted from noncycloplegic refraction data. To create a myopia growth chart, data were arranged in

the order of SE from hyperopia to myopia to acquire specific percentiles of the SE by age. Myopia progression rates were calculated between two specific ages in each percentile. The mean age of the participants was 11.8 years and the mean SE was −1.82 diopters (D). The SE of the 10th percentile was +0.72 D for participants aged 5 and −0.25 D for those aged 20 years, resulting in a total change in refraction of −0.97 D. In contrast, the SE of the 90th percentile was −0.75 D for participants aged 5 years and −6.73 D for those aged 20 years, showing myopia progression of −5.98 D. The myopia progression rate from 5 to 20 years of age was estimated as −0.06, −0.15, and −0.40 D/year in the 10th, 50th, and 90th percentile groups, respectively. The authors concluded that the myopia growth chart may be used to diagnose the severity or to estimate the progression of myopia. A patient in a higher percentile of myopia for his or her age may have myopia progressing at a faster rate and thus require close observation. This study has some limitations. The KNHANES provides cross-sectional data. The continuity of the change in the refractive error corresponding to a specific percentile cannot be guaranteed. A cohort study for the refractive change should confirm the current findings. Moreover, the refractive data from the KNHANES are collected using noncycloplegic autorefraction. As such, the refractive data suggested in this study could be more myopic than it really was. However, studies on myopia screening using the same autorefractor used in this study showed that the autorefractor had reliable performance for the screening of myopic patients, with a sensitivity and specificity of 88.6% and 86.1%, respectively. Considering that the general purpose of a growth chart is early screening for progressive developmental abnormalities, the myopia growth chart using noncycloplegic refraction might be acceptable for screening patients at a risk of high myopia. Further studies using cycloplegic refractive data may compensate for such limitations. Considering that the refractive data can vary depending on the country and the population in the Republic of Korea has a relatively low ethnic variation, the myopia growth chart presented in this study cannot be directly applied in other countries. However, many countries already have refractive data from previous population-based studies. Thus, a myopia growth chart for specific countries and races can easily be made using those data.

Prevalence, Characteristics, and Risk Factors of Moderate or High Hyperopia among Multiethnic Children 6 to 72 Months of Age

Xuejuan Jiang, Kristina Tarcy-Hornoch, Douglas Stram, Joane Katz, et al
Ophthalmology. July 2019;126(7): 989-999.

The purpose of this study was to describe the prevalence, ocular characteristics, and associated risk factors moderate to high hyperopia in early childhood. The design was a pooled analysis of four population-based studies of pediatric eye diseases. Using cycloplegic refraction data from more than 15000 participants, characteristics including the prevalence, ocular characteristics, and associated risk factors for moderate to high hyperopia ($\geq$4.0D) in children 6 to 72 months of

age was gathered. Moderate to high hyperopia was not uncommon in young children and its prevalence did not decrease with age. A family history of strabismus, maternal smoking during pregnancy, and both non-Hispanic and Hispanic white race were associated with higher risk for moderate to high hyperopia. Young children with moderate to high hyperopia are at much higher risk for strabismus, reduced visual acuity, near stereoacuity and accommodative response, and deficits in early literacy; thus, earlier identification would be beneficial. In addition, 44.3% of children with moderate to high hyperopia had either anisometropia of 1.0D or more and astigmatism of 1.5D or more further increasing risk for strabismus and amblyopia. Despite this risk only 17.6% of 36-72 month-old-children with moderate to high hyperopia wore glasses. A lack of surveillance and treatment in this group can lead to significant visual impairment. This study confirms previous reports of an association between maternal smoking during pregnancy and the higher risk of hyperopia and greater amounts of hyperopia. In addition, even modest levels (<5 cigarettes per day) of maternal smoking during pregnancy conferred a higher risk of moderate to high hyperopia and third trimester smoking may be a greater determinant. Biometric analysis revealed an association between reduced axial length consistent with findings that nicotine may inhibit eye growth in animal models and maternal smoking may be associated with increased risk of anophthalmia and microphthalmia. Further studies are needed to clarify the longitudinal patterns of refractive change in early childhood and biological mechanisms underlying the association between gestational exposure to tobacco smoke and hyperopia and to characterize other social or environmental factors that may account for variations in adjusted risk for hyperopia in different studies.

The Associations between Near Visual Activity and Incident Myopia in Children: A Nationwide 4-Year Follow-up Study

Po-Wen Ku, Andrew Steptoe, Yun-Ju Lai, Hsiao-Yun Hu, et al. *Ophthalmology*. February 2019;126:214-220

Myopia rates in children appear to be influenced by behavior, with reduced incidence associated with outdoor time/sunlight exposure and increased incidence with excess near visual activity. Prospective survey data over a four-year period was obtained from parents quantifying the average time their 7 to 12-year-old children spent reading, using electronic devices, and attending “cram school”, defined as private academic classes outside of regular school hours. The survey also collected data on other factors associated with myopia such as parent education level, income, and environment (urban, suburban, or rural). At study outset, older children living in urban areas with parents who were college-educated (or higher degrees) and higher household income had a significantly greater prevalence of myopia. After four years, younger children who shared those characteristics had a significantly greater incidence of myopia. In addition, children who spent at least 30 minutes per day reading or 2 hours per day in cram

schools had a significantly greater incidence of myopia, while time spent on electronic devices had no effect. The survey relied upon self-reported times from parents, did not break out time spent reading or using electronic devices in cram schools, and did not collect data on the severity of myopia or the rate of myopic progression. The data does provide compelling evidence that efforts to reduce screen time for children may not have much effect on reducing myopia prevalence unless accompanied by similar reductions in time spent reading or studying.

Refractive error and visual impairment in Ireland schoolchildren

Harrington S, Stack J, Saunders K, O'Dwyer V. *Br J* Ophthalmol. August 2019;103:1112-1118

The Ireland Eye Study (IES) is the first study to examine prevalence rates of refractive errors in Ireland children. The paper described the rates of refractive error in children 6-7 and 12-13 years old. Children were recruited and tested on school premises after informed consent. Testing included visual acuity, cycloplegic autorefraction, and lifestyle questionnaires. 37 schools participated between 2016 and 2018 and 1626 children participated. This included 728 in the 6-7 year ag e group and 898 in the 12-13 year age group. The prevalence of spherical equivalent myopia (≤-0.50D), hyperopia (≥+2.00D), and astigmatism (≤-1.00D) in the younger group was 3.3%, 25%, and 19.2% respectively. This was 19.9%, 8.9% and 15.9% in the older age group. Myopia prevalence was greater and hyperopia prevalence less in the older group. There was no significant difference in astigmatism between the two groups. Most children had with-the-rule astigmatism in both groups. The rates of visual impairment, defined as ≥0.3 logMAR with glasses if worn, was 3.7% in the younger group and 3.4% in the older group. Overall the myopia prevalence was similar to other European studies, although the rates of visual impairment as defined in the study were higher than reported rates in Northern Ireland, possibility indicating some barriers to access to eye care in Ireland.

Early life factors for myopia in the British Twins Early Development Study

Williams K, Kraphol E, Yonova-Doing E, Hysi P, et al. *Br J* Ophthalmol. August 2019;103:1078-1084

Due to the increasing prevalence of myopia, the authors of this study aimed to better understand early factors in children that may correlate with the onset of myopia. They examined the Twins Early Development Study (TEDS), which is a longitudinal twin cohort in the UK. Twins born between 1994 and 1996 were examined, and ultimately examined 1991 participants. Questionnaires were sent to

the participants' optometrists to obtain refractive data. The median age at refraction was 16.7 years. The mean spherical equivalent was -0.35D (SD 1.80). Myopic glasses were first worn at a mean of age 11. Amblyopia was reported in 5.4% and strabismus in 4.3%. Overall 25.9% of the population was myopic. Using multivariable logistic regression models, factors associated with myopia included level of maternal education, fertility treatment (inverse association), summer birth, and hours spent playing computer games. The inverse relationship noted with fertility treatment was a novel findings that would require further study. Note that the question regarding computer games was done in 2008, which probably predates hand-held tablets/devices that are commonplace today. Also the authors cautioned that although the overall TEDS study is representative of the UK, the subsample analyzed in this study may not be.

Astigmatism and its components in 12-year-old Chinese children: the Anyang Childhood Eye Study

He L, Shi-Ming L, Ya-Zhou J, Meng-Tian K, et al. *Br J* Ophthalmol. June 2019;103:768-774.

Prevalence rates of astigmatism in children vary greatly among different populations. In China, rates in China vary between 14-26% based on location and methods of measurement. However detailed information is lacking. This large school-based study in Anyang City aimed to report the prevalence and distribution of astigmatism and its components in 12 year old Chinese children. A total of 1783 children with mean age of 12.7 years were included in this study. The IOLMaster 500 was used to measure anterior corneal curvature, and cycloplegic measurements were made using an autorefractor. Total astigmatism was given by the cycloplegic refraction, corneal astigmatism by the difference in corneal powers of the principal meridians, and internal component of astigmatism by mathematical calculation. Prevalence rates of refractive astigmatism >=1.0D was 17.4%. Rates of corneal and internal astigmatism were 20.9%. Mean amounts were 0.57D refractive, 1.11D corneal, and 0.72D internal astigmatism. Refractive astigmatism was similar between boys and girls, although girls had a higher prevalence and higher means of corneal and internal astigmatism. Overall the prevalence of refractive astigmatism was higher than reported in other studies. Most of the children had with-the-rule astigmatism. The authors theorize that higher rates may be due to tight eyelids and narrow palpebral apertures in the Asian population.

Environmental Risk Factors Can Reduce Axial Length Elongation and Myopia Incidence in 6- to 9-Year-Old Children

Tideman JWL, Polling JR, Jaddoe, VWV, Vingerling JR, et al. ***Ophthalmology.*** 2019 Jan;126(1):127-136

It is becoming increasingly clear that an important cause of the myopia rise in the world is the changing lifestyles of school children. The goal of this study was to

identify the risk factors for eye growth at a young age that may help to characterize children at risk for whom lifestyle advice and interventions could be beneficial. This study was embedded in the Generation R Study, population-based prospective cohort study of pregnant women and their children in Rotterdam the Netherlands. Children born between April 2002 and January 2006 were invited at age 6 and 9 years of age for examination which included axial length (AL) and corneal radius (CR) measured with an IOLMaster 500. Corneal radius was obtained from average of K1 and K2 from IOL master. Also, daily life activities and demographic characteristics were obtained by questionnaire. Among 4,734 children who completed examination at age 6 and 9, 3,362 children (71%) were eligible for cycloplegic refractive error measurements. Of these, 2,175 children had ocular biometry data at 9 years of age and cycloplegic refractive error. Linear regression models on AL elongation were used to create a risk score based on the regression coefficients resulting from environmental and ocular factors. The predictive value of the prediction score for myopia (≤-0.5 diopter) was estimated using receiver operating characteristic curves. To test if regression coefficients differed for baseline AL-to-CR ratio, interaction terms were calculated with baseline AL-to-CR ratio and environmental factors. The results show that from 6 to 9 years of age, average AL elongation was 0.21±0.009 mm/year and myopia developed in 223 of 2,136 children(10.4%), leading to a myopia prevalence at 9 years of age of 12.0%. Seven parameters were associated independently ($P < 0.05$) with faster AL elongation: parental myopia, 1 or more books read per week, time spent reading, no participation in sports, non-European ethnicity, less time spent outdoors, and baseline AL-to-CR ratio. The discriminative accuracy for incident myopia based on these risk factors was 0.78. Axial length-to-CR ratio at baseline showed statistically significant interaction with number of books read per week ($P < 0.01$) and parental myopia ($P < 0.01$). Almost all predictors showed the highest association with AL elongation in the highest quartile of AL-to-CR ratio; incidental myopia in this group was 24% (124/513). The authors concluded that determination of a risk score can help to identify school children at high risk of myopia and suggest that behavioral changes can offer protection particularly in these children. Also notable in this study is that the highest effect of the environmental factors was found for those children with the highest risk of myopia.

Possible Causes of Discordance in Refraction in Monozygotic Twins: Nearwork, Time Outdoors and Stochastic Variation

Ding X, Hu Y, Guo X, Guo X, et al. *Invest Ophthalmol Vis Sci*. Nov 2018;59:5349-54.

This study evaluated the impact of differences in nearwork and time spent outdoors on difference in refraction in monozygotic (MZ) twins. Data on MZ twins aged 7 to 18 years from the Guangzhou Twin Eye Study were used. A standard questionnaire was administered by personal interview to estimate time spent on nearwork and time spent outdoors. Spherical equivalent (SE) was measured by cycloplegic autorefraction. The interaction between age and nearwork or time spent outdoors was also estimated. A total of 490 MZ twin pairs (233 male and

257 female) were eligible in this analysis, the mean age was 13.14 ± 2.49. In the mixed-effects model, nearwork difference was a risk factor of discordance in myopic SE (β = -0.11 diopter (D)/h, P = 0.009), the overall association between time outdoors difference and SE discordance was not significant (β = -0.89 (D)/h, P = 0.120) although an interaction between time spent outdoors difference and age was detected (β = 0.07 (D)/h, P = 0.002). Furthermore, difference in nearwork and time outdoors explained about 1.8% and 2.5% of the variation in SE discordance, respectively. Given the very marked genetic similarity of MZ twins, and the small effects of known risk factors on SE discordance, the authors suggest that the SE discordance across MZ twins largely results from stochastic variations at the genomic or epigenetic levels, or from uncollected environmental factors. A limitation of this study is possible recall bias due to the use of a questionnaire to collect myopia-related environmental data in a retrospective fashion.

Distribution and Severity of Myopic Maculopathy Among Highly Myopic Eyes

Xiao O, Guo X, Wang D, Jong M, et al. *Invest Ophthalmol Vis Sci*. Oct 2018;59:4880-85.

The purpose of this study was to document the distribution of the severity of myopic maculopathy in a cohort of highly myopic patients and to explore the associated risk factors. A total of 890 Chinese highly myopes aged between 7 and 70 years (median age 19 years) and with spherical refraction -6.00 diopter (D) or worse in both eyes were investigated. All participants underwent detailed ophthalmic examination. Myopic maculopathy was graded into 5 categories according to the International Photographic Classification and Grading System using color fundus photographs: category 0, no myopic retinal lesions, category 1, tessellated fundus only; category 2, diffuse chorioretinal atrophy; category 3, patchy chorioretinal atrophy; category 4, macular atrophy. Category 2 or greater were further classified as clinically significant myopic maculopathy (CSMM). Data from 884 of 890 right eyes were available for analysis. The proportions of category 1, category 2, category 3, and category 4 were 20.0% (177 eyes), 20.2% (178 eyes), 2.6% (23 eyes), and 0.2% (2 eyes), respectively. The proportion of CSMM increased with more myopic refraction (odds ratio 1.57; 95% confidence interval: 1.46-1.68), longer axial length (odds ratio 2.97; 95% confidence interval: 2.50–3.53), and older age (40–70 years compared to 12–18 years, odds ratio 6.77; 95% confidence interval: 3.61–12.70). However, there was a higher proportion of CSMM in children aged 7 to 11 years than those aged 12 to 18 years (20.9% vs. 11.0%, P = 0.008). Older age, more myopic refraction, and longer axial length were associated with more severe myopic maculopathy. Although CSMM was uncommon among younger participants, children with early-onset high myopia have a disproportionately increased risk. The strengths of this study include large sample size and recruitment from the optometry service rather than retinal clinic, suggesting generalizability. Limitations include cross-sectional study design preventing understanding of causality, lack of assessment of posterior staphyloma

due to limited field of photographs, and inclusion of only Chinese participants (generalizability to other races is unknown).

Dim Light Exposure and Myopia in Children

Landis EG, Yang V, Brown DM, Pardue MT, et al. *Invest Ophthalmol Vis Sci*. Oct 2018;59:4804-11.

Experimental myopia in animal models suggests that bright light can influence refractive error and prevent myopia. Additionally, animal research indicates activation of rod pathways and circadian rhythms may influence eye growth. In children, objective measures of personal light exposure, recorded by wearable light sensors, have been used to examine the effects of bright light exposure on myopia. The effect of time spent in a broad range of light intensities on childhood refractive development is not known. This study evaluated dim light exposure in myopia. The authors reanalyzed previously published data to investigate differences in dim light exposure across myopic and nonmyopic children from the Role of Outdoor Activity in Myopia (ROAM) study in Queensland, Australia. The amount of time children spent in scotopic (<1–1 lux), mesopic (1–30 lux), indoor photopic (>30–1000 lux), and outdoor photopic (>1000 lux) light over both weekdays and weekends was measured with wearable light sensors. Significant differences were found in average daily light exposure between myopic and nonmyopic children. On weekends, myopic children received significantly less scotopic light ($P = 0.024$) and less outdoor photopic light than nonmyopic children ($P < 0.001$). In myopic children, more myopic refractive errors were correlated with increased time in mesopic light ($R = -0.46$, $P = 0.002$). These findings suggest that in addition to bright light exposure, rod pathways stimulated by dim light exposure could be important to human myopia development. Optimal strategies for preventing myopia with environmental light may include both dim and bright light exposure. Limitations of the study include relatively small sample size (102 patients), limited age range of children (10-15 years), and evaluating light exposure only during waking hours. Future studies should include younger children, be designed to determine causation (interventional), and also evaluate light exposure during sleep.

Incidence Of and Factors Associated With Myopia and High Myopia in Chinese Children, Based on Refraction Without Cycloplegia.

Sean K. Wang, Yangfeng Guo, Chimei Liao, Yanxian Chen, et al.
JAMA Ophthalmology. September 2018; 136(9):1017-1024.

This was an observational cohort study to determine the incidence of myopia and high myopia based upon evaluation of non-cycloplegic refraction in 4741 children in primary and junior high school in Guangzhou, China. From 2010 to 2015, children were randomly chosen from the city’s 11 districts, with inclusion at grade 1

(mean age of 7.2 years) and grade 7 (mean age of 13.2 years). The authors defined myopia as the spherical equivalent refraction (SER) of -0.50 diopters or less and high myopia defined as the SER of -6.00 diopters. Baseline mean SER was 0.31diopter for children in grade 1 and mean SER was -1.60 diopters for children in grade 7. The baseline prevalence of myopia was 12% in grade 1 students and 67.4% in grade 7 students. The authors found that the incidence of myopia was 20% to 30% each year for both cohorts. Moreover, the incidence of high myopia was < 1% in the primary school cohort and was 2.3% in the junior high school cohort. Trends were overall similar in boys and girls, for SER and axial length (AL) measurements. For all measurements, AL measurements were shorter for girls when compared to boys. The authors report mean AL in grade 1 students: girls at 22.48 and boys at 23.5; mean AL in grade 7 students: girls at 23.90 and boys at 24.42. The authors also report a progression of myopia between grades before reaching junior high school. In particular, between grades 1 and 2, 19.1% non-myopic students developed myopia and between grades 5 and 6, 30.2% non-myopic students developed myopia. This report highlights the high incidence of myopia in this cohort of Chinese students, from grade 1 and onward, based upon refraction without cycloplegia. With the increase in myopia as children aged, by grade 9, 79.4% of students were myopic and 7.0% of students were high myopes. The authors acknowledge the the main limitation of their study was the measure only the noncycloplegic refraction, which may overestimate myopia. The authors suggest that if the high incidence and prevalence of myopia at grade 1 is acknowledged with cycloplegic refraction, treatment and prevention of myopic progression should start at the beginning of primary school rather than junior high school. At the very least, the authors of this study reported that myopic progression by junior high school and the high incidence and prevalence of myopia is reason enough to treat and prevent further refractive amblyopia in these students.

A preliminary study of astigmatism and early childhood development

Harvey EM, McGrath ER, Miller JM, Davis AL, et a.. *J AAPOS*. Aug 2018;22(4):294-298.

The purpose of this paper is to determine whether uncorrected astigmatism in toddlers is associated with poorer performance on the Bayley Scales of Infant and Toddler Development, 3rd edition (BSITD-III). Subjects include were 12- to 35-month-olds who failed an instrument-based vision screening at a well-child check. A cycloplegic eye examination was conducted in all the patients. Full-term children with no known medical or developmental conditions were invited to participate in a BSITD-III assessment conducted by an examiner masked to the child's eye examination results. Independent samples t tests were used to compare Cognitive, Language (Receptive and Expressive), and Motor (Fine and Gross) scores for children with moderate/high astigmatism (>2.00 D) versus children with no/low refractive error (ie, children who had a false-positive vision screening). The sample included 13 children in each group. The groups did not

differ on sex or mean age. Children with moderate/high astigmatism had significantly poorer mean scores on the Cognitive and Language scales and the Receptive Communication Language subscale compared to children with no/low refractive error. Children with moderate/high astigmatism had poorer mean scores on the Motor scale, Fine and Gross Motor subscales, and the Expressive Communication subscale, but these differences were not statistically significant. The results suggest that uncorrected astigmatism > 2.00 D in toddlers may be associated with poorer performance on cognitive and language tasks but it does not seem to be associated with poorer performance on gross motor tasks. The results cannot tell whether correcting the astigmatism with spectacles would improve performance. Further studies assessing the effects of uncorrected refractive error on developmental task performance and of spectacle correction of refractive error in toddlers on developmental outcomes are needed to support the development of evidence-based spectacle prescribing guidelines.

Myopia Prevention and Outdoor Light Intensity in a School-Based Cluster Randomized Trial.

Wu PC, Chen CT, Lin KK, Sun CC, et al. *Ophthalmology* 2018 Aug;125(8):1239-1250

This is a report from Taiwan's school-based Recess Outside Classroom Trial program to increase the outdoor time for school aged children to reduce myopia progression. The program includes recess outside the classroom, incentive-based outdoor homework and other assignments. The authors investigated the effectiveness of this program and aimed to identify the protective light intensities necessary for such measure. A light meter was used to measure the light intensity. This is a multi-area, cluster-randomized controlled trial including 16 schools in four geographic areas with various weather conditions. A total of 693 students in grade 1 (age 6- to 7- years old) were enrolled. Two hundred sixty-seven schoolchildren were in the intervention group and 426 were in the control group. In the intervention group schoolchildren were encouraged to go outdoors at least 11 hours weekly. The intervention also incorporated near work breaks (10 minute break for every 30 minutes of near work). Data collection included eye examinations, cycloplegic refraction, noncontact axial length measurements, light meter recorders, diary logs, and questionnaires. Of note, the control group already received some intervention to minimize myopia, but not as intensive or deliberate as the intervention group. After 1 year of intervention, the authors found that the intervention group showed significantly less myopic shift and axial elongation compared with the control group (0.35 diopter [D] vs. 0.47 D; 0.28 vs. 0.33 mm; P = 0.002 and P = 0.003) and a 54% lower risk of rapid myopia progression (odds ratio, 0.46; 95% CI, 0.28-0.77; P = 0.003). The myopic protective effects were significant in both nonmyopic and myopic children compared with controls. Regarding spending outdoor time of at least 11 hours weekly with exposure to 1000 lux or more of light, the intervention group had significantly more participants compared with the control group (49.79% vs. 22.73%; P < 0.001). Schoolchildren with longer outdoor time in school (≥200 minutes) showed significantly

less myopic shift (measured by light meters; ≥1000 lux: 0.14 D; 95% CI, 0.02-0.27; P = 0.02; ≥3000 lux: 0.16 D; 95% CI, 0.002-0.32; P = 0.048). The school-based outdoor promotion program effectively reduced the myopia change in both nonmyopic and myopic children. Thus, outdoor activities with strong sunlight exposure may not be necessary for myopia prevention. Relatively lower outdoor light intensity activity with longer time outdoors, such as in hallways or under trees, also can be considered. Despite a short duration of follow-up and weakness in gathering light exposure data outside of school, this study suggests that school based interventions can help control myopia and that less than expected light intensity may be necessary to achieve this outcome.

Reducing the Progression of Myopia

Recent updates on myopia control: preventing progression 1 diopter at a time

Rebecca S. Weiss and Sunju Park *Curr Opin Ophthalmol* July 2019 30:215-19

The authors review current treatment modalities in myopia control. The prevalence of myopia is increasing worldwide and there is an inverse correlation between time spent outdoors and myopic progression in children in one longitudinal study. Other studies conclude that increased outdoor time may be protective against myopia onset. Bifocals have not shown significant prevention but in one study, contact lenses that are designed for peripheral hyperopic defocus may show some promise for future myopia control. Orthokeratology has been found to have a statistically significant reduction in axial length elongation however there are risks of microbial keratitis. In addition, with discontinuation of use, axial length elongation was faster compared to controls and continued ortho-K users. Lastly, the authors discuss atopine treatment. They mention the ATOM 1 and 2 studies but discuss more in depth the LAMP studies looking at low dose atropine intervention and found that reduction in spherical equivalent and axial elongation decreased as the dose decreased and the next phase will be looking at long term follow up with respect to washout and maintenance of results. Another study looked at dose dependence based on familial history of progressive myopia. Wu et al developed an algorithm based on dose response and adjunctive therapies. The authors discuss that atropine treatment may need to be customized for each patient based on a variety of factors but that it is the most promising of all the modalities.

Use of Orthokeratology for the Prevention of Myopic Progression in Children

Deborah K. VanderVeen, Raymond T. Kraker, Stacy L. Pineles, Amy K. Hutchinson, et al *Ophthalmology*. April 2019;126:623-636

This study reviewed the literature supporting the use of orthokeratology for myopia control. This technology utilizes specially designed gas-permeable contact lenses, worn overnight, to reshape the corneal surface. The current maximum correctable refractive error is -6.0 diopters of myopia and -1.75 diopters of astigmatism. The lens is only FDA-approved to treat refractive error; use for myopia control in children is off-label. Thirteen studies were deemed of sufficient quality for analysis, one with a level 1 rating, eleven with a level 2 rating, and one with a level 3 rating. The studies all support a modest reduction in the rate of axial length and refractive error increase for orthokeratology, larger for younger subjects, compared with standard spectacle or soft contact lens treatment. The drop-out rate was consistently between 20-30%, typically for poor refractive error correction, poor comfort, or corneal staining, and the effect on myopia control had a large standard deviation consistent with a large variation in individual outcomes. The preponderance of evidence demonstrates that orthokeratology provides some myopia control, but other treatments like low-dose atropine provide equivalent or better myopia control with a better safety profile.

Miscellaneous

Refractive error and vision problems in children: association with increased sedentary behavior and reduced exercise in 9-year-old children in Ireland.

Quigley C, Zgaga L, Vartsakis G, Fahy G *JAAPOS* 2019 June; 23 (3): 159.e1-159.e6

An association between vision problems, including refractive error, and decreased exercise and increased sedentary behavior would be an important factor in identifying children at risk for becoming overweight. The purpose of this cross-sectional study was to investigate whether refractive error and vision problems in children are associated with increased sedentary behaviour and reduced participation in physical activity and sport and, secondarily, to examine the relationship between vision problems and body mass index. The study was conducted as part of the Growing Up in Ireland (GUI) Study, the longitudinal study of 9-year-old children in Ireland, a nationally representative study of children in Ireland. Data was collected between August 2007 and May 2008. Body mass index (BMI) was calculated at the time of the interview. The presence of a vision problem requiring treatment, including refractive error error, was detected by *report of the primary care giver*, usually the mother. Association between vision problems and sedentary behavior, physical activity, and level of participation in sports was investigated in adjusted regression analysis. A total of 8,568 children (mean age, 9 ± 0.13 years; 4,024 [48.68%] males) were included. The presence of refractive error or a vision problem was reported for 1,000 (11.68%) children. Most children had normal weight, but 1,497 (17.5%) were overweight, and 446 (5.2%) were obese. A positive association between vision problems and sedentary behavior (P=0.00089) and an inverse association with exercise (P = 0.01)

were found. Overall, vision problems were not associated with BMI. The authors conclude that in this study cohort, refractive error and vision problems were were associated with increased sedentary behavior and decreased physical activity, although no causal relationship was established. This is a very large, nationally representative sample with very detailed information regarding physical activity and sedentary behavior. However, little is available on the vision problems. The study is limited by the patient-reported nature of the data.

Predictors of Spectacle Wear and Reasons for Non-wear in Students Randomized to Ready-made or Custom-made Spectacles

Morjaria P, Evans J, Gilbert C. *JAMA Ophthalmology*. April 2019;137(4):408-414.

The authors investigated the predictors of spectacle wearing and the reasons of non-wearing in students randomized to ready-made or custom-made spectacles. Students aged 11 to 15 years who had improvement in visual acuity with correction by at least 2 lines in the better eye, were recruited from government schools in Bangalore, India. Recruitment took place during the first six months of 2015 and 460 students were recruited. Of note, spectacle wear was assessed by masked observers at unannounced visits to schools 3 to 4 months after spectacles had been distributed. In particular, students not wearing their spectacles were asked an open-ended question(s) to elicit reasons for non-wear. Of 460 students recruited and randomized, 52.2% were male and there were 46 students aged 11 to 12 years and 13 to 15 years. Follow up was analyzed in 78.7% (362 of 460) and 25.4% (92 of 362) were not wearing their spectacles. Authors noted that poorer presenting visual acuity (VA) and improvement in VA with correction predicted spectacle wear. The main reason students gave for non-wear was teasing or bullying by peers. Girls reported parental disapproval as a reason more frequently than boys. At 4 months follow up, the majority of the students receiving spectacles were wearing them. The authors noted that compared to other studies, predictors of spectacle wear, poorer presenting VA, and greater improvement in VA with correction are similar. However, in particular, the authors note that interventions to reduce teasing and bullying are required, and education of parents is particularly needed for girls in this setting.

IMI – Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies

Daniel I Flitcroft, Mingguang He, Jost B Jonas, Monica Jong, et al. *IOVS.* Special Issue February 2019;60:M20-M30.

This review devises standardized definitions for myopia to be used in clinical research. They refined the proper terms of categorization into myopia, secondary myopia, axial myopia, and refractive myopia. They defined myopia as having a spheri-

cal equivalent refractive error of ≤-0.50 D. High myopia was defined as ≤-6.00 D. Finally, pathologic myopia was defined as eyes with structural complications due to myopia. This is a change from many prior definitions of pathologic myopia as it no longer relates diopteric power to pathology. These standardized terms should allow for easier comparisons between studies of myopia and its complications.

IMI – Report on Experimental Models of Emmetropization and Myopia

David Troilo, Earl L Smith III, Debora L Nickla, Regan Ashby, et al *Invest Ophthalmol Vis Sci*. Special Issue February 2019;60:M31-M88.

This extensive review looked at numerous experimental models to provide an overview of myopia and emmetropization of different animal models. They noted that macaque and marmoset monkeys, tree shrews, guinea pigs, mice, chickens, and zebrafish demonstrate the development of axial myopia in response to visual deprivation, regulate axial length with optical peripheral defocus and recover from defocus once that is removed. They also note that subjects have higher degrees of astigmatism at birth which usually normalizes by school age and that patients with higher degrees of myopia or hyperopia have higher degrees of astigmatism. Astigmatism may also play a role in emmetropization or lack thereof. Examination of ocular circadian rhythms and diurnal light cycles have shown that a disruption in normal rhythms and cycles result in a myopic shift. Increased luminance was shown to decrease myopic shifts. They also identified numerous genes, choroidal activity, and biochemical receptors that affect emmetropization including but not limited to retinal dopamine, Vasoactive Intestinal Peptide, acetylcholine, serotonin, glucagon and insulin.

IMI – Interventions for Controlling Myopia Onset and Progression Report

Christine F Wildsoet, Audrey Chia, Pauline Cho, Jeremy A. Guggenheim, et al *Invest Ophthalmol Vis Sci*. Special Issue February 2019;60:M106-M131.

This article reviews the different treatment options for delaying onset of myopia or controling its progression. They looked at optical, pharmacological, environmental (behavioral), and surgical options. With spectacle correction, large amounts of undercorrection and peripheral myopic defocus were noted to decrease myopic progression. Orthokeratology, multifocal and progressive contact lenses were also shown to be a retardant of myopia. In regards to pharmacological therapy, Atropine has been the main medication used and in 0.01% concentration due to the lack of side effects and lack of rebound effect. Other pharmacologic treatments are currently being studied including timolol, pirenzepine, and 7-methylxanthine. Increased

time with sunlight has shown greater efficacy in decreasing the incidence in myopia than decreasing the progression of myopia. Surgically, scleral strengthening injections, and posterior scleral reinforcement with a single scleral strip have been shown to reduce myopic progression though the latter did have a wide range of complications.

IMI – Clinical Myopia Control Trials and Instrumentation Report

James S Wolffsohn, Pete S Kollbaum, David A Berntsen, David A Atchison, et al *Invest Ophthalmol Vis Sci*. Special Issue February 2019;60:M132-M160.

This study reviewed numerous clinical trial regarding myopia control and gave recommendations for proper conduct for future myopia control trials. They noted that there must be a study length of at least 2 years plus one year of a washout period. Inclusion criteria including age 6-12 years, myopia of at least -0.75 D, astigmatism no greater than 1.00 D, and anisometropia <1.50 D should be used. Axial length measurements and refractive error should both be primary outcomes, whiles secondary and exploratory outcomes may vary with some of the most important ones including outdoor activity and pupil size.

IMI – Industry Guidelines and Ethical Considerations for Myopia Control Report

Lyndon Jones, Bjorn Drobe, Jose M Gonz´alez-M´eijome, Lyle Gray, et al *Invest Ophthalmol Vis Sci*. Special Issue February 2019;60:M161-M183.

This study reviews the ethical implications of conducting a myopia control study on a population that is unable to give informed consent. They state that it is not only the responsibility of the treating physician and parent(s) to understand potential implications of experimental treatments, but of every stakeholder in the studies. This also include regulatory bodies and manufacturers of the potential treatments. While studies in vulnerable populations are difficult to perform both clinically, and ethically, they are absolutely necessary to treat these populations for disease states that revolve around them. These studies must go through utmost scrutiny before, during, and after implementation.

IMI – Clinical Management Guidelines Report

Kate L Gifford, Kathryn Richdale, Pauline Kang, Thomas A. Aller, et al *Invest Ophthalmol Vis Sci*. Special Issue February 2019;60:M184-M203.

This study reviews best clinical guidelines for clinical management of myopia and prevention of myopia. The clinician must first understand which patients are at a

risk of myopia progression. These include patients with lower hyperopic refraction at a younger age, increased number of myopic parents, and poor visual environment. Clinicians with patients who are pre-myopic must have similar conversations to those with risk of progressive myopia. It is important that these discussions are had with lay terminology and discussion of risks, benefits and alternatives must be had in lay terminology. They also outline their preferred standard outline for examination. Treatments must be conformed to each specific patient. Clinicians must also know for how long to treat and at what point to change treatments if poor compliance or outcomes are noted.

Longitudinal Changes in Choroidal and Retinal Thickness in Children with Myopic Shift

Peiyao Jin, Haidong Zoi, Xun XU, Ta Chen Chang, et al. *Retina.* June 209 ;39(6):1091-1099

Evidence suggests that the choroid may contribute to myopic pathogenesis. This study aims to assess the choroid over a one-year period. This was a longitudinal study assess the OCT of the choroid in children in Shanghai, China. 118 children were included in this study. Ophthalmic examinations including refraction, keratometry, axial length, and OCT measurements were taken of all study participants. At the 1 year follow up, 88 children developed a myopic shift. Among the children with a myopic shift, the central foveal choroid was significant diminished. There was no change in the choroid of children without a myopic shift. Choroidal thickness decreased in all subfields during myopic shift. There was no significant difference observed in axial length or retina on OCT with and without myopic shift. The authors concluded that in children with a myopic shift, there was concurrent decrease in choroidal thickness without significant change in retinal thickness suggesting the choroidal changes come prior to retinal changes.

A randomized clinical trial using atropine, cyclopentolate, and tropicamide to compare refractive outcome in hypermetropic children with a dark iris; skin pigmentation and crying as significant factors for hypermetropic outcome.

van Minderhout HM, Joosse MV, Grootendorst DC, Schalij-Delfos NE. *Strabismus.* 2019 Jun 24:1-12.

In this double-blind randomized prospective study, the authors evaluated the refractive outcome of various cycloplegic agents in children with dark irides, dark skin pigmentation and who cried during instillation of the drops. Crying upon or immediately following eye-drop application had a significant impact on hypermetropic outcome in all three dilation regimens (atropine 0.5%, two drops cyclopentolate, cyclopentolate with tropicamide).Atropine 0.5% revealed significantly more hypermetropia than two drops of cyclopentolate or cyclopentolate with tropicamide. Darker pigmented skin resulted in lower hypermetropia in all interven-

tions, particularly when the child was crying. Combined cyclopentolate-tropicamine was better in medium pigmented crying subjects compared to cyclopentolate alone and equal to atropine 0.5%. Based on their findings, the authors recommend the combination of cyclopentolate 1% with tropicamide 1% when dilating children.

Electrophysiological and Psychophysical Studies of Meridional Anisotropies in Children With and Without Astigmatism

Tiong Peng Yap, Chi D. Luu, Catherine M. Suttle, Audrey Chia, et al *Invest Ophthalmol Vis Sci*. May 2019;60:1906–1913.

This study evaluated whether there were any differences in astigmatic versus non non-astigmatic children while viewing pattern onset-offset visual evoked potentials and psychophysical grating acuity. Twenty non-astigmatic subjects aged 3-8 years and 9 astigmatic subjects aged 4-7 years without any other ocular disease and 20/20 best corrected vision were examined. Meridional anisometropy was noted in all subjects, regardless of astigmatism. It was found that there was a weaker response in all subjects to both vertical and oblique gratings when compared to horizontal gratings. This may play a role in both optotype design as well as grating acuity measurements. While this was a very small study with a wide variation in refractive error, this lends foresight into further studies which may allow for better examination of visual acuity in both verbal and non-verbal children.

A Randomized Clinical Trial of Immediate versus Delayed Glasses for Moderate Hyperopia in 1- and 2-Year-Olds

Marjean T. Kulp, Jonathan M. Holmes, Trevano W. Dean, Donny W. Suh, et al for the Pediatric Eye Disease Investigator Group *Ophthalmology*. June 2019;126:876-887

When moderate hyperopia is detected in a young, asymptomatic child, there are conflicting reports in the literature regarding the need for treatment. This study was prospectively designed to compare outcomes in 1- to 3-year-old children with moderate (+3 to +6 diopter) hyperopia treated with partial spectacle correction versus observation. Children who developed any manifest strabismus, strabismus surgery, subnormal (for age) vision in either eye, and/or subnormal (for age) stereoacuity were defined as treatment failures. The study enrollment was stopped at only 45% of the desired size because of slow recruitment. The study groups were further confounded because fewer than half of the children prescribed glasses wore them more than 75% of the time during the first year the glasses were prescribed. At 3 years, 21% of the glasses group reached failure criteria compared with 34% of the observation group, an insignificant difference. The primary cause of treatment failure was subnormal stereoacuity, with fewer

than 10% of each group developing manifest strabismus and similar small numbers in each group demonstrating subnormal vision in either eye. Although at enrollment subjects were evenly divided into groups based on level of hyperopia (+3, +4, and +5 diopters, respectively), no subgroup analysis broke out data based on level of initial hyperopia. Incomplete study enrollment prevents strong conclusions, but treating moderate levels of hyperopia with spectacles likely provides a small benefit to children, primarily in the form of improved stereoacuity.

Meeting the need for corrective spectacles in visually impaired Chinese school children: the potential of ready-made spectacles

Zhu Z, Ellwein L, Wang S, Zhao J, et al. *Br J* Ophthalmol. August 2019;103:1106-1111

Ready-made spectacles (RMS) are glasses with equal spherical correction in each lens that can be made in bulk at low costs. They have been using in screening and glasses distribution programs in areas where access to care is limited. Their use is limited though due to the extent of astigmatism and anisometropia in patients. This study aimed to evaluate how suitable RMS are for needing the needs of visually impaired children in China. Three study sites (from the Refractive Error Study in Children study) were examined. 12,334 children met inclusion criteria. Reasonable candidates for RMS were defined as those with ≤0.75D astigmatism and ≤0.5D anisometropia. The percentage of children meeting these amounts ranges from 62.8% to 64.0% depending on baseline uncorrected visual acuity. If the tolerances were increased to ≤1.25D astigmatism and ≤1.50D anisometropia, the percent meeting criteria increased to 85.8-87.4%. Therefore RMS could theoretically alleviate visual morbidity in 2/3's of children with visual impairment in China (those with decreased uncorrected visual acuity that improves with refractive correction). This is a cost-effective strategy that could be used in underserved areas with poor access to higher level care.

Intraocular pressure and myopia progression in Chinese children: The Anyang Childhood Eye Study

Li S, Iribarren R, Li H, Kang M, et al. *Br J* Ophthalmol. March 2019;103:349-354

Several studies have shown that intraocular pressure (IOP) is not generally associated with myopia prevalence of progression. However it is not known where variations in the range of normal IOP could affect ocular growth and subsequent myopia development. The Anyang Childhood Eye Study (ACES) is a prospective study of myopia development in Chinese schoolchildren. This study presents findings of baseline IOP and its relationship to myopia progression. 1558 students were included in the study. Cycloplegic autorefraction and non-contact tonometry was performed. The mean baseline IOP was 15.87 mmHg. The mean IOP was higher in girls by 0.57 mmHg (p=0.024). Over 2 years, the mean change in spherical equivalent in the entire group was -1.05D. In those progressing 1D or more the baseline IOP was 15.69 mmHg. In those progressing less than 1 D the

baseline IOP was 16.09 mmHg (p=0.022). In looking at myopes alone, the results were similar (mean IOP was lower in faster progressing eyes). Overall myopia progression over 2 years was inversely related to IOP, suggesting that IOP has little or no relationship to myopia progression. The authors then spend considerable time theorizing on why this may be, suggesting that the lower IOP in progressing eyes may indicate more compliance sclera. However a lot of the discussion is conjecture and further studies are needed.

Spectacles utilization and its impact on health-related quality of life among rural Chinese adolescents.

Qian DJ, Zhong H, Li J, Liu H, Pan CW. *Eye* (Lond). 2018 Aug 29. doi: 10.1038/s41433-018-0197-x.

This study measured the magnitude and predictors for spectacles utilization and to quantify its impact on health-related quality of life (HRQOL) among rural Chinese adolescents using a school-based survey of 2346 grade-7 students (mean age: 13.8 years). Criteria to define the need for glasses included an uncorrected visual acuity (VA) of 20/40 or worse correctable to 20/40 or better in the better-seeing eye. Refractive criteria included of myopia of less than 0.5 diopters (D), hyperopia of more than +2.0 D, or astigmatism of more than 0.75D in both eyes. The HRQOL was measured using self-reported versions of 23 item Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales (PedsQL 4.0). A total of 579 (24.7%) adolescents had an uncorrected VA of 20/40 or less. Of those 483 (83.4%) needed vision corrections but only 172 (35.6%) used them. Predictors for glasses included higher parental education levels (OR= 2.73; 95% CI, 1.29-5.77), negative attitude regarding spectacles (OR = 0.49; 95% CI, 0.25-0.97), and poorer uncorrected VA (OR = 31.27; 95% CI, 3.76-260.23). Not use of glasses was associated to lower HRQOL score, psychosocial health (65.91 vs. 70.59; P = 0.028), emotional health (56.85 vs. 63.24; P = 0.012), and social functioning (72.99 vs. 78.60; P = 0.036).
In conclusion in rural China few adolescents meeting the criteria for less than 20/40 vision wear glasses. Despite of the low number there is a negative impact of decrease visual acuity in the quality of life of those individuals

Positional Change of Optic Nerve Head Vasculature during Axial Elongation as Evidence of Lamina Cribrosa Shifting: Boramae Myopia Cohort Study Report 2.

Lee KM, Choung HK, Kim M, Oh S, Kim SH. *Ophthalmology* 2018 Aug;125(8):1224-1233.

Anatomic changes associated with axial growth can cause stress on the optic nerve vasculature in a way that makes it more vulnerable to glaucomatous damage. In myopia, retinal vessels are reported be located more temporally suggesting that the central retinal vascular trunk may have shifted from its original location in early development. In this study, the authors investigated the positional

change of central retinal vasculature and vascular trunk to deduce the change in the lamina cribrosa (LC) during axial elongation. To capture these changes, the authors measured the angle between the central retinal vascular arcades from the center of the disc (center of the glaucoma progression analysis (GPA) mode, angle) and from the vascular trunk (angle) and compared the two angles. Twenty-three otherwise healthy myopic children (46 eyes) were prospectively followed with serial full ophthalmologic examination and axial length measurement every 6 months for 2 years. Using spectral-domain OCT, circle scans centered around the optic disc in the GPA mode, which enabled capturing of the same positions throughout the entire study period, and enhanced depth imaging of the deep optic nerve head complex were performed. Infrared imaging of the circle scans was used to measure the changes in the angles between the first and final visits. The angle between the major superior and inferior retinal arteries was measured along the circle scan twice: from the center of the circle scan and from the central retinal vascular trunk, respectively. The positional change of the retinal vascular trunk also was measured. Over the study period, the vascular angle measured from the center of the circle scan did not change ($P = 0.247$), whereas the angle measured from the central retinal arterial trunk decreased with axial elongation, indicating that the vascular bundle moved more nasally in the disc ($P < 0.001$). A generalized estimating equation analysis revealed that the factors associated with angle decrease were axial elongation ($P = 0.004$) and vascular trunk dragging ($P < 0.001$). The extent of vascular trunk dragging was associated with axial elongation ($P < 0.001$) and increased border length with marginal significance ($P = 0.053$), but the extent of dragging could not be explained fully by their combination. The major directionality of dragging was mostly to the nasal side of the optic disc, with large variations among participants. Based on their findings, the authors suggested that nasal dragging of the central vasculature may contribute to the vulnerability of the myopic eyes to glaucomatous optic neuropathy.

Longitudinal Changes of Optic Nerve Head and Peripapillary Structure during Childhood Myopia Progression on OCT: Boramae Myopia Cohort Study Report 1

Kim M, Choung HK, Lee KM, Oh S, Kim SH. *Ophthalmology* 2018 Aug;125(8):1215-1223.

Axial elongation in myopic eyes is accompanied by scleral remodeling of the optic nerve head (ONH) and peripapillary area where glaucomatous changes occur. The authors conducted a prospective study in Korea documenting the longitudinal changes of the ONH and peripapillary tissues during childhood myopia progression using spectral-domain (SD) OCT. The participants underwent fundus photography, SD OCT, and axial length (AXL) measurements every 6 months for 2 years. A total of 23 participants (46 eyes) were recruited, 9 were boys. Mean age was 9.6 yrs. (range 6.7 to 12.5 yrs.). Based on the morphologic features on fundus photographs, masked observers classified each eye into 4 groups based on the ONH shape and the presence of β-zone parapapillary atrophy (PPA):

Group A (ONH unchanged without β-zone PPA; 11 eyes), group B (ONH changed without β-zone PPA at baseline; 10 eyes), group C (ONH changed with β-zone PPA at baseline; 15 eyes), and group D (ONH unchanged with β-zone PPA; 10 eyes). The configuration of the border tissue (BT) at the temporal margin of the ONH was assessed, and the ONH parameters, including Bruch's membrane opening distance (BMOD), border length (BL), and BT angle (BTA), were measured on horizontal SD OCT scans. Group B showed the greatest AXL increase per year (group B > group C > group A = group D; $P < 0.001$). During the follow-up periods, the BT configuration initially was changed from internally oblique to externally oblique (group B) and was stretched, resulting in optic disc ovality and γ-zone PPA development (group C). In group C, BL was increased significantly nasally and BTA was decreased significantly, whereas BMOD remained stable ($P < 0.001$, $P < 0.001$, and $P = 0.100$, respectively). In the multivariate analysis using a generalized linear mixed-effect model, the changes of BL and BTA were associated with axial elongation ($P = 0.028$ and $P = 0.010$, respectively). Based on the study findings, the authors concluded that there is development and nasal expansion of γ-zone PPA during myopia progression. During the ONH and peripapillary changes, the BL was increased nasally and the BTA was decreased, whereas the BMOD remained relatively stable. The association of axial elongation with ONH and peripapillary tissue changes may facilitate understanding of the relationship between myopia and glaucoma. This is a much-needed study looking at the childhood myopia progression. However, the groups were not comparable in age or axial length. Group A did not seem to have undergone a significant myopic change and Group D may already have gone through a myopic change. Only group B went through a significant myopic change in the study.

4.**VISION IMPAIRMENT**

The Development and Assessment of Crayons that Produce Textured Lines for Individuals Who Are Visually Impaired

Suraj Kandalam, Tyler Ferro, Dianne T.V. Pawluk *Journal of Visual Impairment & Blindness* 2019, Vol 113(2) 165-179

For sighted children, the use of crayons plays an important role in childhood development. For children who are visually impaired, using standard crayons is difficult. This article describes the development and initial assessment of a set of tactile crayons that can produce different textured lines and areas on standard paper. An assessment of the need for tactile crayons was performed which validated interest in tactile crayons as a learning tool that would fill a needs gap. Six tactile crayons were developed along the texture dimensions of sticky or slippery, rough or smooth, and hard or soft. Participants were able to discriminate the six crayons with a mean accuracy of 77%, and of the six, they could identify the four most easily discriminable with 86% accuracy. These results both validate the

usefulness and feasibility of tactile crayons and demonstrates the potential of tactile crayons to aid childhood development and student learning.

Evaluation of an Accessible, Real-Time, and Infrastructure-Free Indoor Navigation System by Users Who Are Blind in the Mall of America

Nicholas A. Giudice, William E. Whalen, Timothy H. Riehle, Shane M. Anderson et al. *Journal of Visual Impairment & Blindness* 2019, Vol 113(2) 140-155

Indoor positioning systems with standard GPS receivers is neither accurate nor reliable since satellite signals cannot penetrate large office buildings. Large-scale adoption and implementation of indoor navigation systems for blind navigators has not been widely done or successful. This article describes an evaluation of MagNav, a speech-based, infrastructure free navigation system. The research was conducted at the Mall of America. Comparisons were made for route-guided performance between the use of updated, real-time route instructions (system-aided condition) and a system-unaided (memory-based condition) where the same instructions were only provided in advance of route travel. Sighted controls who navigated under typical visual perception but used the system for route guidance were used as a best-case scenario control. Blind navigators receiving real-time verbal information from the MagNav system performed route travel faster, more accurately, and more confidently compared to conditions where the same route information was only available to them in advance (similar to asking for directions). This research is compelling in showing the usefulness and importance of development of accessible navigation systems that minimize memory demands

The Impact of Diplopia on Reading

Lijka, Beckie, et al. *Br Ir Orthopt J* 2019; 15(1): 8-14

The impact of strabismus and diplopia on quality of life (QOL) has been well documented. They can have emotional, psychological, and functional negative effects. Reading is a common way to assess the impact of visual conditions which impacts QOL. The Radner Reading Chart (RRC) was used to compare the effect of induced diplopia (small (6Δ) and large (12Δ) separation) on reading speed and accuracy. Reading speed was significantly slower in both the small separation and large separation groups compared to the control group, worse in the small separation group. The small separation induced vertical diplopia group had significantly reduced accuracy compared to both control and large separation groups. The authors conclude that vertical diplopia has a significant impact of reading function bot in speed and accuracy and the smaller the deviation the greater the impact. When a diplopic patient is unable to fuse their corrected deviation, treatment may include using Fresnel prisms to further separate the images making the angle of deviation higher.

Efficacy of Care for Blind Painful Eyes

Oluwatobi O. Idowu, Davin C. Ashraf, Evan Kalin-Hajdu, et al. *Ophthalmic Plast Reconstr Surg* Mar/Apr 2019;35:182–186

Pain relief for a blind painful eye often follows an escalating paradigm of interventions. This study compares the efficacy of common interventions. A retrospective chart review of blind painful eye cases was conducted at a single tertiary institution from April 2012 to December 2016. Demographics, etiology, treatment, and pain level were assessed. Among 99 blind painful eyes, 96 eyes initially received medical therapy (topical steroids, cycloplegics, and/ or hypotensives), with pain relief in 39% of eyes. Minimally invasive interventions (laser cyclophotocoagulation, retrobulbar injection, or corneal electrocautery) were performed 41 times in 36 eyes, 34 of which had failed medical therapy, and led to pain relief in 75% of eyes. Evisceration or enucleation was performed in 28 eyes, and long-term pain relief was achieved in 100% of eyes. Surgery allowed discontinuation of oral analgesics in 100% of cases versus 20% for minimally invasive therapy ($p = 0.005$) and 14% for medical therapy ($p = 0.0001$). Compared with medical therapy, minimally invasive therapy was 2.5 times more likely to achieve lasting pain relief ($p = 0.003$) and surgical therapy 35.6 times more likely to achieve lasting pain relief ($p = 0.011$). High initial pain score was associated with nonsurgical treatment failure. Medical therapy provides pain relief in a moderate number of patients with a blind painful eye. When medical therapy fails, minimally invasive therapy and surgical interventions are successively more effective in relieving ocular pain. High initial pain score is a risk factor for nonsurgical therapy failure and may merit an earlier discussion of surgical intervention.

Visual impairment and Eye Disease Among Children of Migrant Farmworkers.

Rebecca Russ Soares, Michael Rothschild, Danny Haddad, Phoebe Lenhart. J *Ped Ophthal & Strabismus*.2019;56(1):28-34

The purpose of this study is to determine the prevalence of reduced visual acuity and ocular disease in the children of migrant farmworkers in Georgia. A retrospective chart review of data acquired by a vision screening was performed on 156 Haitian and Hispanic children of migrant farmworkers attending a summer school in Georgia. Reduced visual acuity at presentation was analyzed and stratified by ethnicity, type of ocular disease, and immediate resolution with refractive correction. The authors found that 20% of migrant farmworker children have a high prevalence of reduced visual acuity in the worse eye. Of those with worse-eye reduced visual acuity, 83% had uncorrected refractive error. The prevalence of uncorrected refractive error from astigmatism and high astigmatism was significantly higher among Hispanics than Haitians. The prevalence of amblyopia suspects among migrant farmworker children was 3%. Of the amblyopia suspects, 80% were anisometropic. The authors concluded that Children of migrant farm-

workers in Georgia have a higher rate of reduced visual acuity, largely from uncorrected refractive error, when compared to other Hispanic and African American children in the United States with a prevalence more aligned to children in Asian and Latin American countries than school children in the United States. This illustrates the need for improved access to screening and care in this vulnerable population. The study has certain limitations: Due to the retrospective nature of this analysis, the eye charts in each group were not standardized. As such, visual acuity may have been underestimated in 4 to 5 year olds and over estimated in older children using the HOTV charts. Also, there was no additional follow-up to determine the best-corrected visual acuity of patients once they had been wearing their new correction for a few weeks. Furthermore, although the prevalence of uncorrected refractive error was high, this prevalence only accounts for presenting vision; it may not account for children who had but did not bring their spectacles. Finally, because this was a screening measure, amblyopia suspects were referred to follow-up if needed. However, given the transient nature of the population, we were unable to track follow-up visual acuity or response to penalization therapy. Future studies examining long-term visual outcomes in such patients, while logistically difficult, would be worthwhile.

Frequency of Visual Deficits in Children With Developmental Dyslexia.

Apart Raghuram, Sowjanya Gowrisankaran, Emily Swanson, David Zurakowski, et al. *JAMA Ophthalmology* October 2018; 136 (10): 1089-1095.

This was a prospective, uncontrolled observational study from May to October 2016 in an outpatient ophthalmology clinic in 29 children with developmental dyslexia (DD) and 33 typically developing (TD) children. The authors wanted to assess the frequency of visual deficits (vergence, accommodation, and ocular motor tracking) in children with DD compared with a control group. Demographics included mean age of 10.3years for the DD children and mean age of 9.4years for the TD children. The authors report statistically significant accommodation deficits in the DD group compared to the TD group (55% versus 9%, respectively) and statistically significant ocular motor tracking abnormalities in DD group compared to the TD group (62% versus 15%, respectively). Overall, children in the DD group were diagnosed with more than 1 visual deficiency (79%) as compared to children in the TD group (33%) especially abnormalities in ocular motor tracking and accommodation. Reporting statistically significant visual deficiencies in children with DD as compared to TD children, the authors' suggest that it is important to evaluate visual function in children with dyslexia, including an evaluation of vergence, accommodation, and ocular motor tracking. Limitations of the study is the small sample size and the unmasked examiners. Furthermore, the authors suggest that additional studies should assess if treatment of particular visual deficiencies will help improve visual symptoms for children with DD.

An Analysis of Parents' Reports on Educational Services for Their Children with Albinism

Corn, Anne L.; Lusk, Kelly E. *Journal of Visual Impairment & Blindness*. Nov/Dec 2018, Vol. 112 Issue 6, p667-682.

The purpose of this study is to gain information from parents in the United States about their children with albinism. The article focuses on information and services related to the education of children with albinism. This article complements a second article in the same journal looking at information and services related to which complements an adjacent article from the same authors focusing on the information and services related to medical care and low vision care. An online questionnaire was used to collect data. Parents had opportunities to submit additional information. One hundred ninety-two families, representing 223 children with albinism from 40 U.S. states, completed surveys. Results revealed that while most children were receiving direct instruction or consultation from teachers of students with visual impairments, many parents were not able to provide information about the level of assessment, reading rates, or the nature of the services. Parents are generally satisfied with services provided as well as their level of involvement in their children's educational service plans. The article makes recommendations to: 1) provide additional information about educational interventions for infants and children with albinism to physicians who diagnose albinism; 2) provide information to parents about the Individuals with Disabilities Education Act (IDEA) so that they are more aware of which low vision services are available under IDEA's provisions for medical evaluations and assistive devices; 3) provide support for the social and emotional development of children with albinism; 4) conduct research on educational practices with students with albinism. In addition to other important points, this study highlights the importance of the practitioner partnering with parents of children with autism to ensure parents have a strong foundational understanding of the condition and are aware of services available to them.

Reports from Parents about Medical and Low Vision Services for Their Children with Albinism: An Analysis

Corn, Anne L.; Lusk, Kelly E. *Journal of Visual Impairment & Blindness*. Nov/Dec2018, Vol. 112 Issue 6, p655-666.

The purpose of this study is to gain information from parents in the United States about their children with albinism. The article focuses on information and services related to medical care and low vision care. This article complements a second article in the same journal looking at information and services related to the education of children with autism. An online questionnaire was used to collect data. Parents had opportunities to submit additional information. One hundred ninety-

two families, representing 223 children with albinism from 40 U.S. states, completed surveys. The data revealed that the majority of families have no known family history of albinism, and 55.8% of children met criteria for legal blindness. Less than half (48%) of children using optical devices received a clinical low vision evaluation by a specialist. The study highlights the importance of obtaining a medical and clinical low vision evaluation and providing education to families on the value of obtaining both exams. The study also recommends a longitudinal study of the medical services and low vision care provided to these children.

Exploring the Functional Impact of Childhood Vision Impairment: An e-Delphi Study

Susan L. Silveira & Robyn Cantle Moore *Journal of Binocular Vision and Ocular Motility*, 2018; 68:4, 110-121

A new method that assesses both the functional and the clinical impact of childhood vision impairment at various ages, developmental stages, levels of vision loss, and with co-existing disabilities is needed. The purpose of the study is the exploration of the functional impact of childhood vision impairment using the Delphi technique. The Delphi technique uses a series of questionnaires; this study had participants complete three online questionnaires with feedback emailed to them in between the questionnaires. The participants were orthoptists and specialist teachers in vision impairment (STVIs). The outcomes were analyzed for evidence of consensus and stability. The ultimate goal of the study was to develop a visual behavior standard (VBS) that presents an understanding of the child's current visual function that may not correlate with clinical measurements.

The epidemiology of childhood blindness and severe visual impairment in Indonesia

Muhit M, Karim T, Islam J, Hardianto D, et al. *Br J* Ophthalmol. November 2018;102:1543-1549.

The magnitude of childhood blindness is unknown in Indonesia, therefore this study aimed to define epidemiological characteristics of childhood blindness in two parts of Indonesia. A community based program in two areas identified children age 0-15 years. The programs included schools for special education and community based rehabilitation programs. Standard WHO data forms were used, and defined blindness as visual acuity less than 3/60, severe visual impairment as visual acuity 3/60 to less than 6/60, and visual impairment 6/60 to 6/18. Unilateral blindness was excluded. 195 children were assess, of which 113 had blindness or severe visual impairment. Overall prevalence of blindness/severe visual impairment was 0.25 and 0.23 per 1000 children in the two areas. Prevalence of cataract was 0.07/0.05 per 1000 children (again in the two areas). This suggests there are over 17,000 children with blindness/severe visual impairment in Indonesia, including over 4000 blind from cataracts. This highlights a substantial unmet need for these children including screening programs and access to care.

Visual development During the Second Decade of Life in Albinism.

Brandon K.McCafferty, Ann M.Holleschau, John E.Connett, C.Gail Summers
J of Ped Ophth & Strabismus.2018; 55(4): 254-259

The purpose of this retrospective study is to evaluate change in best corrected visual acuity (BCVA) during the second decade of life and the effects of albinism type and extraocular muscle surgery on BCVA in children with albinism. Forty one patients with albinism with clinic visits recording binocular BCVA at least once between the ages of 10 and 13 years (visit A) and again between the ages of 17 and 20 years (visit B) were included. Type of albinism, age at each visit, and interval eye muscle surgeries were recorded for each patient. The study showed that Forty (98%) patients showed BCVA improvement or stability between visits A and B. There was no significant effect of interval extraocular muscle surgery on BCVA. Those carrying either a clinically presumed or moleculary confirmed diagnosis of oculocutaneous albinism types 1B and 2 had the best visual outcomes, consistent with previous studies. The authors conclude that in the majority of patients with albinism, significant improvement in BCVA occurs during the second decade of life. Extraocular muscle surgery was not a significant factor in BCVA improvement in albinism. Overall, the assessments support the finding of improvement of visual acuity in children with albinism at earlier ages and provide new information beneficial in predicting visual outcomes in the second decade of life. The study is limited by its retrospective nature as well as the small sample size, which limits the usefulness of data analysis by specific type of albinism. This is further accentuated by the lack of molecular data on all patients; knowing the specific causative mutations on all patients would allow phenotype-genotype correlations. Finally, the patients were not randomly assigned to having extraocular muscle surgery in this retrospective study.

Symbol Discrimination Speed in Children With Visual Impairments

Barsingerhorn AD, Boonstra FN, and Goossens J. *Invest Ophthalmol Vis Sci*. Aug 2018;59:3963-72.

This purpose of this study was to determine whether visual discrimination speed was slower in children with visual impairments compared to children with normal vision. Five- to twelve-year-old children with visual impairments due to ocular dysfunction (VI_o; n = 30) or cerebral visual impairment (CVI; n = 17) performed a speed-acuity test in which they indicated the orientation of Landolt-C symbols as quickly and accurately as possible. The reaction times for symbols ranging between -0.3 and 1.2 logMAR relative to acuity threshold were compared with normative data. To test whether children were already slow in merely detecting symbols, we also compared their reaction times on a simple visual detection task (VDT) to normative data. An auditory detection task (ADT) was used to probe for other, more general deficits. Of the children with visual impairments, 88% had

abnormally long reaction times in the speed-acuity test. This deficit was partly explained by their reduced acuity, but 40% still needed more time to discriminate acuity-matched optotypes. Children responded late in the VDT too, especially those with CVI, but this impairment could not fully account for their slow symbol discrimination. In children with CVI, reaction times in the ADT were affected as much as those in the VDT, suggesting more general sensorimotor problems in CVI. The speed-acuity test offers additional insight in visual impairment. Children with VI_o and CVI are abnormally slow in discerning foveal details. Magnification of materials is often insufficient to compensate for this deficit, partly because stimulus detection is already hampered. A larger study including multiple children per ocular diagnoses (retinal abnormalities, nystagmus, strabismus, etc.) would help elucidate whether certain diagnoses have a higher risk of response delays.

5. NEURO-OPHTHALMOLOGY

Impaired Visual Search in Children with Rett Syndrome

Susan A. Rose, Sam Wass, Jeffrey J. Jankowski, Judith F. Feldman, Aleksandra Djukic Pediatric *Neurology* 92 (2019) 26-31

Rett Syndrome is a severely disabling neuro-developmental disorder caused by mutations in the X-linked MECP2 gene. Eye tracking technology (Tobii X2-60 infrared eyetracker) was used to investigate selective attention (the ability to focus on or select a particular element or object in the environment) in this population. The study used a search task in conjunction with the eye-tracking technology. The study sample included 28 females with Rett Syndrome and 32 age-matched controls. Each trial included a target (a red apple) and several distractors (blue apples, red cylinders). The distractors varied in number and were different from targets by a single feature (such as color or shape to produce a pop-out effect) or in conjunction of features requiring serial searching. Children searched for the target in arrays containing five or nine objects, and trials ended when the target was fixated, or time expires (4000ms). Children with Rett Syndrome had more difficulty finding the target than controls (50% vs 80%) in both single and with conjunction of features. Success rate for children with Rett Syndrome was not influenced by display size or age. When successful, children with Rett Syndrome took significantly longer to respond (392 to 574ms longer). It is unclear what factors underlie the difficulties in these children, but a few ideas are postulated: 1) they have difficulty shifting and/or engaging attention from the distractors; 2) visual search is impaired in children with Rett Syndrome because they have difficulty distributing attention across the display; 3) efficient search of children with Rett Syndrome is compromised by a tendency to focus on local (rather than global) features. This article provides the first evidence that selective attention is compromised in Rett Syndrome.

Neurofibromatosis Type 1:A population-Based Study

Bashar M. Bata, David O. Hodge, Brian G. Mohney. *J of Ped Ophthalmol & Strabismus.*2019; 56(4): 243-247

The purpose in to report the incidence, demographics, and clinical manifestations of neurofibromatosis type 1 among a population-based cohort of patients. The medical records of all patients diagnosed as having neurofibromatosis type 1 while residing in Olmsted County, Minnesota, from January 1, 1980, through December 31, 2009, were retrospectively reviewed. Fifty patients were diagnosed as having neurofibromatosis type 1 during the 30-year period, yielding an incidence of 1.2 per 100,000 individuals. The mean age at diagnosis was 11.7 years (95% confidence interval [CI]: 0.2 to 47) and 26 (52%) were males. Twenty-eight patients were new mutations, yielding a de novo mutation rate of 56%. During a mean follow-up of 9.8 years (range: 3 weeks to 32 years), café-au-lait macules were diagnosed in 49 individuals (98%), neurofibromas in 26 (52%), and skeletal anomalies in 14 (28%). Three (5.9%) individuals were diagnosed as having glioma of the central nervous system (95% CI: 1.2 to 9.7%) at a mean age of 13 years (range: 5 to 26 years), including 1 patient with optic nerve glioma diagnosed at the age of 26 years. Only 1 (2%) patient was diagnosed as having malignant nerve sheath tumor. The authors concluded that although the estimated prevalence and de novo mutation rate of neurofibromatosis type 1 in this population-based study are similar to previous reports, the prevalence of optic nerve gliomas was much lower. There are several limitations to the findings of this study. Its retrospective design is limited by incomplete data and an evolving understanding of neurofibromatosis and its clinical manifestations. This experience is reflected in the fact that some patients went undiagnosed until an older age even though they possessed enough diagnostic criteria to be diagnosed at a much younger age. Some of the patients may have sought care outside Olmsted County, thereby decreasing the true incidence in this population. The de novo mutation rate might also be an underestimate given the variable expressivity of the disease and the fact that the majority of parents were not genetically tested to confirm whether or not they have the disease. Furthermore, the rate of optic nerve glioma may have been underestimated because there is not enough data on which of those received surveillance in the form of brain imaging. Finally, this cohort is also limited by occurring in a relatively homogenous white population, making extrapolation to other populations problematic.

Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder

Pittock SJ, Berthele A, Fujihara K, Kim HJ, et al. *N Engl J Med.* May 2019. E-pub ahead of print.

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune, inflammatory disorder characterized by recurrent attacks of optic neuritis and myelitis, from which patients typically do not recover. At least two thirds of NMOSD cases are associated with aquaporin-4 antibodies (AQP4-IgG) and complement-mediated damage to the central nervous system. Aquaporin-4 (AQP4) is a water

channel protein expressed mainly by astrocytes in the central nervous system. AQP4-IgG triggers the complement cascade, which leads to inflammation and the formation of the membrane attack complex and subsequent astrocyte destruction. In a previous small, open-label study involving patients with AQP4-IgG–positive disease, eculizumab, a terminal complement inhibitor, was shown to reduce the frequency of relapse.

In this randomized, double-blind trial, 143 adults were randomly assigned in a 2:1 ratio to receive either intravenous eculizumab or placebo. The eculizumab was given weekly for four weeks at 900 mg per dose and then every two weeks thereafter at 1200 mg per dose. The continued use of stable-dose immunosuppressive therapy was permitted. The primary end point was the first relapse, as defined by a committee of two neurologists and one neuro-ophthalmologist retrospectively reviewing clinical data, masked to treatment type. A secondary outcomes was a disability score on the Expanded Disability Status Scale (EDSS), which ranges from 0 (no disability) to 10 (death).

130 (91%) of the patients were women of mean age 44 +/- 13 years. Relapses occurred in 3 of 96 patients (3%) in the eculizumab group and 20 of 47 (43%) in the placebo group (hazard ratio, 0.06; 95% confidence interval [CI], 0.02 to 0.20; P<0.001). The mean change in the EDSS score was –0.18 in the eculizumab group and 0.12 in the placebo group (least-squares mean difference, –0.29; 95% CI, –0.59 to 0.01). Upper respiratory tract infections and headaches were more common in the eculizumab group. There was one death from pulmonary empyema in the eculizumab group.

Patients with AQP4-IgG–positive NMOSD who received eculizumab had a significantly lower risk of relapse than those who received placebo. There was no significant between-group difference in measures of disability progression. Although this clinical trial involved adults, neuromyelitis optica can also affect children. Pediatric ophthalmologists should be aware of a new medication in a new medication class that can be used for a blinding disease. Of note, this study was funded by Alexion Pharmaceuticals, which makes eculizumab.

Vestibular Eye Movements Are Heavily Impacted by Visual Motion and Are Sensitive to Changes in Visual Intensities

Tobias Wibble, Tony Pansel *Invest Ophthalmol Vis Sci*. March 2019; 60:1021-1027.

This study evaluated eye movements in healthy subjects, 6 under the age of 35 years and 6 over the age of 49 years, who were introduced to visual, vestibular, and visual-vestibular stimulation. Torsional response, skewing response, and a torsion-skewing ratio were measured for each type of stimulation as well as increasing intensity of visual stimulus. The younger group showed increasingly faster torsional response, and higher torsional velocity with vestibular and visual-vestibular stimuli,

though intensity of visual stimulus did not show any significant effect. The older group did not show any difference in torsional response. There was an increase in skewing velocities for both groups from visual to vestibular stimuli. There was also noted to be an increase in torsion-skewing ratio with increased intensity of visual stimulus in both the visual and visual-vestibular stimuli. This small study shows that eye movements may play an important role in the diagnosis of vertigo. When no clear etiology of the vertigo can be elucidated, it may be of interest to record eye movements to see if they are playing a role in the patient's symptoms.

Study of Optimal Perimetric Testing in Children (OPTIC): evaluation of kinetic approached in childhood neuro-ophthalmic disease

Patel D, Cumberland P, Walters B, Cortina-Borja M, et al. *Br J* Ophthalmol. August 2019;103:1085-1091.

The purpose of this study was to investigate the differences between Goldmann and Octopus kinetic perimeters for visual fields testing in children. The "gold-standard" Goldmann perimeter is no longer commercially available, so evaluation of newer equipment is needed. 30 children aged 5-15 (mean 11.1 years) with either neuro-ophthalmic conditions or known neuro-ophthalmic visual field defects were recruited. Goldmann perimetry was performed first, followed by 5 minutes of rest and the Octopus perimetry. Note that test order was not randomized. Overall 90% completed the Goldmann testing vs 72.4% for Octopus. The most common reason for not completing the test was inability to plot the blind spot due to poor cooperation. The testing time was similar between the perimeters. Test quality (using the Examiner Based Assessment of Reliability tool) was deemed similar for the two perimeters for children 8 and older. For children under 8 years better quality was obtained with Goldman testing (4/5) vs Octopus (2/5). Visual field loss severity scores showed broad agreement. The type of field defect matched in 29/42 (69%) tests. The octopus tended to depict more extensive field loss, and the Goldmann depicted a larger blind spot. The Octopus also tended to underestimate severe visual field defects. Overall the authors felt that the outputs of these two perimeters are not directly interchangeable in this group, and it is not recommended to use the perimeters interchangeably when monitoring children longitudinally. This is important for those practitioners transitioning to the Octopus to develop appropriate strategies to interpret findings in their patients.

Optokinetic nystagmus in patients with SCA: A bedside test for oculomotor dysfunction grading.

Seshagiri DV, Pal PK, Jain S, Yadav R. *Neurology.* Sep 2018;91(13):e1255-e1261.

The authors examined the utility of OKN testing as a bedside tool for quantifying oculomotor dysfunction in the setting of spinocerebellar ataxia in a cohort of 73 genetically confirmed patients. In this prospective study, the authors found that there was a differential response to vertical and horizontal OKN depending on whether the patient had SCA1, 2 or 3. This impairment in response corresponded favorably to the motor disability as evaluated by the International Co-operative Ataxia Rating Scale and therefore may be a more sensitive measure of determining oculomotor disease in these patients.

Inclusion of optic nerve involvement in dissemination in space criteria for multiple sclerosis

Brownlee WJ, Miszkiel KA, Tur C, Barkhof F, et al. *Neurology.* Sep 2018; 91(12):e1130-e1134.

The authors examine the inclusion of optic neuritis as a criterion for dissemination in space as part of the revised McDonald criteria for MS using 160 patients with clinically isolated syndrome. Inclusion of symptomatic optic neuritis improved the sensivity of the McDonald 2017 DIS criteria from 83% to 95% but was less specific from 68% to 57%. When evaluated in patients with clinically isolated syndrome without optic neuritis (of whom there were 31 of the 160), the inclusion of optic neuritis as a criterion did not improve the diagnostic accuracy of the McDonald 2017 criteria. The authors conclude that when considering predilection for development of MS, symptomatic optic neuritis should be included as part of the DIS criteria as it improves the diagnostic accuracy of the McDonald 2017 criteria.

Detection and characterisation of visual field defects using Saccadic Vector Optokinetic Perimetry in children with brain tumours

Murray IC, Schmoll C, Perperidis A, Brash HM, et al. *Eye*. Oct 2018;32:1563-73.

The purpose of this study was to determine the ability of Saccadic Vector Optokinetic Perimetry (SVOP) to detect and characterise visual field defects in children with brain tumours using eye-tracking technology, as current techniques for assessment of visual fields in young children can be subjective and lack useful detail. This was a case-series study of children receiving treatment and follow-up for brain tumours at the Royal Hospital for Sick Children in Edinburgh from April 2008 to August 2013. Patients underwent SVOP testing and the results were compared with clinically expected visual field patterns determined by a consensus panel after review of clinical findings, neuroimaging, and where possible other forms of visual field assessment. Sixteen patients participated in this study (mean age of 7.2 years; range 2.9–15 years; 7 male, 9 female). Twelve children (75%) successfully performed SVOP testing. Of the 4 children in which SVOP failed due to poor eye tracking, one was due to heavy mascara use, one had

congenital glaucoma with buphthalmos and cloudy cornea in one eye, one had extremely poor vision and unsteady fixation due to severe optic atrophy, and reason for failure in the fourth patient was not elucidated. SVOP had a sensitivity of 100% and a specificity of 50% (positive predictive value of 80% and negative predictive value of 100%). In the true positive and true negative SVOP results, the characteristics of the SVOP plots showed agreement with the expected visual field. Six patients were able to perform both SVOP and Goldmann perimetry; these demonstrated similar visual fields in every case. SVOP is a highly sensitive test that may prove to be extremely useful for assessing the visual field in young children with brain tumours, as it is able to characterise the central 30° of visual field in greater detail than previously possible with older techniques. The automated nature of SVOP requires minimal experience to operate the system, children find the test easy with engaging animations and it takes only ~5 minutes to perform. Future studies on longitudinal follow-up of children with visual pathway tumors will help determine repeatability and reliability of the test and demonstrate changes of visual field defects in relation to changes in tumour size over time and response to medical or surgical interventions.

Efficacy and Safety of Low-to –Moderate Dose Oral Corticosteroid Treatment in Ocular myasthenia Gravis.

Yoon Gon Lee, Ungsoo Samuel Kim.*J Ped Ophthal & Strabismus*.2018;55(5):339-342

The purpose of this study is to evaluate the response to corticosteroid treatment as primary therapy for ocular myasthenia gravis. Twenty-nine patients (19 men and 10 women; average age: 49 ± 16.5 years) who were diagnosed with myasthenia gravis were included in the study and started receiving treatment with a corticosteroid. Patients with a blowout fracture, hyperthyroidism, diabetes mellitus, hypertension, cardiovascular disease, or history of strabismus surgery were excluded. Disappearance of diplopia and ptosis were considered a response to treatment. A total of 6 patients were lost to follow-up. Twenty-three of 29 patients (82.6%) were regarded as having presented a response to treatment. The average treatment duration was 3 weeks for patients responding to primary treatment. Eight patients complained of adverse effects from steroid therapy such as heartburn, insomnia, weight gain, and myalgia. The authors conclude that a low-to-moderate dose of an oral corticosteroid may be considered as a primary treatment in ocular myasthenia gravis because the treated patients had a favorable response to the corticosteroid without severe side effects. The study has a lot of limitations:First, the study was retrospective and conducted in a relatively small number of eyes. There was no comparison of the effectiveness and efficacy between corticosteroid treatment and a cholinesterase inhibitor. Second, most patients suffered from diplopia because the study was performed in a neuro-oph-

thalmology clinic. In ocular myasthenia gravis, ptosis is the most common finding.[20] Thus, there might have been selection bias. However, the study demonstrated the effectiveness of a low-to-moderate dose of a corticosteroid in ocular myasthenia gravis.

Prevalence of Strabismus Among Children With Neurofibromatosis Type 1 Disease With and Without Optic Pathway Glioma.

Gad Dotan, Hanya M.Qureshi, Hagit Toledano-Alhadef, Nur Azem et al. *J Ped Ophthalm & Strabismus*.2019;56(1):19-22

The purpose of this study is to evaluate the prevalence of strabismus in Neurofibromatosis type 1(NF-1) by comparing children with normal neuroimaging to those with optic pathway glioma. A retrospective data collection of all children with NF-1 with neuroimaging studies examined at a single medical center between 2000 and 2016. Of the 198 children with NF-1 reviewed, 109 (55%) were male, 121 (61%) had normal neuroimaging, and 77 (39%) had an optic pathway glioma. Mean age at presentation was 6.3 ± 4.7 years and mean follow-up was 4.8 ± 3.1 years. Strabismus was present in 29 (15%) children and was significantly more prevalent in children with NF-1 with optic pathway glioma (21 of 77 [27%]) than in those with normal neuroimaging (8 of 121 [7%], $P < .001$). Sensory strabismus was only found in children with optic pathway glioma, accounting for most cases (12 of 21 [57%]). A strong association between strabismus and optic pathway glioma is demonstrated by an odds ratio of 5.29 ($P < .001$). Children with NF-1 with optic pathway glioma have a 4.13 times higher relative risk of developing strabismus than children with NF-1 without it ($P = .001$). The direction of ocular misalignment in children with NF-1 with optic pathway glioma was not significantly different than that observed in children without optic pathway glioma ($P = .197$, Fisher's exact test). Only 5 (17%) children with NF-1 with strabismus (3 with optic pathway glioma) underwent corrective surgery to align their eyes. The authors concluded that optic pathway glioma in children with NF-1 is associated with an increased risk of strabismus, especially sensory strabismus. Although exotropia is the most common ocular misalignment associated with optic pathway glioma, the direction of strabismus cannot be used as an accurate predictor for the presence of optic pathway glioma. Many children with NF-1 with strabismus do not undergo corrective surgery. This study's results should be interpreted within the context of its limitations. Because data were collected retrospectively based on chart reviews, it is subject to variability depending on the accuracy and completeness of records. Furthermore, because all children with NF-1 included were examined in a tertiary referral medical center, they may not accurately represent the entire pediatric population of patients with NF-1.

Optic Nerve Head Drusen: An Update

Edward Palmera, Jesse Gale, Jonathan G. Crowstond, and Anthony P. Wellsa,

Neuroophth Dec 2018, 42(6), 367–384

Optic nerve head drusen are benign acellular calcium concretions that usually form early in life, just anterior to the lamina cribrosa. Improving imaging using optical coherence tomography suggests they are common and may be present in many clinically normal discs. These drusen may change in appearance in early life, but are generally stable in adulthood, and may be associated with visual field defects, anterior ischemic optic neuropathy, or rarer complications. Based on long-term clinical data and optical coherence tomography, we propose a refined hypothesis as to the cause of optic disc drusen. Here we summarize recent findings and suggest future studies to better understand the forces involved.

Visual outcomes after chemotherapy for optic pathway glioma in children with and without neurofibromatosis type 1: results of the International Society of Paediatric Oncology (SIOP) Low-Grade Glioma 2004 trial UK cohort

Falzon K, Drimtzias E, Picton S, Simmons I. *Br J* Ophthalmol. October 2018;102:1367-1371.

Although survival rates are good, children with optic pathway gliomas (OPG) can experience significant visual impairment. Management decisions are sometimes difficult due to the variable natural history of these tumors. This study aimed to report visual outcomes following chemotherapy for OPG in children with or without neurofibromatosis type 1 (NF1). The authors performed a prospective, multicenter study between 2004 and 2012. 90 children (180 eyes) with complete follow-up and visual acuity outcomes were included. 46 children had NF1 associated OPG and 44 had sporadic OPG. Visual acuity loss was the most frequent indication to initiate therapy in both groups. Average follow-up was 6.5 years. At the start of chemotherapy, 26% and 49% of eyes in NF1 and sporadic groups respectively had VA >= 0.7 logMAR. At completion, in the NF1 group 49% had acuity <=0.2, 23% 0.3-0.6, and 28% had VA>= 0.7 logMAR. In the sporadic group, 32% had <=0.2, 11% 0.3-0.6, and 57% had VA >= 0.7 logMAR. Children with sporadic OPG were significantly less likely to have visual outcomes <= 0.6 logMAR compared to the NF1 group. Overall the two groups had about the same rate of visual acuity improvement, stabilization, or worsening, but the children with sporadic OPG had a poorer visual outcome. Better initial visual acuity, increasing age, absence of post-chiasm tumor, and presence of NF1 were associated with better visual acuity outcomes. Overall timely treatment arrested the decline in VA in most children and some children regained vision.

Ocular Neuromyotonia: Case Reports and Literature Review.

Stockman AC, Cassiman C, Dieltiëns M, Janssens H, et al. *Strabismus*. 2018 Sep;26(3):133-141.

Ocular neuromyotonia is a rare disorder cause by contraction of an extraocular muscle by a damaged nerve leading to delayed muscle relaxation. The authors present 8 patients and review the literature, as well as present an alternative association with low Vitamin D levels. Of the 49 cases in the literature, the patients had an average age of 46 years (range 7-77 years) and were predominantly female (75%). The most commonly affected nerve was CN 6 (65.3%). The majority of cases were associated with oncological radiation (80%), presenting anywhere from 2 months to 18 years after treatment. In one of the authors' cases, the ONM complaints disappeared after supplementation with vitamins B12 and D, which suggests that neural conduction along the myelin sheath that results from hypovitaminosis may a possible mechanism. Of the published cases in the literature, 23 of 49 were treated with carbamazepine with an 87.8% success rate. The authors suggest that in the absence of a history of cranial radiation, a neurological cause or thyroid dysfunction should be considered in the workup and that carbamazepine is an effective treatment.

Gene therapy in optic nerve disease

Adam DeBusk and Mark L. Moster *Curr Opin Ophthalmol* 2018, 29: 234-238 (May 2018)

The authors review current gene therapy trials for Leber's Hereditary Optic Neuropathy as well as other possible modalities for gene therapy. LHON is caused by a point mutation in mitochondrial DNA with 3 common mutations. The 11778 mutation has been the primary focus as it is the most common and the lowest likelihood of spontaneous visual recovery. Adeno-associated viruses type 2 (AAV2) are the vector utilized because of their high efficiency and safety of transduction to inner retinal layers after intravitreal injection. In addition, they have a low risk of tumor formation. Patients (9 eyes) were recruited and given a single dose. No ocular or systemic adverse events were identified as well as no decrease in vision below baseline. However, results showed that there was regression after improvement in the subjects which suggests that gene expression may reduce over time. There are other targets for gene therapy which may help in nerve regeneration such as the mammalian target for rapamycin (mTOR), Rho/Rho associated coiled containing kinase (ROCK), Neuroglobin (Ngb) and the Kruppel-like factor family. The authors summarize that gene therapy is promising. However, in order to be viable the gene expression must persist long enough to have a therapeutic effect, and not succumb to regression. In genetic disorders, the expression would need to have long-term expression. The axons need to be able to take the correct pathway to target neurons in the brain and also because some of these targets are oncogenes and tumor suppressor genes the risk of tumor formation must be addressed.

Retinal and optic nerve changes in microcephaly: An optical coherence tomography study

Eleni Papageorgiou, Anastasia Pilat, Frank Proudlock, Helena Lee, et al. *Neurology*. Aug 7 2018;91:e571-e585.

In this case-controlled prospective study, the authors seek to characterize the optic disc and retinal morphology in 27 patients with microcephaly using hand held OCT. The hypothesis is that given the relationship between ocular and brain development, there may be abnormalities in ocular development in the setting of microcephaly. With respect to the retina, 85% of patients had abnormalities on OCT, 70% with abnormalities of the fovea, and 15% with abnormalities of the retinal periphery. Findings included abnormal foveae, disruption of the ellipsoid zone, and parafoveal thinning. These findings were detectable on funduscopy in only 1/3 of patients. With respect to the optic nerve, 4 patients were noted to have optic nerve hypoplasia both by funduscopy and by OCT. rNFL thinning was also noted. The study highlights the use of OCT to identify ophthalmic changes which may not be readily detectable on clinical exam in patients with microcephaly. However the etiologies which contributed to microcephaly in these patients were heterogeneous and therefore the utility of applying these OCT findings in differentiating amongst different causes of microcephaly appears to be limited.

Handheld Spectral Domain Optical Coherence Tomography Imaging Through the Undilated Pupil in Infants Born Preterm or with Hypoxic Injury or Hydrocephalus

Tran-Viet D, Wong BM, Mangalesh S, et al. *Retina* August 2018; 38:1588-1594.

This pilot study investigated the feasibility of undilated SD-OCT imaging of the retina, choroid, and optic nerve in preterm infants and children with neurologic abnormalities. Images were obtained through an undilated pupil of 11 infants/children over 28 imaging sessions, 27 at the bedside without sedation and one under anesthesia. The infants had ROP (n=8), hypoxic ischemic encephalopathy (n=2), or obstructive hydrocephalus (n=1). Pupil sizes ranged from 1.0 to 3.5 mm. The authors captured fovea and optic nerve scans in 25/28 imaging sessions, with scans of adequate quality to discern prespecified foveal and optic nerve morphology. The choroidal-scleral junction was visible in all but 6 of the 25 sessions. In this study, a highly skilled imager was required to align the handheld imaging system and capture the key structural retinal features through small pupils. Lighter, more compact, and higher speed handheld OCT technology would address this major limitation and hopefully advance the ability to monitor ophthalmic and neurologic microstructural abnormalities, reflecting injury and response to injury in the CNS, in infants with pharmacologically undilated pupils.

Natural history of primary paediatric optic nerve sheath meningioma: case series and review

Narayan D, Traber G, Figueira E, Pirbhai A, et al. *Br J* Ophthalmol. August 2018;102:1147-1153

Optic nerve sheath meningioma (ONSM) is a rare tumor of the optic nerve that is particularly associated with Neurofibromatosis type 2 (NF2). Treatment in the past was commonly surgical resection, but fractionated radiation is more commonly used today. The authors of this paper performed a retrospective case series of 8 patients with ONSM from 1994-2016 in Switzerland and Australia. There were 6 female and 2 male patients, with mean age of 11. One patient had bilateral tumors. Decrease visual acuity was the most common presenting complaint. 3/9 had acuity less than 20/200. 6/9 had eye movement limitations and 4/9 had proptosis. 2/8 patients had NF2. 6 of the patients were observed while the other 2 received radiotherapy. Two of the observation patients, both presenting with good initial acuity, did not experience tumor growth after long-term follow-up. The other 4 that were observed experienced deterioration of vision. The authors conclude that it is possible that some cases may be observed, but generalized conclusions cannot be made from this small case series.

Acquired Intermittent Pediatric Horner Syndrome due to Neuroblastoma

Cohen LM, Elliott A, Freitag SK *Ophthal Plast Reconstr Surg.* 2018;34(2):e38-e41

This is a case report which involves a 3-month-old male who developed intermittent left upper eyelid ptosis at the age of 1 month that was gradually increasing in frequency and duration. Examination revealed anisocoria and left upper and lower eyelid ptosis, consistent with a left Horner syndrome. Imaging showed a mass in the left superior posterior mediastinum, which was resected, and pathology was consistent with neuroblastoma. Eight months thereafter, the patient underwent left upper eyelid ptosis repair. Cases of infantile acquired Horner syndrome due to neuroblastoma are rare. To the authors' knowledge, there has only been one case described that presented with intermittent symptoms. The authors report the second case of intermittent acquired Horner syndrome due to neuroblastoma. This case demonstrates the importance of recognizing that Horner syndrome may present with subtle and intermittent symptoms. In a pediatric patient, one should maintain suspicion for neuroblastoma.

Idiopathic Intracranial Hypertension

Perimetry

Optic Nerve Imaging

Retinal and optic nerve changes in microcephaly: An optical coherence tomography study

Eleni Papageorgiou, Anastasia Pilat, Frank Proudlock, Helena Lee, et al. *Neurology* August 2018;91:e571-e585

This was a prospective case-control study to investigate the morphology of the retina and optic nerve (ON) in microcephaly. The study included 27 patients with microcephaly and 27 healthy controls. All participants underwent ophthalmologic examination and handheld optical coherence tomography (OCT) of the macula and ON head. The thickness of individual retinal layers was quantified at the foveal center and the parafovea (1,000 μm nasal and temporal to the fovea). For the ON head, disc diameter, cup diameter, cup-to-disc ratio, cup depth, horizontal rim diameter, rim area, peripapillary retinal thickness, and retinal nerve fiber layer thickness were measured.

Results showed seventy-eight percent of patients had ophthalmologic abnormalities, mainly nystagmus (56%) and strabismus (52%). OCT abnormalities were found in 85% of patients. OCT revealed disruption of the ellipsoid zone, persistent inner retinal layers, and irregular foveal pits. Parafoveal retinal thickness was significantly reduced in patients with microcephaly compared to controls, nasally (307 ± 44 vs 342 ± 19 μm, $p = 0.001$) and temporally (279 ± 56 vs 325 ± 16 μm, $p < 0.001$). There was thinning of the ganglion cell layer and the inner segments of the photoreceptors in microcephaly. Total peripapillary retinal thickness was smaller in patients with microcephaly compared to controls for both temporal (275 vs 318 μm, $p < 0.001$) and nasal sides (239 vs 268 μm, $p = 0.013$). The authors conclude that retinal and ON anomalies in microcephaly likely reflect retinal cell reduction and lamination alteration due to impaired neurogenic mitosis. OCT allows diagnosis and quantification of retinal and ON changes in microcephaly even if they are not detected on ophthalmoscopy

Myasthenia Gravis

Incidence and Ocular Features of Pediatric Myasthenias

Mansukhani SA A, Bothun ED, Diehl NN, et al. *Am J Ophthalmol.* 2019 April; 200: 242-249.

The authors of this study used a retrospective cohort analysis to report the incidence, demographics, and ocular findings of children with ocular myasthenia. They reviewed the medical records of all children at one academic institution under the age of 19 over a 50 year period. A total of 364 children were

evaluated and of those 60% had Juvenile myasthenia gravis (JMG), 38% had congenital myasthenia syndrome (CMS) and 2% had Lambert-Eaton syndrome. The median age of diagnosis was 13.5, 5.1, and 12.6 years respectively. The median time to diagnosis was 5 months. The authors calculated the incidence of ocular myasthenia using the information from the Rochester Epidemiology project as 0.35 per 100 000 under 19 years old. Most JMG and CMS had ocular involvement and of those children with at least a year of follow up, most improved and complete remission was achieved in about a third of children with JMG. The authors concluded that MG in children is exceedingly rare, has two major forms (both of which are likely to cause ocular involvement), and that improvement is more common in the juvenile form. The limitations of this study included those related to retrospective studies. Additionally, since the definition of myasthenia gravis has changed over the last 50 years, the authors were applying newer definitions to patients from years ago, which may have underestimated the rate of disease. Additionally, serology was not available on all children. Overall this paper contributes new information about the ocular involvement in pediatric myasthenia and provides a nice summary of myasthenia gravis in children.

Ocular Myasthenia gravis: an update on diagnosis and treatment

Elizabeth Fortin, Dean M. Cestari, and David H. Weinberg *Curr Opin Ophthalmol* 2018, 29: 477-484 (Nov 2018)

Ocular myasthenia gravis (OMG) typically presents with pupil sparing ptosis and/or diplopia. It can be challenging to make the diagnosis because OMG can overlap with other efferent ophthalmic conditions and it has a lower rate of seropositivity to AChR antibodies compared with the systemic form. Variability in ophthalmoplegia, Cogan's lid twitch to induce ptosis, and assessment of orbicularis function are some ways to clinically elucidate the diagnosis. Nonpharmacologic testing includes the ice and rest tests. Edrophonium can be used in the clinic and has a sensitivity of 88-97% in the detection of OMG. Serologic testing can include AChR antibodies although they are only present in about half of the patients with OMG. LDL-related receptor-related protein 4 antibodies are found in 1-5% of all patients with MG and patients with positivity tend to have a milder course. Muscle-specific tyrosine kinase antibodies are present in 1-10% of patients and are more prevalent in women. Anti-MuSK positive patients have similar incidence of ophthalmic findings as those with AChR-positive antibodies but the ocular symptoms tend to be milder. 10% of patients with MG will be seronegative for all 3 antibodies. Single fiber EMG is the most useful test for patients with OMG especially when seronegative. Sensitivity for OMG is 80% and is usually performed on the orbicularis. It can also predict the severity of the disease. CT or MRI of chest should be done in all patients to assess for thymoma. In addition, 15% of patients diagnosed with MG will have another autoimmune disorder, most commonly thyroid disease, followed by SLE and RA. It is more common in patients with early onset disease and thymic hypoplasia. Treatment is commonly with pyridostigmine and in OMG ptosis improves more than motility

deficits. Immunosuppressive agents such as prednisone may help to reduce symptoms and in some studies treatment of OMG early on may reduce generalization of the disorder. Azathioprine is most frequently used as an SSA in OMG. Mycophenolate mofetil can be used as an adjunct to steroids in the treatment of OMG. Thymectomy has not been recommended in OMG without thymoma as it has not been shown to prevent generalization or improvement of disease.
The article reviews the diagnostic criteria for OMG and the treatment modalities available.

Optic Neuritis

Validation of a symptom-based questionnaire for pediatric CNS demyelinating diseases.

Waldman AT, Yeshokumar AK, Lavery A, Liu G, et al. *JAAPOS* 2019 June; 23 (3): 157.e1-157.e7

Optic neuritis is a manifestation of numerous neuroinflammatory disorders. Recognition of current and prior symptoms may facilitate identification of an underlying multifocal neurologic disease. The purpose of this study was to determine whether a symptom-based questionnaire could inform clinical decision making by identifying children with visual complaints who may have a systemic demyelinating disorder. Children with visual changes from non-demyelinating disease were compared with patients with confirmed pediatric-onset multiple sclerosis (MS) or neuromyelitis optica spectrum disorder (NMOSD). Participants completed a 21-item questionnaire to capture their recent (<30 days) and remote (>30 days) symptoms of neurologic dysfunction. The questionnaire scores were compared using t tests, and the 95% confidence interval for each group was used to determine a threshold score suggesting demyelinating disease. A total of 51 participants were enrolled (30 females [59%]) with a mean age of 14.6 years (range, 4-21): 25 in the non-demyelinating disease group and 26 with MS/NMOSD. The mean questionnaire score for the non-demyelinating group was 5.0 points (95% CI, 3.3-6.9); for the MS/NMOSD group, 9.4 points (95% CI, 7.4-11.4) for the MS/NMOSD group (P<0.002). Questionnaire results were dichotomized using a score of ≥7 as indicative of demyelinating disease, with 69% sensitivity and 72% specificity. An abbreviated questionnaire, using 8 questions that differed between groups, had a sensitivity of 65% and specificity of 92%. The authors conclude that a symptom-based questionnaire is sensitive and specific for identifying children with CNS demyelinating disease and may be useful as a screening tool for children with vision complaints and possible demyelination. Further studies are likely warranted to establish the value of this questionnaire in newly diagnosed patients with demyelinating disorders.

Optical coherence tomography is highly sensitive in detecting prior optic neuritis.

Xu SC, Kardon RH, Leavitt JA, Flanagan EP, et al. *Neurology*. Feb 2019;92(6):e527-e535.

In this retrospective study, the authors examined the use of OCT to detect episodes of prior optic neuritis in a cohort of 51 patients. The goal of the study was to evaluate whether OCT was an effective tool for detecting a prior episode of optic neuritis in patients with unilateral optic neuritis. By utilizing interocular differences as measured with OCT, the authors determined that an interocular difference of ≥9 µm for rNFL or ≥6 µm for GCIPL were reflective of prior optic neuritis. The reduction in GCIPL was a more sensitive measure (76% for GCIPL and 37% for RNFL) to reflect prior optic neuritis as compared to age matched controls. This study defines thresholds for interocular differences which may provide a quantitative way of detecting prior optic neuritis and establishes which measure of OCT is most effective in screening when the history is unknown.

Pediatric Optic Neuritis

Sharon S. Lehman and Judith B. Lavrich *Curr Opin Ophthalmol* 2018 29: 419-422 (Sept 2018)

The authors review the challenges faced by clinicians in the diagnosis and management of pediatric optic neuritis. Most treatment has been guided by adult studies that have been performed. However, the clinical presentation differs in children including bilateral optic nerve swelling, preceding viral illness and more significant visual deficit. On OCT evaluation the nerve fiber layer and ganglion cell layer are reduced in thickness. Using OCT, VEP and serologic testing for myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) is associated with demyelinating diseases other than MS in adults and children. Aquaporin 4 (AQP4-IgG or NMO-IgG) is specific for NMO. The serologic markers may delineate which patients will have more relapses and greater disability. In children with NMO aggressive therapy is necessary to prevent damaging relapses as these patients have a higher risk of disability. The paper highlights the challenges and the possible diagnostic and treatment tools that may be important in the future although prospective studies are warranted.

6. NYSTAGMUS

Clinical evaluation of graded Anderson's procedure in idiopathic infantile nystagmus.

Ganesh SC, Rao SG, Narendran K. *Strabismus*. 2019 Jun 20:1-4.

The authors investigate the effect of a graded recession of yoke muscles in patients with idiopathic infantile nystagmus based on the initial head turn. They included 37 patients (26 males) with a mean age of 12.3±8.64 years. All patients improved after surgery, with a mean decrease in the head turn from 22.5 degrees to 7.48 degrees ath the post-operative month 1 visit. The binocular visual acuity

improved and all patients were orthotropic in primary gaze. The authors conclude that this modification is useful particularly in moderate head turns and overall is helpful as it involves fewer operated muscles, only has recessions and can be revised.

Reading Individual Words Within Sentences in Infantile Nystagmus

Esha Prakash, Rebecca J. McLean, Sarah J. White, Kevin B. Paterson, et al *Invest Ophthalmol Vis Sci*. May 2019;60:2226–2236.

This study evaluated eye movements for both patients with Infantile Nystagmus and controls while reading. The goals were to evaluate if patients with IN could increase the duration and number of first pass foveations which would lead to overall faster reading. Participants were both age and IQ matched. While control participants had significantly increased gaze duration for uncommon words, this lead to decreasing the overall reading time as they had a decrease number of second pass foveations, and similar gaze and nongaze durations and for common and uncommon words. Patients with IN had increased acquisition times, gaze, and nongaze durations for uncommon words, as well as increased second pass foveations for smaller words. This study demonstrated that patients with IN had significantly decreased reading speeds due to increased first-pass foveations on both uncommon and long words. The findings of this study should be discussed with all parents of patients with IN. If accommodations are available for increased time for patients with IN, it may be appropriate to afford them of these accommodation

Longitudinal Studies and Eye-Movement-Based Treatments of Infantile Nystagmus Syndrome: Estimated and Measured Therapeutic Improvements in Three Complex Cases

Louis F. Dell'Osso, Faruk H. Orge, Jonathan B. Jacobs & Zhong I. Wang
Journal of Binocular Vision and Ocular Motility, 2018; 68:4, 122-133

Infantile Nystagmus Syndrome (INS) is difficult to accurately differentiate from fusion maldevelopment nystagmus syndrome clinically. Eye-movement date analysis can help distinguish the two, it can also accurately determine the angle of the null point for surgical correction, differentiate good versus poor foveation, estimate therapeutic improvements, and document improvements after surgery. The authors assessed 3 patients before and after Kestenbaum procedures using the EyeLink II system for eye movement. The authors found that the eye-movement data provided definitive diagnoses, quantified the nystagmus signal and allowed for estimation of the potential therapeutic improvements along with objective measurements of the post-therapy improvements.

Long-Term Follow-up of Spasmus Nutans

Rupin N. Parikh, John W. Simon, Jitka L. Zobal-Ratner & Gerard P. Barry
Journal of Binocular Vision and Ocular Motility, 2018; 68:4, 137-139

Spasmus nutans is an acquired asymmetric, fine amplitude, high frequency nystagmus commonly accompanied by head bobbing and torticollis. The majority of cases present within the first year of life with spontaneous resolution by 4 years of age. Rarely spasmus nutans is associated with CNS lesions and patients commonly undergo neuro-imaging. Twenty-two patients with spasmus nutans were included in the study with an equal number of females and males. The series investigated the evolution of clinical findings. The authors found that the nystagmus associated with spasmus nutans does not resolve as quickly as reported in the literature. The authors only encountered the classic triad in 4 of the 22 patients. There was an association with developmental abnormalities and Down syndrome with spasmus nutans. Strabismus occurred in 64% of patients in this study, which has not been defined as a classic characteristic. Despite finding zero incidence of a space occupying lesion on neuro-imaging the authors still recommend scanning all patients with spasmus nutans.

Visual functioning in adults with Idiopathic Infantile Nystagmus Syndrome (IINS).

Das A, Quartilho A, Xing W, Bunce C, Rubin G, MacKenzie K, Adams G, Dahlmann-Noor A, Theodorou M. *Strabismus*. 2018 Dec;26(4):203-209.

The NEI Visual Function Questionnaire (VFQ-25) has been validated to assess the quality of life for many different ophthalmic conditions. In this manuscript, the authors investigate the impact of infantile nystagmus syndrome (INS) on the quality of life in adults using the VFQ-25. Of the 38 patients recruited, 35 completed the questionnaire. The overall scores were lower than the “normal” score. There was no association of the scores with the level of near or distance visual acuity and the scores for near and distance activities did not differ significantly. The effect of nystagmus on quality of life was similar or worse than other diseases affecting vision, including AMD, diabetes and optic neuritis. The authors postulate that although participants reported reasonable social functioning scores, the substantial effect of IINS in this study was on mental health, role difficulties, and well-being, to a greater extent than would be expected from the documented level of visual acuity.

The role of Superior oblique Posterior Tenectomy Along With Inferior rectus recessions for the Treatment of Chin-up Head Positioning in Patients With Nystagmus.

Ann G.Escuder, Milan P.Ranka, Kathy Lee, Julie N.Nam et al *J of Ped Ophth & Strabismus*.2018; 55(4): 234-239

The purpose of this retrospective study is to evaluate the clinical outcomes of bilateral superior oblique posterior 7/8th tenectomy with inferior rectus recession on improving chin-up head positioning in patients with horizontal nystagmus. The medical records were reviewed from 2007 to 2017 for patients with nystagmus

and chin-up positioning of 15° or more who underwent combined bilateral superior oblique posterior 7/8th tenectomy with an inferior rectus recession of at least 5 mm. Thirteen patients (9 males and 4 females) were included, with an average age of 7.3 years (range: 1.8 to 15 years). Chin-up positioning ranged from 15° to 45° degrees (average: 30°). Three patients had prior horizontal muscle surgeries, 1 for esotropia and 2 for horizontal null zones causing anomalous face turns. Ten patients underwent other concomitant eye muscle surgery: 3 had esotropia, 1 had exotropia, and 2 had biplanar nystagmus null point requiring a horizontal Anderson procedure. Four patients underwent simultaneous bilateral medial rectus tenotomy and reattachment. All patients had improved chin-up positioning. Eight patients had complete resolution, whereas 5 had minimal residual chin-up positioning. Three patients developed an eccentric horizontal gaze null point with compensatory anomalous face turn with onset 2 weeks, 2 years, and 3 years postoperatively. Average follow-up was 42.7 months. No postoperative pattern deviations, cyclodeviations, or inferior oblique overaction were seen. No surgical complications were noted. The authors conclude that bilateral superior oblique posterior 7/8th tenectomy in conjunction with bilateral inferior rectus recession is a safe and effective procedure for improving chin-up head positioning in patients with horizontal nystagmus with a down gaze null point. The study limitations include being a retrospective study without a comparative surgical group. Furthermore torsion was assess only by fundoscopic examination.

Characteristics and Long-term follow-up of Isolated Vertical Nystagmus in Infancy.

Imran Jivraj, Shannon J.Beres, Grant T.Liu *J of Ped Ophth & Strabismus*.2018; 55(3): 159-163

The purpose of this study is to determine the clinical characteristics and long-term outcomes of infants who presented with isolated vertical nystagmus. The medical records of 114 infants who were diagnosed as having nystagmus from 1996 to 2016 were screened. Patients with vertical nystagmus within the first year of life who had unremarkable magnetic resonance imaging of the brain and demonstrated age-appropriate visual behavior were included. The parents of the patients in the final study cohort were contacted by telephone to obtain long-term follow-up information. Eight patients comprised the final cohort. Vertical nystagmus was first observed at a mean age of 1.4 months (range: 1 to 2.5 months) and resolved in 87.5% of patients at a mean age of 3.8 months (range: 2 to 10 months). Vertical nystagmus was intermittent in 62.5%, upbeat in 62.5%, and pendular in 37.5% of patients. One patient's nystagmus did not resolve. Seventy-five percent of patient guardians participated in the telephone questionnaire. The mean age of patients at follow-up was 3.5 years (range: 0.5 to 8.1 years). Isolated iris transillumination was discovered in one patient without other features of albinism. Fifty percent of patients had speech delay requiring intervention. No other developmental delays or general medical conditions were identified. In a cohort of otherwise neurologically intact male infants with vertical nystagmus but

age-appropriate visual behavior and unremarkable neuroimaging studies, the authors found a high rate of resolution of nystagmus within the first year of life. There was no emergence of significant ophthalmic or neurologic impairment; however, speech delay was noted in half of the patients who could be reached for follow-up. Further studies that perform longitudinal ophthalmic and neurological assessments will be required to confirm these initial findings.
The current retrospective study has several limitations. Clinical observation of age-appropriate fixation behavior and structural ophthalmic examinations were demonstrated in all patients and excluded significant retinal or optic nerve pathology; therefore, further testing with ERG was not performed universally. Cases of mildly impaired visual acuity from subtle macular or optic nerve pathology that may have been identified with optical coherence tomographic imaging of the retina or optic nerve could have been missed.[8]Although the presence of neurological signs and symptoms was elicited during the neuro-ophthalmologist's history and clinical examination, formal neurological examinations were not performed. All patients received an MRI of the brain, but an EEG was not performed universally.

Simulation of Oscillopsia in Virtual Reality

Randall, D., et al. *Br Ir Orthopt J* 2018; 14(1): 45-49

Patients with acquired nystagmus commonly have oscillopsia, which can be debilitating for them. The patients with oscillopsia can have associated nausea, vertigo, and loss of balance. Patients feel isolated and neglected. The aim of the study was to create a virtual reality (VR) simulation of oscillopsia to aid in communication with others what a patient with oscillopsia perceives. Eye tracking hardware was used to record different nystagmus eye movements which were then applied to a virtual reality app for smartphones. Users with nystagmus or oscillopsia can then utilize the app to understand and appreciate what others experience day to day. The apps purpose is to raise awareness and aid in communication.

7. PREMATURITY.

Ophthalmic Features of Premature Infants

Comparison of optic disk features in preterm and term infants.

Kuruvilla SE, Simkin S, Welch S, Dai S. *J AAPOS*. Oct 2018; 22(5): 376-380.e372.

The purpose of this retrospective study was to compare the optic disk features of preterm and term infants. Digital fundus images of preterm infants were compared with those of infants born at term, imaged within 1 week of birth. The optic disk horizontal diameter to vertical diameter ratio, the disk-macula to disk-diameter ratio, and the presence or absence of double ring sign was noted. Images of

649 infants (324 preterm and 325 term) were analyzed. Of the preterm infants, 129 (40%) had a complete double ring sign, compared to 4% in term infants. The double ring was seen more frequently in infants of European descent and was more common with younger gestational age. The mean horizontal to vertical disk diameter in preterm infants on first examination was 0.75 ± 0.063, increasing to 0.80 ± 0.069 at final examination. Term infants had a horizontal to vertical disk diameter ratio of 0.79 ± 0.064. At final examination, the ratio of disk-to-macula distance to the horizontal disk diameter was 3.9 in preterm infants and 3.7 for term infants. This cohort of preterm infants often had a double ring sign around the optic disk in the absence of optic nerve hypoplasia. Preterm disks tend to be more vertically oval, and become less oval closer to term. The mean disk-to-macula to disk-diameter ratio among normal preterm infants was higher than previously reported. Despite its retrospective nature this large-sample study highlights that the mere presence of a double ring does not warrant further investigation in preterm infants unless other features of optic nerve hypoplasia are present.

Visual Function and Fundus Morphology in Relation to Growth and Cardiovascular Status in 10-Year-Old Moderate-to-Late Preterm Children

Lind A, Dahlgren J, Raffa L, et al *Am J Ophthalmol.* 2018 November; 195: 121-130.

This prospective cohort study from Sweden examined 33 (10 girls) former moderate-to-late preterm (MLP) children at the age of 10 and compared them to 28 age- and sex- matched controls. The goal was to evaluate for any differences visual function and fundus morphology between these groups in relation to growth, metabolic status, and blood pressure. The authors found that the former MLP children were more likely to have myopia, smaller optic disc area, smaller rim area, fewer branching points, and higher index of tortuosity of the retinal vasculature than their full term counterparts. There was some association of refraction and arteriole tortuosity with IGF-1 levels and of letpin/adiponectin ratio to tortuosity of the veins. The authors concluded that MLP is associated with changes in refraction and fundus structure. The authors point out the main limitations of small sample size and high patient drop out rate. This paper is a reminder that MLP children can also have ocular complications and should be counseled about these risks.

Relationship between Retinal Thickness Profiles and Visual Outcomes in Young Adults Born Extremely Preterm: The EPICure@19 Study.

Balasubramanian S, Beckmann J, Mehta H, Sadda SR, et al*. Ophthalmology.* 2019 Jan;126(1):107-112.

Children born preterm are at increased risk of developing a range of ocular and vision disorders later in life. It is known that foveal reflex is reduced in premature

infants and that several spectral-domain (SD) studies have shown abnormal foveal contour, absence of foveal depression and retention of inner retinal layers at the foveal center and macular edema. This is the first study correlating the retinal findings to visual function in adults born extreme preterm (EP), before 26 weeks of gestation. All data for this study was obtained from EPICure study, large well-characterized study on young adults born before 26 weeks of gestation, as part of a long-term follow-up study called the EPICure@19 study. Extreme preterm participants were aged 18 to 20 years and a full-term born age-matched comparison group was recruited for assessment. A total of 354 eyes (226 eyes of former EP infants and 128 age-matched full-term control eyes) from 177 young adults were evaluated. Among EP participants, 50% of eyes (112/226) were not previously diagnosed with retinopathy of prematurity (ROP), 38% of eyes (84) had ROP not deemed to require treatment in the neonatal period, and 13% of eyes (30) had neonatal cryotherapy or laser ablation for ROP. Subjects underwent eye examinations including best-corrected visual acuity (BCVA) and Heidelberg Spectralis macular SD OCT imaging. Retinal layers were auto-segmented and thickness profiles were computed at the fovea by the instrument software. Compared with control eyes, the inner and outer retinal layers of EP eyes were significantly thicker and BCVA was significantly reduced. Retinal layer thicknesses and BCVA were similar for untreated EP eyes and those without neonatal ROP. In contrast, treated eyes had increased inner and outer retinal layer thickness and decreased vision. Inner retinal layer thickness was moderately correlated with worse BCVA ($r = 0.30$, $P < 0.001$), but outer retinal layer thickness was not ($r = -0.01$, $P = 0.80$). Multivariate regression indicated ganglion cell layer thickness was a significant independent predictor of BCVA. Extremely premature birth influences maturation of the fovea and visual outcomes into early adult life. Increased ganglion cell layer thickness was associated with worse BCVA. Eyes requiring neonatal treatment for ROP had associated worse BCVA at the age of 19 years. Of note, it is interesting that these EPs when compared to full-term controls did not have a significant difference in refractive error.

Visual and Hearing Impairments After Preterm Birth

Mikko Hirvonen, Riitta Ojala, Paivi Korhonen, et al. *Pediatrics* August 2018; 142 (2) e:20173888

Pre-term birth is associated with significant hearing loss and visual impairment. The aim of the study was to determine the incidence of sensory impairments in a large national birth cohort and to establish prenatal and neonatal risk factors predictive of these disabilities. The authors used the medical birth registry in Finland between 1991 and 2008 which contains information about the gestational age (GA) of the baby at birth as well as weight. The children were divided into 3 GA subgroups: 1) VP which is less that 32 wks gestation; 2) MP which is 32 through 33 wks gestation; 3) LP 34 wks up to 37 wks gestation and 4) term which is 37

wks or greater of gestational age. Diagnoses of sensory disturbances were obtained through ICD coding in the hospital discharge register and Social Insurance Institution. The incidence of sensory impairments decreased with advancing GA at birth ($p<0.001$). The most prominent risk factors for impairment were intracranial hemorrhage and convulsions. VP and LP were associated with increased risk of hearing loss, while VP (OR = 1.94), MP (OR=1.42), and LP (OR = 1.31) predicted an increased risk of visual impairment. Other factors associated with visual impairment included maternal smoking and mother being over the age of 40. Strabismus and refractive disorders decreased with increasing GA at birth. The strength of the study derives from the large study population, duration of the study period, quality of data reported in the Finish medical system, and the ability to link different databases within the national medical system. Weaknesses of the study include the unknown number of undiagnosed disabilities, accuracy of the coding, and the time delay between the registry data and the publication of the study. Overall, the study provides valuable predictive information for medical providers and families with pre-term babies and suggests that physicians should have a low threshold to refer children born prematurely to evaluate for sensory disabilities.

Handheld Spectral Domain Optical Coherence Tomography Imaging Through the Undilated Pupil in Infants Born Preterm or with Hypoxic Injury or Hydrocephalus

Tran-Viet D, Wong BM, Mangalesh S, et al. *Retina* August 2018; 38:1588-1594.

This pilot study investigated the feasibility of undilated SD-OCT imaging of the retina, choroid, and optic nerve in preterm infants and children with neurologic abnormalities. Images were obtained through an undilated pupil of 11 infants/children over 28 imaging sessions, 27 at the bedside without sedation and one under anesthesia. The infants had ROP (n=8), hypoxic ischemic encephalopathy (n=2), or obstructive hydrocephalus (n=1). Pupil sizes ranged from 1.0 to 3.5 mm. The authors captured fovea and optic nerve scans in 25/28 imaging sessions, with scans of adequate quality to discern prespecified foveal and optic nerve morphology. The choroidal-scleral junction was visible in all but 6 of the 25 sessions. In this study, a highly skilled imager was required to align the handheld imaging system and capture the key structural retinal features through small pupils. Lighter, more compact, and higher speed handheld OCT technology would address this major limitation and hopefully advance the ability to monitor ophthalmic and neurologic microstructural abnormalities, reflecting injury and response to injury in the CNS, in infants with pharmacologically undilated pupils.

Vision in former very low birthweight young adults with and without retinopathy of prematurity compared with term born controls: the NZ 1986 VLBW follow-up study

Darlow B, Elder M, Kimber B, Martin J, et al. *Br J* Ophthalmol. August 2018;102:1041-1046

Little comprehensive data exists on visual outcomes in adult former very preterm or very low birthweight (VLBW) infants. This study looked at visual outcomes of VLBW infants born in 1986 in New Zealand, before ROP treatment was available, and compared them with healthy term born controls. 229 patients (ages 27-29 years) were assessed over a 2 day period along with 100 controls. Data included visual acuity, glasses prescriptions, contrast sensitivity, autorefraction, retinal photographs, and a questionnaire of vision-related activities. 45 of the patients had a history of ROP, and these subjects had a reduced visual acuity compared to both those without ROP and controls. There were no significant differences in myopia except for cases of high myopia (>5D) which was heavily weight towards those with history of ROP or <1000g birth weight. Results were compared to data collected when the patients were 7-8 years old and found the rates of poor visual acuity were stable. Also the rates of mild myopia increased regardless of whether there was a history of ROP. The VLBW cohort did report more difficulties with everyday activities due to eyesight and less frequently were drivers.

Prematurity and Outcomes

Amblyopia risk factors in premature children in the first three years of life.

Lauren Hennein; Euna Koo; Julie Robbin; Alejandra G. de Alba Campomanes. *J of Ped Ophth & Strabismus*.2019;56(2):88-94

The purpose of this study id to determine the incidence of amblyopia risk factors during the first 3 years of life in premature children. This prospective cohort included 145 premature children (gestational age of less than 37 weeks) who were evaluated for amblyopia risk factors every 6 months until age 3 years. The incidence rate, cumulative incidence, and prevalence of any amblyopia risk factor were assessed in retinopathy of prematurity (ROP) and non-ROP screened groups. Multivariate logistic regression was performed to evaluate variables associated with the development of an amblyopia risk factor. The study showed that the 3-year incidence rates of amblyopia risk factors were similar between the non-ROP and ROP screened groups (18 versus 19 cases per 1,000 person-years, respectively). The 3-year cumulative incidence was also similar: 32% (95% confidence interval [CI]: 18 to 47) in the non-ROP and 14% (95% CI: 5 to 28) in the ROP screened group ($P > .05$). In the ROP screened group, the prevalence rates were 20% or greater at most time points. In the non-ROP screened group, the prevalence rates were 11% to 14% during the first 18 months and increased to more than 20% at 24 months and thereafter. Astigmatism was the most prevalent amblyopia risk factor in both groups (7% to 18%).This study

demonstrated that at 3 years, the cumulative incidence, incidence rate, and prevalence of all amblyopia risk factors in premature children did not statistically significantly differ between those who were eligible for ROP examinations compared to those who were not. Vision screening in these patients around 24 to 30 months that focuses on detection of refractive errors may be warranted. A prospective study with a full-term control group would be useful to assess the difference in incidence of all amblyopia risk factors and to further assess the need for ophthalmologic examinations in premature children. This study has a lot of limitations such as the lack of a control group of full-term children, poor compliance with outpatient comprehensive eye examinations over the study period despite this being a high-risk population in a relatively captive health care system, study population was largely Hispanic and of lower socioeconomic status, and thus our results may be more generalizable to these populations.

8.ROP

ROP and Telemedicine/Screening

Factors in Premature Infants Associated With Low Risk of Developing Retinopathy of Prematurity

Wade KC, Ying GS, Baumritter MS; et al. *JAMA Ophthalmology*. February 2019;137(2):160-166.

This study evaluated characteristics of infants at low risk for development of retinopathy of prematurity (ROP) in North American neonatal intensive care units, especially whom post-discharge screening may be of limited value. In addition, the authors did a post hoc analysis of prospectively collected in-hospital ROP examination results among infants enrolled. In order to characterize the infants at low risk for ROP, the authors characterized infants without ROP and performed logistic regression on the subset of infants who were 27 to 33 weeks' gestational age to determine characteristics associated with the absence of ROP during all in-hospital examinations. A total of 1257 infants born at 22 to 35 weeks' gestation with birth weights less than 1251 g underwent 4,113 ROP examinations between 31 and 47 weeks' post-menstrual age. Overall, 1,153 examinations (38%) showed no ROP, and 456 infants (36%) did not have ROP prior to study center discharge or study end point. Among infants without ROP during examinations at 32 and 33 weeks' post-menstrual age, 16 (9.4%) and 14 (5.3%) subsequently underwent ROP treatment, respectively. At hospital discharge, there was no ROP in 59% of infants of 27 to 33 weeks' gestational age, compared with 15% of those who were less than 27 weeks' gestational age ($P \leq .001$). With more than 85% follow-up among infants without ROP by 37 weeks' post-menstrual age, none

were treated for ROP. In a multivariate analysis of infants born at 27 to 33 weeks' gestation, larger birth weight and higher gestational age were statistically significantly associated with absence of ROP. In summary, the findings suggest that, for infants of 27 weeks' gestational age or greater and birth weights larger than 750 g, if no ROP has been detected by discharge at near-term post-menstrual age, then further ROP surveillance has limited value.

Evaluation of remote telemedicine screening system for severe retinopathy of prematurity.

Brett A. Begley, BA; Joseph Martin, CO, COMT; Geoffrey T. Tufty, MD; Donny W. Suh, MD *J Ped Ophth & Strabismus*.2019;56(3):157-161

The purpose of this study is to evaluate the validity of remote telemedicine screening for retinopathy of prematurity (ROP) in a population of at-risk preterm infants in Iowa and South Dakota. The medical records for all preterm infants screened for ROP at neonatal intensive care units (NICUs) in Sioux City, Iowa, and Sioux Falls, South Dakota, from September 1, 2017, to July 31, 2018, were retrospectively reviewed. The RetCam Shuttle (Natus Medical Inc., Pleasanton, CA) was used to capture retinal images, which were posted on a secure server for evaluation by a pediatric ophthalmologist. Infants with suspected ROP approaching the criteria for treatment with anti-vascular endothelial growth factor (VEGF) medications were transferred to the Children's Hospital and Medical Center NICU in Omaha, Nebraska, where a comprehensive examination was performed and treatment was administered when indicated. The remaining infants received an outpatient comprehensive examination by one of two pediatric ophthalmologists within 2 weeks of discharge. A total of 124 telemedicine examinations were performed on 35 infants during the study period. Remote telemedicine screening for referral-warranted ROP using the RetCam Shuttle had a sensitivity of 100%, specificity of 97%, positive predictive value of 66.7%, and negative predictive value of 100%. Of the three infants transferred for referral-warranted ROP, two required treatment with anti-VEGF medications. Good outcomes were noted in all cases, and no patients progressed beyond stage 3 ROP. The authors conclude that telemedicine screening reliably detected referral-warranted ROP in at-risk premature infants at two remote sites, with no poor outcomes during the 11-month period. These results demonstrate the validity and utility of remote telemedicine screening for ROP. A limitation of this study was its relatively small sample size. Based on the decision to screen weekly, it is likely that infants in the current study underwent more examinations than necessary. This choice was made, per authors, to prioritize patient safety by limiting the possibility of failing to detect a cases of ROP requiring treatment.

Plus Disease in Telemedicine Approaches to Evaluating Acute-Phase ROP (e-ROP) Study: Characteristics, Predictors, and Accuracy of Image Grading

Qianqian Ellie Cheng, Ebenezer Daniel, Wei Pan, Agnieshka Baumritter, et al for the e-ROP Cooperative Group *Ophthalmology*. June 2019;126:868-875

The e-ROP study is an ongoing observational cohort study evaluating the effectiveness of digital imaging in detecting ROP requiring treatment in premature infants. All infants undergo both standard ophthalmoscopic examinations by e-ROP certified ophthalmologists and RetCam digital imaging analyzed by two trained non-physician readers. Plus disease was identified by clinical exam in 226 eyes; 95% involved the superior or inferior temporal quadrant of the retina, while 73% had both vessel dilation and tortuosity. The predictors of plus disease were consistent with prior studies: low birth weight, younger gestational age, white race, need for respiratory support, and lower weight gain. The trained readers had very poor sensitivity (40-45%) detecting plus disease combined with high specificity (95%). When the criteria for diagnosing plus was adjusted to include preplus disease, the sensitivity jumped to 94-98%, but the specificity declined to 72-81%. Although the authors conclude that non-physician readers can be trained to detect plus disease with good specificity, given the severity of adverse outcomes from delayed or missed plus disease detection, the screening algorithms should be revised to emphasize sensitivity over specificity. Future research will likely involve artificial intelligence analysis of digital imaging, rather than trained readers, to more accurately quantify vascular dilation and tortuosity to detect plus disease in ROP.

Implementation of a Critical Prediction Model Using Postnatal Weight Gain, birth Weight, and gestational Age to Risk Stratify ROP.

Kortany McCauley, Anupama Chundu, Helen Song, Robin High et al. *J Ped Ophthal & Strabismus*.2018;55 (5):326-334

The purpose of this study is to develop a simple prognostic model using postnatal weight gain, birth weight, and gestational age to identify infants at risk for developing severe retinopathy of prematurity (ROP). The medical records from two tertiary referral centers with the diagnosis code “Retinopathy of Prematurity” were evaluated. Those with a birth weight of 1,500 g or less, gestational age of 30 weeks or younger, and unstable clinical courses were included. Multivariate regression analysis was applied to transform three independent variables into a growth rate algorithm. Seventeen of 191 neonates had severe ROP. Weight gain of at least 23 g/d was determined as a protective cut-off value against development of severe ROP. This value maintained 100% sensitivity with 62% specificity to ensure all neonates who require treatment would be captured. Overall, the Omaha (OMA)-ROP model calculated a 58% reduction in eye examinations within the cohort. The authors concluded that inclusion of postnatal growth rate in risk stratification will minimize the number of eye examinations performed without increasing adverse visual outcomes. The OMA-ROP model predicts neonates who gain less than 23 g/d are at higher risk for developing severe ROP. Although

promising, larger cohort studies may be necessary to validate and implement new screening practices among preterm infants. This study is not without limitations. Similar to previously proposed models, the OMA-ROP model was developed from tertiary academic hospitals where infants have a higher ROP risk profile. Therefore, this cohort may not represent the average demographic of the national at-risk neonatal population. Furthermore, our findings are not applicable to infants in developing nations where differences exist in health care systems, patient demographics, and a cohort of older and larger infants who develop ROP and who may represent a different ROP risk profile. Accurate assessment of gestational age may not even be possible in some regions. Both the CO-ROP model and the OMA-ROP model screen based on lower-than-predicted weight gain. Therefore, an infant with higher-than-average weight gain due to non-physiologic reasons (edema, sepsis, or hydrocephalus) could theoretically be missed. Of the current proposed postnatal weight gain models, the WINROP is unique in its identification of such infants. Similarly, clinical factors that cause weight gain but are not associated with increased IGF-1 may generate false-negative signals and should be further assessed.

Development of Modified Screening Criteria for Retinopathy of Prematurity: Primary Results From the Postnatal Growth and Retinopathy of Prematurity Study.

Gil Binenbaum, Edward F. Bell, Pamela Donohue, Graham Quinn, et al. for the G-ROP Study Group. *JAMA Ophthalmology*. September 2018; 136 (9): 1034-1040.

This is a retrospective multi center cohort study of the incidence and early course of retinopathy of prematurity (ROP) from infants having ROP screening from 29 hospitals in the United States and Canada from 2006 to 2012. The authors performed a secondary analysis of the G-ROP study data. Of note, the data collection was standardized with a rigorous certification process for interpretation of medical records. To be enrolled in the study, the infant had to meet 1 of 2 conditions: (1) either eye met criteria for the ETROP type 1 or type 2 ROP or underwent treatment for ROP or (2) both eyes had mature retinal vasculature, immature vasculature in zone III with no prior ROP, or a regression of ROP of less than type 1 or type 2 ROP. Among the 7,483 infants included, 947 (12.7%) had birth weight (BW) of 1500g or more and 1440 (19.2%) had a gestational age (GA) of older than 30 weeks. Regarding the demographics, almost half the infants were white and more than 30% were African American. The authors reported that 43.1% (3224 infants) developed ROP, 6.1% (459 infants) developed type 1 ROP and 6.3% (472 infants) developed type 2 ROP. Furthermore, only 514 infants (6.9%) underwent treatment in 1 or both eyes and 147 infants (2%) had zone 1 disease. In infants with BW of less than 1251g, most had type 1 or 2

ROP (98.1%) and only approximately half of the eyes (49.4%) had retinal vasculature into zone III by 37 weeks postmenstrual age. One critical finding in this study is that these multi center cohort study involved ROP screenings of all eligible infants and not only high-risk infants. The authors remind us that for infants with BW less than 1251g, there is a higher risk of developing severe ROP and they reported 12.5% of severe ROP from low BW infants. Limitations of the study include the retrospective analysis and retinal photography was not used to confirm ROP zone or the presence of plus disease. However, study strengths include the large sample size from ROP screening programs from 29 hospitals with a rigorous data abstraction procedure. The authors suggest that this study is helpful for ophthalmologist, neonatologists, and care coordinators by providing ROP risk profiles across GA and BW groups for these infants.

Screening Examination of Premature Infants for Retinopathy of Prematurity

Walter M. Fierson, American Academy of Pediatrics Section on Ophthalmology, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus, American Association of Certified Orthoptists

Pediatrics. December 2018; 142(6): e20183061.

This policy statement provides an updated outline of evidence-based screening and treatment for infants with retinopathy of prematurity (ROP). From the multicenter trials of Cryotherapy for Retinopathy of Prematurity and Early Treatment of Retinopathy of Prematurity Randomized Trial, researchers confirmed the efficacy of treatment in reducing visual loss with high risk disease. From the information gleaned from these and other studies, the following guidelines have been developed to maximally detect ROP before it becomes severe enough to result in retinal detachment while minimizing the frequency of potentially traumatic examinations. Examinations should be performed by experienced ophthalmologists with binocular indirect ophthalmoscopy or, the authors suggest, an expert ophthalmologist reviewing wide angle retinal photographic images of pre-term infants. All infants less than or equal to 30 weeks or 1500 kg should be screened. The schedule of the screening is based on the gestational age at birth and post-menstrual age beginning at 31 weeks of post-menstrual age for 22-27 week premature infants and 32-34 weeks of post-menstrual age for 28-30 week premature infants. Depending on the stage and aggressiveness of ROP, the babies are re-examined in 1 to 3 week intervals. Termination of examinations occurs with full retinal vascularization, zone III retinal vascularization attained without prior zone I or zone II ROP, postmenstrual age of 45 weeks and no type 1 ROP, regression of retinopathy of prematurity without any change of reactivation or progression, or if anti-VEGF. Treatment with either laser photocoagulation or anti-VEGF injections. Treatment must be initiated if there is plus disease in zones I or II, Zone I ROP of any stage with plus disease, Zone I ROP with stage

3 without plus disease, and Zone II with Stage 2 or 3 with plus disease. Treatment should generally be accomplished as soon as possible at least within 72 hours of diagnosis and the infant should be re-examined in 3-7 days after treatment. The authors discuss the pros and cons of retinal photocoagulation and anti-VEGF injections. Photocoagulation has been proven to be effective in treatment of ROP but will cause mild visual field loss, risk of increased myopia, and significant structural changes. Anti-VEGF injections show promise in stopping ROP with limited structural changes but more prolonged follow up is needed due to reactivation of the ROP and there is uncertainty regarding systemic side effects and developmental delays. Communication with parents about the examinations, findings, and treatment plan is crucial. Systemic approaches to follow up and transitions to outpatient care are very important to follow screening and treatment guidelines and ensure appropriate care for these vulnerable infants. Regardless of whether infants at risk develop treatment requiring ROP, physicians should be aware that these infants are at increased risk for other visual disorders such as strabismus, amblyopia, high refractive errors, cataracts, and glaucoma.

Real-World Simulation of an Alternative Retinopathy of prematurity screening System in Thailand: A Pilot Study.

S.Grace Prakalapakorn, Sharon Freedman, Amy K.Hutchinson, Piyada Saehout et al *J of Ped Ophth & Strabismus*.2018; 55(4): 245-253

The purpose of this study is to evaluate an alternative retinopathy of prematurity (ROP) screening system that identifies infants meriting examination by an ophthalmologist in a middle-income country. The authors hypothesized that grading posterior pole images for the presence of pre-plus or plus disease has high sensitivity to identify infants with type 1 ROP that requires treatment. Part 1 of the study evaluated the feasibility of having a non-ophthalmologist health care worker obtain retinal images of prematurely born infants using a non-contact retinal camera (Pictor; Volk Optical, Inc., Mentor, OH) that were of sufficient quality to grade for pre-plus or plus disease. Part 2 investigated the accuracy of grading these images to identify infants with type 1 ROP. The authors prospectively recruited infants at Chulalongkorn University Hospital (Bangkok, Thailand). On days infants underwent routine ROP screening, a trained health care worker imaged their retinas with Pictor. Two ROP experts graded these serial images from a remote location for image gradability and posterior pole disease. Fifty-six infants were included. The study showed that overall, 69.4% of infant imaging sessions were gradable. Among gradable images, the sensitivity of both graders for identifying an infant with type 1 ROP by grading for the presence of pre-plus or plus disease was 1.0 (95% confidence interval [CI]: 0.31 to 1.0) for grader 1 and 1.0 (95% CI: 0.40 to 1.0) for grader 2. The specificity was 0.93 (95% CI: 0.76 to 0.99) for grader 1 and 0.74 (95% CI: 0.53 to 0.88) for grader 2. The authors concluded that it was feasible for a trained non-ophthalmologist health care worker to

obtain retinal images of infants using the Pictor that were of sufficient quality to identify infants with type 1 ROP.
The results of this study should be considered in light of several limitations. First, the results may not be generalizable to other countries because ROP screening guidelines are region specific. Second, there was a single imager in this study who had a background in ophthalmic photography. Third, although both graders have extensive experience screening and treating ROP, they were not given any specific training before grading these images and the variability of their grading underscores the need for standardized training for image grading, which has been shown to be effective in other ROP screening studies.

ROP and imaging

Optical Coherence Tomography Angiography of the Foveal Avascular Zone in Children with a History of Treatment-Requiring Retinopathy of Prematurity

Norie Nonobe, Hiroki Kaneko, Yasuki Ito, Kei Takayama, et al. *Retina* January 2019; 39:111-117.

Ten patients with history of laser photocoagulation or cryopexy treatment for Stage 3 (Zone >=II) ROP and 10 normal control subjects were included in this retrospective case-control study to examine the characteristics of the foveal vascular structure by OCT angiography. Foveal avascular zone, vessel density, vessel length, and vascular diameter index were measured by OCT angiography using the 3x3-mm ETDRS sectors. The median foveal avascular zone values of the patients with ROP and controls were 0.103 mm^2 and 0.260 mm^2 respectively (p=0.0025). The medians of the vessel density, vessel length, and vascular diameter index of the patients with ROP were 0.218 mm^2/mm^2, 11.75 mm/mm^2, and 18.0 um, respectively, in ETDRS Sector 1 and did not significantly differ from those of the controls. For the average of ETDRS Sectors 2 to 5, the medians of the vessel density, vessel length, and vascular diameter index for the patients with ROP were 0.347 mm^2/mm^2, 18.95 mm/mm^2, and 18.28 um, respectively; vessel density and vessel length were significantly smaller than those of the controls, but there was no difference in vascular diameter index.

This study population was small. Gestational age was not accurately recorded in some patients and therefore a correlation between FAZ formation and gestational age could not be made. In addition, although not statistically significant, there was an age difference at the time of testing between the ROP and control groups. Because this study compared children with history of treatment for ROP to control subjects without any treatment, it is possible that the treatment itself may have caused changes. Also, FAZ data from children with spontaneously regressed ROP was not compared to these groups. Despite these limitations, OCT angiography appears to be useful for non-invasively visualizing retinal vascular construction in children. OCT angiography-guided FAZ was significantly smaller

in patients treated for ROP than in controls, indicating that foveal vascular development may be altered in patients with a history of treatment-requiring ROP.

ROP and Treatment

A Spectrum of Regression Following Intravitreal Bevacizumab in Retinopathy of Prematurity.

Chen TA, Shields RA, Bodnar ZH, et al. *Am J Ophthalmol.* 2019 Feb; 198: 63-69.

The purpose of this study was to describe regression patterns in ROP after (half adult dose, 0.625mg) intravitreal bevacizumab. The authors performed a retrospective cohort study of 92 eyes of 46 patients at one institution over a 5-year period. Patients who did not have complete vascularization by 60 weeks underwent an exam under anesthesia with fluorescein angiogram and those with two disc diameters or more of peripheral non perfusion were lasered. The authors then reviewed the amount of retinal non perfusion on fluorescein angiogram to categorize their patients and found that only 3 of the 93 eyes reached full maturity. Thirty-nine (44%) of patients had vascular arrest alone (VAA), 24 eyes (38%) had vascular arrest with tortuosity (VAT), and 16 eyes (18%) had reactivation of the ROP. Eyes with reactivation had larger areas of ischemia compared to those who had VAA or VAT. The authors concluded that incomplete vascularization is very common after intravitreal bevacizumab. They found that the patients with aggressive posterior retinopathy of prematurity (APROP) were more likely to have reactivated ROP. The authors highlight the need for close follow up for patients who receive intravitreal bevacizumab for ROP and the important role of fluorescein angiography in these patients to determine the amount of peripheral non perfusion. This paper adds to the growing literature reminding the pediatric ophthalmologist and pediatric retina surgeon of the importance of follow up and laser in the treatment of ROP after intravitreal bevacizumab.

Iatrogenic crystalline lens injury in pediatric eyes following intravitreal injections for retinopathy of prematurity.

Murugesan Vanathi, MD; Devesh Kumawat, MD; Rashmi Singh, MD; Parijat Chandra, MD *J Ped Ophth & Strabismus*.2019;56(3):162-167

The purpose of this study is to report the occurrence of lens injury during intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection in infants with retinopathy of prematurity (ROP). ROP cases presenting to a tertiary care center with cataract following intravitreal injection were retrospectively studied. The indication, setting, and method of injection were noted. Ultrasound biomicroscopy (UBM) details were recorded. The main measures were morphology of cataract, posterior capsular defect, and intraocular lens (IOL) placement. Three children

(mean age: 14 ± 8.6 months, two male and one female) received injection elsewhere under topical anesthesia in the neonatal intensive care unit (NICU) for type 1 ROP (stage 3 in zone I or II with significant plus disease) 9 to 18 months earlier. All cases developed cataract caused by intravitreal needle damaging the posterior capsule. In one case, a dense zonular cataract was present and peripheral dehiscence of the posterior capsule became evident only during lens aspiration. The second and third cases had a central posterior subcapsular cataract. Preexisting central dehiscence of the posterior capsule was noted on UBM and confirmed during surgery. A multi-piece IOL was securely placed in all cases. At last follow-up (median: 6 months; range: 3 to 6 months), the IOL was stable and centered in all cases with a clear visual axis. The authors conclude that the increasing occurrence of cataract in treatment-requiring ROP following intravitreal anti-VEGF injections being given by practitioners in the NICU setting under topical anesthesia that hinders optimal visualization and technique is a significant concern. This study is limited by the small number of cases.

Laser Treatment for Retinopathy of Prematurity: A Decade since ETROP

Seema Emami, Maram Isaac, Kamiar Mireskandari , and Nasrin N. Tehrani *Ophthalmology*. April 2019;126:639-641

Recent data support the use of intravitreal bevacizumab over laser in premature infants with severe type 1 ROP, with reduced rates of disease recurrence and better structural outcomes. This study reports the long-term outcomes of type 1 eyes treated with laser since the conclusion of the ETROP study. Dividing outcomes into zone 1 and zone II disease, 93% and 99%, respectively, of laser-treated eyes had favorable structural outcomes. Only a single eye with zone II disease required invasive surgery, a scleral buckle for stage 4a ROP, and only two eyes in the same patient with zone I disease progressed to stage 5 ROP, with one additional eye progressing to stage 4a. Two-thirds of treated eyes demonstrated myopia, with half of those eyes progressing to high myopia more than -5 diopters. Laser remains a viable option to treat type 1 ROP, with a better refractive outcome after intravitreal injection of bevacizumab compared with laser balanced against potential long term systemic or ocular side effects.

Posterior zone 1 retinopathy of prematurity: spectrum of disease and outcome after laser treatment

Katoch D, Dogra M, Aggarwal K, Sanghi G, et al. *Can J Ophthalmol.* February 2019;54(1):87-93.

Premature infants with Zone 1 retinopathy of prematurity (ROP) have been reported to have worse outcomes after ablative therapy compared to those with Zone II ROP. Among those with Zone 1 disease, outcomes can be even worse if

they had very posterior zone 1 ROP at the time of laser ablation. This retrospective study aimed to describe the clinical characteristics and outcomes after laser of this group of infants with posterior zone 1 ROP. The study looked at infants treated for posterior zone 1 ROP at a single institution in India from 2006 to 2015. Posterior zone 1 was defined as the area within a circle with a radius from the center of the optic disc to the center of the macula. This is approximately half of the area covered by the whole of zone 1. 56 eyes of 28 infants were included in analysis, with mean GA 28.65 weeks and mean BW 1154g. Typical aggressive posterior retinopathy (as described by ICROP) was seen in 64.3% of eyes. 25% had an atypical appearance with a raised fibrovascular proliferation of the nasal retina close to the optic nerve and intraretinal shunts. 8.7% had a “mat-like” fibrous proliferation, and 4.4% had threshold ROP. All eyes underwent laser treatment at mean of 35 weeks. 8 eyes required laser supplementation. 6 eyes received intravitreal bevacizumab before laser. Unfavorable outcomes were noted in 44 eyes (78.6%). This included 3 eyes with stage 4A, 15 eyes with stage 4B, and 23 (52.27%) with stage 5. 2 eyes had vitrectomy and stabilized, but the rest progressed. Among the 6 eyes that received bevacizumab before laser, 5 had a favorable outcome and 1 did not. There were several limitations of this study included unknown details of neonatal illness and oxygen exposure in many infants, no angiography was performed, and its retrospective nature. The authors also note the low rates of bevacizumab used in this study, the use of which may have allowed better anatomical outcomes in this group.

Systematic review and meta-analysis of the negative outcomes of retinopathy of prematurity treated with laser photocoagulation

Liang J *EJO* March 2019,29(2) 223–228

Retinopathy of prematurity is a leading cause of potentially avertable childhood blindness around the world. And laser photocoagulation is currently performed as a gold standard for retinopathy of prematurity treatment, but it may contribute to elevated myopia and decreased visual field. Therefore, the objective of this meta-analysis is to explore the negative impact of laser photocoagulation for retinopathy of prematurity in terms of anatomic outcomes and structural outcomes. Studies were retrieved through literature searches in PubMed and EMBASE from 1990 to 2017 in English. Case-control studies that reported anatomic and structural changes or significant complications after laser coagulation or cryotherapy for retinopathy of prematurity were eligible. This meta-analysis included eight original studies related to laser treatment for retinopathy of prematurity at any stages. A total of 1422 infants were participated, of which 1156 documented subthreshold or threshold retinopathy of prematurity without laser treatment were selected as comparison group and the rest treated with diode or argon laser coagulation were chosen for experiment group. Taking all included studies into account, spherical equivalent (mean difference −2.53, 95% confidence interval: –5.23 to 0.18, I2 = 96%, P < 0.00001), anterior chamber depth (mean difference −0.52, 95% confidence interval: −0.76 to −0.28, I2 = 55%, P = 0.11), astigmatism (odds ratio 3.19, 95% confidence interval: 1.61 to 6.32, I2 = 0%, P = 0.54), and

myopia (odds ratio 8.08, 95% confidence interval: 3.79 to 17.23, I2 = 37%, P = 0.21) were associated with laser treatment for retinopathy of prematurity. Axial length (mean difference −0.01, 95% confidence interval: –0.28 to 0.27, I2 = 0%, P = 0.62) and anisometropia (odds ratio 4.21, 95% confidence interval: 0.54 to 33.17, I2 = 1%, P = 0.31) had no statistical significance on laser coagulation for retinopathy of prematurity. This meta-analysis showed that spherical equivalent, anterior chamber depth, astigmatism, and myopia were associated with the negative outcomes of laser coagulation, while axial length and anisometropia had no statistical importance on the defects of laser coagulation. Therefore, patients treated with laser coagulation should follow periodic cycloplegic refraction and receive early optical correction.

A Dosing Study of Bevacizumab for Retinopathy of Prematurity: Late Recurrences and Additional Treatments

Wallace DK, Trevano, WD, Hartnett ME, Kong L, et al. *Ophthalmology*. 125; 12 Dec 2018: 1961-1966.

Intravitreal bevacizumab (IVB) is increasingly used to treat severe retinopathy of prematurity (ROP), but it enters the bloodstream, and there is concern that it may alter development of other organs. Previously, this study group reported short-term outcomes of 61 infants enrolled in a dose de-escalation study, where one eye was injected with 0.25 mg, 0.125 mg, 0.063 mg or 0.031 mg of IVB. The lowest dosage of 0.031 mg was effective after 4 weeks in 9 out of 9 infants. There was a concern that these low doses, however, will lead to higher recurrence of the disease. Here, the authors report the late recurrences and additional treatments and structural outcomes for infants receiving lower doses of IVB. This was a masked, multicenter, dose de-escalation study including 61 premature infants with type 1 ROP. If type 1 ROP was bilateral at enrollment, then the study eye was randomly selected. In the study eye, bevacizumab intravitreal injections were given at de-escalating doses of 0.25 mg, 0.125 mg, 0.063 mg, or 0.031 mg; if needed, fellow eyes received 1 dose level higher: 0.625 mg, 0.25 mg, 0.125 mg, or 0.063 mg, respectively. After 4 weeks, additional treatment was at the discretion of the investigator. Of 61 study eyes, 25 (41%; 95% confidence interval [CI], 29%–54%) received additional treatment: 3 (5%; 95% CI, 1%–14%) for early failure (within 4 weeks), 11 (18%; 95% CI, 9%–30%) for late recurrence of ROP (after 4 weeks), and 11 (18%; 95% CI, 9%–30%) for persistent avascular retina. Re-treatment for early failure or late recurrence occurred in 2 of 11 eyes (18%; 95% CI, 2%–52%) treated with 0.25 mg, 4 of 16 eyes (25%; 95% CI, 7%–52%) treated with 0.125 mg, 8 of 24 eyes (33%; 95% CI, 16%–55%) treated with 0.063 mg, and 0 (0%; 95% CI, 0%–31%) of 10 eyes treated with 0.031 mg. By 6 months corrected age, 56 of 61 study eyes had regression of ROP with normal posterior poles, 1 study eye had developed a Stage 5 retinal detachment, and 4 infants had died of preexisting medical conditions. The fellow eyes treated with IVB had similar outcome. Due to small sample size, the study was not powered to address the relationship between the dose and recurrence rate. The authors concluded that retinal structural out-

comes are very good after low-dose, as low as 0.031 mg, bevacizumab treatment for ROP, although many eyes received additional treatment. This is the first study aimed at determining the ideal anti-VEGF dosing in infants with ROP.

Macular Structures, Optical Components, and Visual Acuity in preschool Children after Intravitreal Bevacizumab or Laser Treatment

Lee YS, See LC, Chang SH, et al. *Am J Ophthalmol.* 2018; 192: 20-30.

This is a comparative interventional case series of 80 eyes of 42 patients who had type I ROP treated either by intravitreal Bevacizumab (IVB) or laser. The patients had spectral domain OCT of their macula between the ages of 4 and 6 to determine if treatment modality would affect the macular structures at preschool age. The authors also looked at refraction and biometry metrics to compare the two groups. Thirty-three eyes of 17 patients had IVB only, 24 eyes of 13 children had laser only, and 23 eyes of 12 children had both laser and IVB. Baseline characteristics were evaluated and there was a difference in the gestational age at birth with the Laser +IVB group having younger GA and a trend towards a lower BW. Patients treated with IVB had less myopia, deeper anterior chambers, but similar axial lengths and corneal curvatures. The IVB treated eyes had thinner retinal thicknesses in the fovea, parafovea, and perifovea. There was a higher incidence of having a foveal depression in the the IVB group. The IVB group had better uncorrected visual acuities but did not have improved best corrected visual acuities. Interestingly, there were clear structural differences in the eyes in the two groups, but no differences in the BCVA suggesting that the development of the foveal depression does not affect BCVA. Some of the limitations of this study included small sample size, lack of randomization, selection for patients who could cooperate with OCT testing and visual acuity testing, and the baseline differences between the two groups. However, this is an important study since it is the first to describe the visual acuity, morphology of the retina, and the biometry of the eyes in IVB and laser treated eyes in the preschool years with a large cohort of patients.

Short-term Outcomes After Intravitreal Injections of Conbercept versus Ranibizumab for the Treatment of Retinopathy of Prematurity

Jin E, Yin H, Li X, et al. *Retina* August 2018; 38:1595-1604.

This study investigated intravitreal injection of conbercept (IVC) as a treatment for ROP, comparing the structural outcomes and recurrence of ROP among patients treated with IVC or intravitreal ranibizumab (IVR). The primary outcome was treatment success, defined as regression of plus disease; secondary outcomes included recurrence of plus disease, times of injection, and final disease regression. 48 eyes (24 patients) with ROP were included in the study. 20 eyes (10 patients) received IVC, and 28 eyes (14 patients) received IVR. In the IVC

group, 17 (85%) of 20 eyes received only one injection, and the regression of plus disease occurred 4.3 weeks later. 3 eyes (15%) received a second IVC injection, and plus disease regression occurred within 3 weeks. For the IVR group, 15/28 (53.6%) eyes received a second IVR injection. No retinal detachment was observed in either group.

Infants in this Chinese study who developed severe ROP were more mature and heavier than infants who were similarly affected in other studies, including ETROP, potentially limiting the generalizability of the results. Another limitation is the study's retrospective nature and lack of matched laser-treated group. The number of included patients is small and the follow-up somewhat limited (mean 52.6 weeks in IVC group and 42.9 weeks in IVR group), and long-term safety and efficacy studies are needed. However, with a structure different than ranibizumab and bevacizumab, conbercept may represent a new choice of anti-VEGF treatment for ROP.

ROP Epidemiology and Outcomes

Temporal profile of retinopathy of prematurity in extremely premature compared to premature infants.

Vincent D. Venincasa, MD; Victoria Bugg, MD; Justin Dvorak, PhD; Kai Ding, PhD; et al.*J of Ped Ophthal & Strabismus*.2019;56(2):116-123

The purpose of this study is to compare the time course of retinopathy of prematurity (ROP) in premature (≥ 28 to 34 weeks' gestational age) and extremely premature (< 28 weeks' gestational age) infants. This study was a retrospective single-center chart review that included 582 eyes (122 premature, 464 extremely premature) of 299 infants (65 premature, 234 extremely premature) diagnosed as having ROP who were born between January 1, 2010, and December 31, 2015. Data collected were analyzed with shared frailty models, chi-square, and Fisher's exact tests. Extremely premature infants were diagnosed as having ROP earlier than premature infants at 33.6 weeks (95% CI [confidence interval]: 33.4 to 33.9) versus 36.0 weeks (95% CI: 34.7 to 36.4, $P < .0001$). The time from diagnosis to spontaneous regression was more than 4 weeks longer for extremely premature infants than premature infants with stage 1 ROP (82.0 vs 50.0 days, $P < .0001$), and more than 6 weeks longer for extremely premature infants than premature infants with stage 2 ROP (99 vs 55 days, $P < .0001$). Extremely premature infants had more bilateral ROP (96.6% vs 87.1%, $P < .01$) and were three times more likely to require treatment than premature infants (29.7% vs 9.9%, $P < .0001$). On average, infants who required treatment weighed 137 grams less at birth ($P < .0001$) and gained 37.7 grams less per week than infants who underwent spontaneous regression ($P < .0001$). The study concluded that extremely premature infants developed ROP earlier, had more bilateral ROP, took longer to achieve spontaneous regression, and required treatment more often than premature infants. Infants who required treatment had a lower birth weight and rate of

weight gain than infants who underwent spontaneous regression. This study has several limitations. Data are from a single center via a retrospective analysis. Although the diagnosis of ROP and classification of type 1 ROP are standardized at this institution, four different ophthalmologists examined the infants. In addition, 382 of 2,907 (13.1%) total encounters were missing weight measurements, most commonly from the final follow-up.

Impact of early postnatal weight gain on Retinopathy of prematurity in very preterm infants in southwestern Ontario.

Yingxiang Li, MD; Meera Shah, BSc; Michael R. Miller, PhD,Davud S.C.Lee,MB et al *J of Ped Ophth & Strab*.2019; 56(3): 168-172

The purpose of this study is to examine the relationship between postnatal growth and development of retinopathy of prematurity (ROP) among infants in southwestern Ontario. The medical records of 431 preterm infants, born between January 1, 2008, and June 1, 2015, with a gestational age (GA) of less than 31 weeks or birth weight (BW) of less than 1,250 g were reviewed. Information collected included pregnancy and birth history, neonatal characteristics, ROP status, comorbidities, and postnatal weight measurements at specified intervals. Infants diagnosed as having ROP and no ROP were compared. The study showed that low weight velocity from day 7 to day 28 ($P < .001$), high weight velocity from birth to first day of full enteral feeding (FEF) ($P < .001$), long duration from birth to FEF ($P < .001$), and long duration from FEF to discharge/transfer ($P < .001$) were associated with ROP. After controlling for GA and BW, the durations, birth to FEF, and FEF to discharge/transfer remained significant ($P < .05$). In a multivariable logistic regression analysis adjusting for GA, bronchopulmonary dysplasia, and surgical ligation for patent ductus arteriosus, the only independent risk factor of ROP was duration from FEF to discharge/transfer ($P < .05$). The authors concluded that the duration from birth to the establishment of FEF in very preterm infants may be an additional risk factor for the development of severe ROP. Used in conjunction with BW and GA, the duration from birth to FEF may improve the reliability and efficiency of current screening tools for ROP. However, this was highly associated with the three strongest predictors of ROP: GA, BPD, and surgical ligation for PDA. Duration from birth to FEF may thus represent a surrogate marker that correlates to ROP and comorbidities in very pre-term and VLBW infants. Future studies may assess how FEF may be achieved more quickly in preterm infants, and whether earlier achievement of FEF in preterm infants reduces the risk of developing ROP. The study is is limited in that certain known risk factors for the development of ROP, including the use of oxygen therapy, were not considered in the analysis. Factors affecting postnatal weight gain, including IGF-

I, and parenteral and enteral nutrition, were also not measured. Although the severity of ROP is an important determinant of disease management and clinical outcomes,[2] the severity of ROP was not assessed in the current study.

Increased incidence of retinopathy of prematurity and evolving treatment modalities at a Canadian tertiary centre

Isaza G, Donaldson L, and Chaudhary V. *Can J Ophthalmol.* April 2019;54(2):269-274

This study is retrospective review of infants screened from 2010 to 2016 at a large Canadian referral center. The authors aimed to determine ROP incidence and risk factors for disease in this population. A total of 623 infants were screened for ROP during the time limits. Overall incidence of ROP was 67.1% (418 infants). Severe ROP (stage 3 or worse) was seen in 88 (14.1%) infants). The overall mean GA was 27.1 weeks in the group, with a mean GA of 26.4 weeks for those with ROP. Among infants with GA 26 weeks or less the incidence of severe ROP was 30.1% (74/249). No infant born more than 29 weeks had severe ROP. Mean BW of the group was 1032g, with mean of 929g in those with ROP. No infants progressed to stage 4 or 5. Plus disease was present in 9.3% of ROP, and every infant with plus disease had stage 3 ROP. Treatment was performed in 44/418 infants (10.5%). 14 infants received laser and 26 anti-VEGF injection. 4 patients had combination treatment. Overall predictors or ROP were gestational age, birth weight, and length of NICU stay. The authors compared overall incidence to earlier data from the same institution and found overall increase from 40.4% to 67.1%. They speculate this may be due to inter-observer variability, increased attention to early stages of disease, and increased number of very premature infants. They have also noted the rapid adoption of intravitreal anti-VEGF injections at their institution in recent years.

Neurodevelopmental Outcomes of Preterm Infants with Retinopathy of Prematurity Treatment

Girija Natarajan, Seetha Shankaran, Tracy Nolen, et. al *Pediatrics*. August 2019; 144(2): e20183537.

This study aimed to determine whether there is a difference in adverse outcomes between bevacizumab therapy and surgery for retinopathy of prematurity in extremely pre-term infants. The study was a retrospective analysis of prospective data on preterm infants 22-26 +6/7 weeks gestational age. The primary outcomes were death and severe neurodevelopmental impairment (NDI) at 18-26 months' corrected age (a composite score of Bayley Scales of Infant and Toddler Development Classification Scale greater than or equal to 2, and bilateral blindness or hearing). The study included 405 infants from multiple health centers.

The results demonstrated that the bevacizumab group were a sicker cohort with lower median birth weight, longer durations of conventional ventilation, and longer supplemental oxygen. Rates of death or severe NDI did not differ between the groups. But, the bevacizumab group had a greater odds of death and developmental scores were significantly lower in the bevacizumab group. There may be significant selection bias given that the physicians chose which patients received injection versus laser and that the bevacizumab group was a sicker group of patients. This study was the first to observe that mortality through infancy was significantly higher in the bevacizumab group than the surgery group. Although not conclusive, these results do highlight the need for rigorous appraisal of the risks and benefits of bevacizumab in a large randomized trial with neurodevelopmental follow up.

Implementation of a Critical Prediction Model Using Postnatal Weight Gain, birth Weight, and gestational Age to Risk Stratify ROP.

Kortany McCauley, Anupama Chundu, Helen Song, Robin High et al. *J Ped Ophthal & Strabismus*.2018;55 (5):326-334

The purpose of this study is to develop a simple prognostic model using postnatal weight gain, birth weight, and gestational age to identify infants at risk for developing severe retinopathy of prematurity (ROP). The medical records from two tertiary referral centers with the diagnosis code “Retinopathy of Prematurity” were evaluated. Those with a birth weight of 1,500 g or less, gestational age of 30 weeks or younger, and unstable clinical courses were included. Multivariate regression analysis was applied to transform three independent variables into a growth rate algorithm. Seventeen of 191 neonates had severe ROP. Weight gain of at least 23 g/d was determined as a protective cut-off value against development of severe ROP. This value maintained 100% sensitivity with 62% specificity to ensure all neonates who require treatment would be captured. Overall, the Omaha (OMA)-ROP model calculated a 58% reduction in eye examinations within the cohort. The authors concluded that inclusion of postnatal growth rate in risk stratification will minimize the number of eye examinations performed without increasing adverse visual outcomes. The OMA-ROP model predicts neonates who gain less than 23 g/d are at higher risk for developing severe ROP. Although promising, larger cohort studies may be necessary to validate and implement new screening practices among preterm infants. This study is not without limitations. Similar to previously proposed models, the OMA-ROP model was developed from tertiary academic hospitals where infants have a higher ROP risk profile. Therefore, this cohort may not represent the average demographic of the national at-risk neonatal population. Furthermore, our findings are not applicable to infants in developing nations where differences exist in health care systems, patient demographics, and a cohort of older and larger infants who develop ROP and who may represent a different ROP risk profile. Accurate assessment of gestational age may not even be possible in some regions. Both the CO-ROP model

and the OMA-ROP model screen based on lower-than-predicted weight gain. Therefore, an infant with higher-than-average weight gain due to non-physiologic reasons (edema, sepsis, or hydrocephalus) could theoretically be missed. Of the current proposed postnatal weight gain models, the WINROP is unique in its identification of such infants. Similarly, clinical factors that cause weight gain but are not associated with increased IGF-1 may generate false-negative signals and should be further assessed.

Refractive Trend of Stage 3 Retinopathy of Prematurity.

Sneha Padidam, Kim Le, Xihui Lin.*J Ped Ophthal & Strabismus*.2018;55(6):403-406

The purpose of this retrospective review was to analyze the refractive trend in patient with Stage 3 Retinopathy of Prematurity (ROP) over a 7- year time period. Of the 70 eyes that were included in the study, 46 received laser ablation and 24 did not. There was a similar distribution between zone II and zone III disease in both groups (*P* = .87). The average final refraction in the laser group was −0.83 diopters (D) in comparison to +1.61 D in the no laser group. The final refractive change was −3.55 D in the laser group and −0.25 D in the no laser group. A greater myopic shift was observed in the first 2 years of life than between years 2 and 7 in both groups. The authors conclude that infants who underwent laser treatment for stage 3 ROP tended to have higher myopia than those with stage 3 ROP who did not require treatment. This study has several limitations. First, it was a retrospective study without a randomized control group. Although the laser and no laser groups with a similar disease extent were analyzed, it was still difficult to account for disease severity because the laser group had more patients with plus disease. All of the patients in the bevacizumab group had plus disease. Additionally, most of the patients in this study were Hispanic and these findings may not be as widely reproducible in another population.

Incidence and Early Course of Retinopathy of Prematurity: Secondary Analysis of the Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study.

Graham E. Quinn, Gui-shang Ying, Edward F. Bell, Pamela K. Donohue, et al. for the G-ROP Study Group. *JAMA Ophthalmology*. December 2018; 136 (12): 1383-1389.

This was a large retrospective cohort study of 7483 infants who had serial retinopathy of prematurity (ROP) examinations in 29 hospitals in the United States and Canada between 2006 and 2011. Of note, this article has some overlap of findings and data points and collection in the earlier article from JAMA Ophthalmology September 2018. The authors sought to establish the incidence, onset, and early ROP course in infants undergoing ROP screening. Of note, this study includes all eligible infants for ROP screening, not only high-risk infants for ROP.

Demographics for the children undergoing ROP examinations included a mean birth weight (BW) of 1099g and a mean gestational age (GA) of 28 weeks. The authors reported that 3224 (43.1%) infants developed ROP, 459 (6.1%) developed type 1 ROP and 472 (6.3%) developed type 2 ROP. Regarding treatment, 514 (6.9%) infants underwent ROP treatment in 1 or both eyes and 147 (2.0%) had zone 1 disease. The authors report that secondary analysis shows that more than 40% of at-risk premature infants develop some stage of ROP and most ROP regresses without treatment. Of note, severe ROP was noted in 12.5% infants, especially with BW of less than 1251g. The authors suggest, similar to their earlier manuscript, that these stratified ROP results provide ROP risk profiles across BW and GA categories. Finally, the authors suggest that more specific guidelines are needed for low-risk infants with older GA and larger BW regarding the current criteria for ROP screening.

Incidence, risk factors and severity of retinopathy of prematurity in Turkey (TR-ROP study): a prospective multicenter study in 69 neonatal intensive care units

Bas A, Demirel N, Koc E, Isik D, et al. *Br J* Ophthalmol. December 2018; 102:1711-1716.

This is the first multicenter study to analyze risk factors for ROP in Turkey. The authors performed a prospective cohort study between April 2016 and April 2017 in 69 NICUs. Included in the analysis were infants with birth weight <=1500g or gestation age <=32 weeks (or if not these then unstable clinic course) Overall 6115 infants were analyzed. 27% overall had some stage of ROP, with 6.7% having severe ROP. Risk factors for severe ROP (based on multivariate logistic regression analysis) included lower birth weight, smaller gestational age, total days on oxygen, late-onset sepsis, frequently of red blood cell transfusions and relative weight gain. 414 infants needed treatment, of which 95.4% had BW<=1500g. 19 treated babies had BW 1501-2000g. 16% of the treated infants did not fulfill ETROP requirements for treatment (i.e. they were treated earlier than type I ROP). The authors conclude that screening criteria in Turkey should be wider than in developed countries, with criteria including infants <1700g or <=32 weeks if seen in university hospitals, and <1700g or <=34 weeks if seen in state or private hospitals.

ROP - Other Topics

Comparison of Biphasic vs Static Oxygen Saturation Targets Among Infants With Retinopathy of Prematurity

Shukla A, Sonnie C, Worley S et al. *JAMA Ophthalmology.* April 2019;137(4):417-423.

This was a retrospective cohort study comparing biphasic vs static oxygen saturation targets in infants with retinopathy of prematurity (ROP) at a level III neonatal intensive care unit (NICU) in Cleveland, Ohio from 2010 to 2017. The study included infants born at a corrected gestational age (CGA) of 31 weeks or younger or a birth weight of 1500 g or less. Of note, the biphasic protocol had target saturations of 85% to 92% at younger than 34 weeks' CGA and greater than 95% at 34 weeks' CGA or older in comparison to the group with a constant 91% to 95% target. Of the 596 eligible infants, 562 had ophthalmic examinations and 54% were boys. Mean CGA and birth weight were 29 weeks and 1151 g, respectively. Findings included an increase in Type 1 ROP in the cohort with static, constant 91% to 95% target ($P = .03$). Of note, there was a delay in vascularization in the biphasic 85% to 92% targeted group ($P = .03$). The limitations of this study include the retrospective cohort and that it was completed at one level III NICU center. However, this study's findings reinforce previous studies, in which lower target oxygen saturation in biphasic versus static conditions are associated with decreased incidence and severity of ROP without increasing mortality.

Persistent Avascular Retina in Infants with a history of Type II Retinopathy of prematurity: to treat or not to treat?

Rasha Al-Taie, Samantha K.Simkin, Erica Doucet, Shuan Dai. *J of Ped Ophth &Strabismus.*2019; 56(4): 222-228

The purpose of this prospective observational study is to investigate the persistent avascular retina in infants with type 2 retinopathy of prematurity (ROP) that persisted after 45 weeks post menstrual age when regular ROP screening ceased by performing fundus fluorescein angiography(FFA). FFA was completed on 72 eyes of 36 infants (53% male), with a mean gestational age of 26.0 ± 2.2 weeks and a mean birth weight of 834.6 ± 216.3 grams. The mean age at discharge from ROP screening was 47.6 weeks' post-menstrual age. All patients had type 2 ROP at the worst stage of their disease, with predominantly stage 2 disease. FFA was performed at a mean age of 18.8 ± 10.3 months post-menstrual age. All patients had detectable avascular retina in peripheral zone II or III on FFA. Peripheral vessel leakage was present in 3 eyes of 2 infants (5.5%), who both subsequently received peripheral laser treatment. The authors concluded that persistent avascular retina after 45 weeks post-menstrual age can have active leakage in a small percentage of patients. Infants with type 2 ROP but without complete vascularization can present management dilemmas when screening and treating them. The long-term impact of peripheral avascular retina is still not known, and, until such information becomes available, retinal imaging with FFA is recommended, with potential laser treatment for those with high-risk features. Currently, long-term outcomes of patients with confirmed leaking are unclear and further research on the benefits of lasers is required. All infants with persistent avascular retina after ROP screening require regular outpatient clinical follow-up with dilated fundus examination. Some of the patients without FFA leakage could still potentially pose longer term risk, although this is unlikely given its peripheral location. Patients with small areas of vascular leakage may be safe

to be watched, but further data are needed to validate such an approach. This study is limited by the relative small number of children and the short duration of follow-up.

Thrombocytopenia as a Risk Factor for Retinopathy of Prematurity

Selim Sancak, Handan H. Toptan, Tulin Gokmen Yildirim, Guner Karatekin, et al. *Retina.* April 209 ;39(4):706-711

ROP has been associated with numerous risk factors including the upregulation of VEGF leading to retinopathy. Platelets preserve and supply proangiogenic mediators such as VEGF and play a role in the regulation of angiogenesis. The authors then postulated that thrombocytopenia can be a risk factor for ROP. This study identified patients with type 1 ROP in a retrospective cohort with using patients with no ROP as a control. In this study, the authors identified thrombocytopenia as a significant risk factor for type 1 ROP, in addition to erythrocyte and thrombocyte transfusion, bronchopulmonary dysplasia and duration on mechanical ventilation. The predictive factors which affect ROP include BPD and thrombocytopenia. The authors concluded that there was a significant association between thrombocytopenia and type 1 ROP.

Evaluation of a deep learning image assessment system for detecting severe retinopathy of prematurity

Redd T, Campbell J, Brown J, Kim S, et al. *Br J* Ophthalmol. May 2019;103:580-584.

Previous studies have shown that inter-examiner diagnostic variability is high when examining for ROP, even among “expert” clinicians. Therefore there is high interest in artificial intelligence technologies for ROP to improve screening and standardization of diagnosis. The artificial intelligence technique known as deep learning (DL) has already been used for certain eye conditions including diabetic retinopathy. These systems use computer-based imaging analysis to automatically evaluate images and detect disease. The DeepROP algorithm, developed by the Imaging and Informatics in ROP (i-ROP) research consortium has been used to detect plus disease with high accuracy. This system is used in this study to identify broader diagnostic categories of ROP from posterior pole images. A total of 4861 eye examinations from 870 infants were analyzed. Mean BW and GA were 901g and 27+/-2 weeks. A reference standard diagnosis of type 1 ROP was identified in 155 exams (3%). The deep learning system was found to have a 94% sensitivity for type 1 ROP. The negative predictive value was 99.7% - and high value for a screening test where underdiagnoses can have severe implications. The system’s vascular severity score was strongly correlated with expert ranking of overall disease severity. The system was able to detect severe ROP based only on the posterior pole vascular morphology. This suggests that severe

ROP rarely occurs in the absence of detectable changers in the posterior vasculature. Overall the results suggest this screening device could be used to improve the objectivity of ROP diagnosis as well as improve access to screening.

Heart rate variability changes and its association with the development of severe retinopathy of prematurity.

Hussein MA, Deng N, Rusin C, Paysse EE, et al. *J AAPOS.* Oct 2018; 22(5): 371-375.

The purpose of this retrospective case-control study was to evaluate for differences in autonomic nervous system (ANS) activity of premature infants with advanced retinopathy of prematurity (ROP). Heart rate variability (HRV) was used as an indicator of ANS activity. It was calculated in two groups of premature infants: (1) a treatment group of 15 infants who developed type 1 ROP and underwent treatment and (2) an age-matched control group of 8 infants, who did not develop ROP or only developed stage 1 ROP. The control group was also matched to the treatment group by weight and risk factors. No normative values are available for these indices in premature infants; Therefore, differences between the control and the study groups were assessed by comparing changes in HRV over time. HRV was analyzed during the first 5 days of life, within 5 days of initial ROP examination, and within 5 days of ROP treatment for the treatment group or, for controls, on the day of last electrocardiogram data prior to discharge. Calculations were performed for the high frequency, low frequency, and low frequency-high frequency values of the HRV components. Between the initial ophthalmologic evaluation and the final evaluation, there was a tendency for reduction in both the low- and high-frequency components of the HRV indices in the treatment group, whereas there was a tendency for an increase in both components of the HRV indices in the control group. None of which were statistically significant. The difference in the rate of change of the high frequency between groups was statistically significant ($P = 0.021$). The authors concluded that disruption in ANS activity may play an important role in the development and severity of ROP. This idea is very interesting, however the data presented was not very compelling, possibly due to study limitations including small sample size.

Effect of Patients' Clinical Information on the Diagnosis of and Decision to Treat Retinopathy of Prematurity

Andreas Gschlieber, Eva Stifter, Thomas Neumayer, Elisabeth Moser, et al. *Retina* November 2018; 38:2253-2259.

This prospective cross-sectional study evaluated the effect of patients' clinical information on experts' diagnoses of ROP and decisions to treat. 7 experts assessed wide-field fundus photographs of eyes of 52 premature infants for ROP diagnosis and the necessity for treatment for 2 days. On Day 1, they were masked to all patient data. On Day 2, they were given information on gestational age and birth weight. After receipt of patients' clinical information, there was a

significant shift in the experts' ratings towards a less aggressive ROP grading stage and less frequent decision for intervention. This was truer for heavier/less premature infants (gestational age >/= 28 weeks or BW >/= 900 grams) than those with very low BW/high prematurity (GA < 24 weeks or BW < 600 grams).

The results of this study suggest that knowledge of patients' clinical information influences the grading of ROP disease and decision for treatment, as ROP staging seemed to be set at a lower level and the decision for treatment at a higher threshold for heavier/less premature babies. The authors raise an important point that the key issue to be addressed is the problem of subjectivity in ROP assessment. Despite the lack of objective metrics of disease severity and the fact that various examination methods exist, examiners ultimately make decisions based on their own interpretations of results. Although inherent subjectivity is a problem, individual decisions are triggered or reinforced by external confounding factors that merit further study.

Parents' Knowledge and Education of Retinopathy of Prematurity in Four California Neonatal Intensive Care Units

Eneriz-Wiemer M, Liu SD, Chu MCY et al. *Am J Ophthalmol.* 2018; 191: 7-13.

The purpose of this study was to evaluate the lack of parental knowledge about Retinopathy of Prematurity (ROP) in order to better understand gaps in screening and treatment. To do this the authors performed a cross sectional study in four NICUs in California with 194 parents of very low birth weight infants between 2013 and 2015 completing phone surveys. They called parents 4 weeks after discharge asked parents what they knew about ROP and how they were educated about this disease. The goal was to talk to parents after the first outpatient ROP visit. They then used multivariate analysis to determine if parental understanding of ROP was associated with English proficiency and literacy, method of education, and infant transfer status. There was a 68% rate of returned survey and of those, half of the parents reported receiving information about ROP status at the patient's discharge. Parents reported treatments for ROP including steroid injections, eye drops, lights, oxygen, and blood transfusions demonstrating a clear lack of understanding. Patients with limited English proficiency had lower odds of knowing that low birth weight and prematurity were risk factors for ROP. The authors did not survey the health care providers on what education was actually provided, and highlighted this as a limitation. The authors concluded that patients with limited English proficiency had less knowledge about ROP.

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

Lee Y-S, Chang SHL, Wu S-C, See L-C, Chang S-H, Yang M-L, Wu W-C. *Eye* (2018) 32, 104–112

The eyes of preterm children have more highly curved corneas, shallower anterior chambers, thicker lenses, and shorter axial lengths (ALs) than those of full-term children; these differences become more significant as the severity of ROP increases. Preterm children with or without a history of ROP have a thinner retinal nerve fiber layer (RNFL) than full-term children. Glaucoma is a progressive optic neuropathy characterized by RNFL thinning and it is recognized as an important cause of visual decline in children with severe ROP after surgery. Myopia, especially high is strongly associated with glaucoma. The mechanical stretching of the ocular structure alone or insufficient ocular perfusion in people with myopia can lead to RNFL damage. An analysis of the ganglion cell layer (GCL) might be a powerful predictor to diagnose and monitor glaucoma. The present study performed detailed measurements of the optic nerve head (ONH) and inner retinal structures (including the peripapillary RNFL and mGCC). This study recruited two cohorts of children: children with a history of treatment- requiring ROP. The second cohort consisted of age-matched healthy controls born at > 37 weeks; Birth weight > 2500 g and they did not present with any ocular disease except refractive errors. ROP grade was categorized by the maximal severity in the acute stage. Patients were excluded if they had stage 4 or 5 ROP and had undergone vitrectomy or scleral buckling. Patients with residual retinal sequelae of ROP, including retinal detachment or macular dragging or fold, were also excluded. To measure the ONH, RNFL, and mGCC, the standard glaucoma module was used. The peripapillary RNFL thickness was measured at a diameter of 3.45 mm around the center of the optic disc. The mGCC consists of three layers: the RNFL, the GCL, and the IPL.The mGCC scan covered a 7 × 7 mmarea in the macula and was centered 1 mm temporal to the fovea to improve coverage of the temporal macula. Four types of data (average, superior, inferior thicknesses, and superior- inferior difference) were used to analyze the mGCC. The mGCC global loss volume (GLV) and focal loss volume (FLV) metrics are designed to detect patterns of loss. The GLV detects diffuse loss, and the FLV detects localized loss over the mGCC map. A total of 41 eyes of 21 preterm children and 34 control eyes of 17 full-term children were included in this study. The mean GA of children in the ROP group was 26.2 ± 2.1 weeks (range, 23–36 weeks) and 39.0 ± 1.7 weeks (range, 37–41 weeks) in the control group (P0.001). The mean BW of the children in the ROP group was 919.4 ± 260.8 g (range, 552–1530 g) and 3195.9 ± 384.3 g (range, 2500–3878 g) in the control group (P0.001). The mean age (years) at examination was 9.6 ± 2.5 in the ROP group and 8.4 ± 1.7 in control group (P = 0.14). In the ROP group, all of the eyes (100%) were zone 2 ROP. Six eyes (14.6%) were stage 2 ROP plus disease, and 35 eyes (85.4%) were stage 3 ROP plus disease. A total of 37 (90.2%) eyes were treated with diode laser photocoagulation, and 4 eyes (9.8%) were treated with diode laser photocoagulation and IVB. A significant greater spherical equivalent was seen in the ROP cohort. (Myopia 4.6 vs 0.4 D). Other analysis revealed similarity in average AL between the two cohorts, significantly shallower ACDs and thicker LTs in the ROP cohort, and no differences in the vitreous depth, baseline intraocular pressure, central corneal thickness. The average RNFL thickness of children with ROP did not significantly differ from that of full-term children (108.4 ± 16.0 μm

and 109.5 ± 12.1 μm, respectively, P = 0.91). The peaks near the superior and inferior sectors showed a temporal deviation in the ROP group, which means that the superotemporal and inferotemporal sectors were thicker, and the superonasal and inferonasal sectors were thinner. The average, superior, and inferior mGCC thicknesses were all thicker in children with a history of ROP than healthy children. mGCC difference between the superior and inferior areas was similar across these two groups (P = 0.20). The spherical powers, cylindrical powers, and spherical equivalent in all patients were positively correlated with RNFL thickness. The AL in all patients was negatively correlated with RNFL thickness. The ACD in all patients was not correlated with RNFL thickness. there was no significant correlation between mGCC thickness and spherical powers, cylindrical powers, spherical equivalent, AL, or ACD among all patients. Preterm children with a history of ROP have poorer best-corrected visual acuity, shallower ACD, greater LT, changes in peripapillary RNFL distribution, and greater mGCC thickness with increased mGCC-FLV compared with full-term children Inner retina in children with a history of ROP was thicker and had a different distribution pattern than those of full- term children. The temporal RNFL thickening in children with a history of ROP was related to the disrupted development of the inner retina rather than the temporal shift of RNFL peaks in axial myopia observed in full-term children.

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

Fleck BW, Williams C, Juszczak E, Cocker K, BJ Stenson BJ, Darlow BA, S Dai S, Gole GA, Quinn GE, Wallace DK, Ells A, Carden S, Butler L, Clark D, Elder J, Wilson C, S Biswas S, Shafiq A, King A, Brocklehurst P, Fielder AR for the BOOST II Retinal Image Digital Analysis (RIDA) Group. *Eye* (2018) 32, 74–80

Variation in the rates of severe ROP between clinical centers have been attributed in part to observer bias. A number of studies have demonstrated interobserver variation when grading ROP using retina images. This study aimed to determine whether international variation in the interpretation of images and subsequent treatment decisions was present. Nine readers from Australia, two from New Zealand, and seven from UK who participated in the BOOST II trials were used. The median (range) number of years' experience of the readers in performing clinical ROP screening examinations was 25 (14–26) for the UK group, 15 (3.5–40) for ANZ, and 21 (10–38) for the international reference group. Each reader assessed 48 eye examinations. Seventeen of the 42 (40.5%) image sets were obtained at the time when a decision to treat was made, or immediately prior to treatment. Thirteen of the 42 (31.0%) image sets were from infants who did not require treatment at the time of imaging, but who were subsequently treated. Twelve of the 42 (28.6%) image sets were from infants who were not treated for ROP at any time. Of the 42 eye examinations reviewed the mean (SD) number of examinations per reader judged as 'plus' disease was 14.1 (6.23) for

UK readers, 8.5 (3.24) for ANZ readers, and 13.2 (6.31) for the international readers (Table 1). The difference between UK and ANZ readers was significant (t-test P = 0.021, mean difference = 5.69, 95% CI = 0.98–10.40). Examinations per reader classified as stage 2 was higher in the ANZ group than in the UK group (t-test, P = 0.026, mean difference = 7.47, 95% CI = 1.00–13.94). For stage 3 there were no significant differences between the groups. The proportion of eye examinations read as each zone was not significantly different between any pair of groups. Agreement was highest within the ANZ group for all measures, with 'moderate' agreement for treatment decisions and for plus disease categories. Agreement was 'fair' for treatment decisions within the UK group. Agreement was poor for most measures within the INT group. UK ophthalmologists demonstrated a lower threshold to treat than Australian and New Zealand ophthalmologists. UK ophthalmologists graded more images as plus disease, and more images as treatment-requiring. There were no significant differences in grading stage 3 disease or ROP zone. The UK ophthalmologists had more inter-observer variation than the Australian and New Zealand ophthalmologists. Intra- observer consistency appeared to be good among all ophthalmologists. The international reference ophthalmologists graded in a similar way to the UK ophthalmologists. it is likely that variation in treatment rates between countries was due to international variation in ROP grading and treatment decisions.

9. STRABISMUS

Strabismus – double vision, binocular vision and visual perception

Comparison of a new digital KM screen test with conventional Hess and Lees screen tests in the mapping of ocular deviations

Thorisdottir RL, Sundgren J, Sheikh R, Blohme J, et al. *JAAPOS*. Aug 2018;22(4):277–280.e6

This paper's goal is to evaluate the digital KM screen computerized ocular motility test and to compare it with conventional nondigital techniques using the Hess and Lees screens. Patients with known ocular deviations and a visual acuity of at least 20/100 underwent testing using the digital KM screen and the Hess and Lees screen tests. The examination duration, the subjectively perceived difficulty, and the patient's method of choice were compared for the three different tests. The accuracy of the test results was compared using Bland-Altman plots between testing methods. A total of 19 patients were included in this study. Examination with the digital KM screen test was less time-consuming than tests with the Hess and Lees screens (P < 0.001 and P = 0.003, respectively, compared with the digital KM screen). Patients found the test with the digital KM screen

easier to perform than the Lees screen test (P = 0.009) but of similar difficulty to the Hess screen test (P = 0.203). The majority of the patients (83%) preferred the digital KM screen test to both of the other screen methods (P = 0.008). Bland-Altman plots showed that the results obtained with all three tests were similar. The authors conclude that the digital KM screen is accurate and time saving and provides similar results to Lees and Hess screen testing. It also has the advantage of a digital data analysis and registration. From this study digital KM screen should be considered over the nondigital Lees and Hess screen testing.

Anatomy

Magnetic Resonance Imaging of the Globe-Tendon Interface for Extrocular Muscles: Is There an "Arc of Contact"?

Clark RA and Demer *AJO* 2018 October; 194: 170-181.

The authors of this paper performed MRIs in 18 normal patients and 14 strabismic patients in order to test the "arc of contact" biomechanical model of extraocular muscle force transfer to the globe. Each extraocular muscle leaves its insertion and wraps around the globe for a contact arc, and then leaves the globe and heads towards its insertion and this "arc of contact" model is what has historically used to understand the angle at which the muscles are acting upon the globe. However this model, mathematically, assumes that the tendon is infinitely thin at that portion where it touches the globe, and that the muscle leaves at a perfectly straight line towards its insertion. The authors sought to test this mathematical model by evaluating the angle at the insertion of the muscles compared to the angle predicted by the "arc of contact" model. Using MRI, the angle measured at the insertion during large ipsiversive ductions and the angle predicted on the "arc of contact" model were compared. The authors found that for the normal extraocular muscles, the measured angle was larger than predicted by the traditional "arc of contact" method. In strabismic patients, the authors found that the measured angle was also greater than predicted for the medial rectus in abducens palsy, after medial rectus resection, but not after lateral rectus recession. The authors make a case that the "arc of contact" model needs updating with information that we obtain from modern imaging techniques. Of note, there is a (strong) letter to the editor highlighting a few extra limitations of the paper, namely the technique of using extreme ipsiversive gaze and suggests an overstatement of their conclusions.

Optical Coherence Tomography in Children With Microtropia.

Manuel Angel Garcia-Garcia, Jose I.Belda, Konrad Schargel, Maria Jose Santos et al *J of Ped Ophth & Strabismus*.2018; 55(3): 171-177

The purpose of this retrospective, observational, and transversal study is to assess whether optical coherence tomography(OCT) could be useful for detecting

and documenting fixation in patients with microtropia. A total of 25 patients were included: 15 with microtropia (study group) and 10 without tropia and with foveal fixation and stereopsis (control group). Retinal fixation observation was performed using spectral-domain OCT on amblyopic children with microtropia. The position between the retinal fixation point and the anatomical fovea was measured, in microns, using the system software tools. Only patients with a high level of cooperation, OCT scan quality signal of 7 or better, and visual acuity of 0.70 logarithm of the minimum angle of resolution (logMAR) or worse in the amblyopic eye were included. The study showed that in the study group, microtropia was previously diagnosed in 67% of cases through the cover test, and was predominantly in the left eye (73%). The average visual acuity of the sound eye was 0.03 decimal and 0.18 logMAR in the amblyopic eye. The microtropia was 3.73 ± 3.34 prism diopters and eccentric fixation (387 ± 199 µm) with OCT was observed in all cases except one. Eccentricity was predominantly in the superonasal quadrant (57%). Both eyes in the control group and the contralateral eyes of the study group showed foveal fixation. The authors conclude that OCT can aid in the detection of eccentric fixation and provide a relative degree of location of the retinal fixation point. Therefore, OCT can play an important role in the detection and measurement of eccentric fixation in eyes with microtropia, providing a high sensitivity compared to other methods. The small experimental sample size and the study design (observational and retrospective) limit the results. Furthermore, comparison with a gold standard or reference test, such as microperimetry, would be of value. Further more the instability of fixation in amblyopic or strabismic eyes is another important bias factor to be considered.

Neuroanatomical Structures in Human Extraocular Muscles and Their Potential Implication in the Development of Oculomotor Disorders.

Ala Paduca, Jan Richard Bruenech *JPOS.* 2018;55(1):14-22

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

the receptors can be questioned and some uncertainties remain. The purpose of this study was to review the related literature and discuss the possible role of ocular proprioceptors in relation to binocular vision and the development of eye motility disorders.

Strabismus – Cranial Nerve palsy

Strabismus – Childhood XT and ET

Duane's retraction Syndrome in a Cohort of South African Children: A 20-year clinic-based review.

Annalien Steyn, Rhian Grotte, Christopher Tinley. *J of Ped Ophth & Strabismus* 2019; 56(4): 248-253

The purpose of this retrospective case series is to describe the clinical features of Duane's retraction syndrome in a cohort of South African children and to analyze the differences between ethnic groups. The charts of 120 patients between 1997 and 2017 at a tertiary referral center in Cape Town, South Africa were reviewed. The study showed that type 2 Duane's retraction syndrome was most common in black children (54%), whereas type 1 was predominant in mixed race (68%) and white (94%) children. In this cohort, 63% of black children with Duane's retraction syndrome were boys, whereas 69% of white children and 59% of mixed race children were girls. Left eye involvement was the most common in all ethnic groups (44%), followed by right eye (41%) and bilateral (14%) involvement. The average age at presentation was 34.2 months (range: 1 to 144 months). Strabismus in primary position was present in 57 patients (46%), of whom 39% had esotropia and 61% had exotropia. A deviation in the primary position was more common in black (71%) children than in mixed race (39%) or white (41%) children. Ametropia was found in 94 patients (79%), amblyopia was present in 15 patients (13%), and 41 patients (34%) underwent surgery. The authors concluded that this is the first study to provide robust data on the profile of pediatric Duane's retraction syndrome in the three main ethnic groups in South Africa, and it showed clear ethnic differences. Among black children, boys are affected more often, the proportion with type 2 Duane's retraction syndrome is more frequent, and surgery is required more often. Among white and mixed race children, girls are affected more often and type 1 Duane's retraction syndrome is predominant. Limitations of this study largely surround its retrospective, clinic-based design. Incidence rates of Duane's retraction syndrome cannot be inferred because it is not population-based. It is possible that a proportion of the children with Duane's retraction syndrome within the population did not present to the clinic and were therefore not included. Unavoidable inaccuracies arose in history-taking due to language barriers, and the authors relying on caregivers' recollections of the onset of deviation, without the aid of photographs. Nevertheless, this

study is the first to provide robust data on the profile of pediatric Duane's retraction syndrome in the three main South African ethnic groups.

A Comparison of the Maximum Deviation Measured in Intermittent Exotropia using Various Clinical Conditions

Algee, Kailee; Walsh Leah; Hahn, Erik *Journal of Binocular Vision and Ocular Motility,* 2019; 69:2, 73-81

Determining the maximum deviation in intermittent exotropia (IXT) is imperative to maximize surgical intervention when indicated. IXT can be partially controlled by fusional mechanisms, such as accommodative convergence, tonic convergence, tenacious proximal fusion, and proximal convergence. Measuring the deviation at near with additional plus lenses (+3D), performing distance measurements with a fixation target at greater than 6m (in this study a distance of 20m was used), and prolonged monocular occlusion (PMO). The purpose of the study was to determine if these specific tests elicit clinically significant differences in the size if deviation amongst IXT patients. The results showed that there was a clinically significant increase in the near deviation with any tests, with the greatest increase in measurements elicited by +3D lenses after PMO. Although the difference in near deviation increase between the +3D lenses after PMO group and the +3D lenses without PMO group was insignificant. At distance fixation the greatest impact on deviation was measured at 20m (with or without prior PMO) statistically, but that did not translate clinically. The authors conclude that +3D lens measurements at near and 20m measurements at distance are the most clinically efficient tests for determining the maximum deviation in IXT patients.

Clinical and surgical risk factors for consecutive exotropia.

Bryselbout S, Promelle V, Pracca F, Milazzo S. *Eur J Ophthalmol.* Jan 2019.

This study retrospectively examined 74 patients with consecutive exotropia to determine risk factors for this surgical outcome. The majority of patients had preoperative amblyopia. Amongst all of the risk factors which were analyzed including age of strabismus onset, oblique dysfunction, anisometropia and stereopsis abnormalities, preoperative amblyopia was the strongest predictor of post operative exotropia. The authors emphasize that this should be considered during surgical planning for an esotropia and will be useful for counseling families regarding potential complications from surgery.

Congenital monocular Strabismus fixus

Kai Jie Wang, Qing Lin Chang, Feng Yuan Man, Juan Ding et al. *J Ped Ophthal & Strabismus.*2018;55(6):363-368

The purpose of this retrospective observational case series is to investigate the clinical characteristics and magnetic resonance imaging (MRI) findings of the extraocular muscle and ocular motor nerves in congenital monocular strabismus fixus. Three patients presented with unilateral non-progressive strabismus fixus with marked limitations of movement in all directions since birth. Of the three patients, one presented with esotropia, one with a large degree of exotropia and hypertropia, and one with an almost normal primary position. All three patients had normal ocular motor nerves, but adherences among the extraocular muscles, posterior Tenon's capsule, and the globe within the muscle cone on MRI. Two patients underwent strabismus surgery, but there were no postoperative improvements in the primary position and eye movements. The authors conclude that extensive adherences among the extraocular muscles, posterior Tenon's capsule, and globe may partially explain the cause of congenital monocular strabismus fixus and why strabismus surgery was ineffective. The findings further highlight the importance of MRI in detecting and characterizing atypical forms of strabismus. There are some limitations to this study. This is a retrospective study with a relatively small sample size. However, this disease is rare, and it will hopefully be of benefit to have a better understanding of the clinical characteristics to offer a tailored treatment plan and have an informed prognosis.

Decompensated Esophoria as a Benign Cause of Acquired Esotropia

Ali MH, Berry S, Demer JL, et al *Am J Ophthalmol.* 2018 October; 194:95-100.

This is a retrospective, interventional case series aimed at determining clinical and magnetic resonance imaging (MRI) characteristics of patients with adult, acquired, comitant esotropia due to decompensated esophoria. The authors looked retrospectively at 8 patients with a mean age of 29 years. These patients had a history of gradually progressive intermittent binocular diplopia and on exam had 31$\underline{+}$12 prism diopters of esotropia at distance and 29 $\underline{+}$12 prism diopters at near. All patients had a neurologic exam and MRI, which were normal. For all patients, orthoptropia and resolution of the double vision was achieved with bilateral medial rectus recession, though some patients continued to have esophoria. The authors concluded that decompensated esophoria is a cause of acquired esotropia in adults and proposed that patients with acute acquired comitant esotropia and no other neurologic signs or symptoms should be considered to have this benign condition. While this is an important entity to describe, the authors fail to point out the small sample size and that neurologic causes, in the absence of clear history of esophoria, should still remain in the differential.

Long-Term Follow-Up of Cyclic Esotropia

Carlos Souza-Dias MD, Burton J. Kushner MD & Luiz Eduardo Rebouças de Carvalho MD *Journal of Binocular Vision and Ocular Motility*, 2018; 68:4, 148-153

A retrospective review of 7 patients with cyclic esotropia who underwent bilateral medial rectus recessions to describe the development and treatment of cyclic esotropia. Cyclic esotropia is extremely rare, it typically manifests on alternate days with the esotropia being present one day for 24 hours followed by 24 hours of no deviation. Some patients may have a 3, 4, or 5-day cycle. The deviation is typically between 30 and 40 prism diopters. Cyclic esotropia may be associated with seizure disorders, hyperkinesia, behavioral problems, menstrual cycles, etc. It can be present for many years, may disappear spontaneously, or may become constant. The mainstay of treatment is surgical, surgical dose is determined by the deviation present on the esotropic days.

The Role of Dynamic Retinoscopy in Predicting Infantile Accommodative Esotropia and Influencing Emmetropization

Deniz Somer, Esra Karabulut, Fatma Gul Cinar, Ugur Emrah Altiparmak & Nurten Ünlü *Journal of Binocular Vision and Ocular Motility*, 2018; 68:2, 54-58

The goal of the study was to determine the role of dynamic retinoscopy in reducing the occurrence of infantile accommodative esotropia and facilitating emmetropia. Infants with greater than 5 diopters of hyperopia in their more hyperopic eye were assessed with cycloplegic refraction and their accommodation was tested with dynamic retinoscopy at 33cm. Infants with normal accommodation were followed without spectacle correction, patients with subnormal accommodation were prescribed partial hyperopic correction to neutralize the with-motion on dynamic retinoscopy. Patients were followed regularly monitoring for the development of esotropia. None of the patients with neutral dynamic retinoscopic responses indicating normal accommodation developed strabismus. Of the patients placed in spectacles to partially correct their hyperopia due to their subnormal dynamic retinoscopy accommodation 53% did not develop strabismus and 47% developed strabismus. The authors found a direct correlation between the degree of hyperopia and the development of esotropia amongst the groups. The emmetropization rate between the groups was not statistically significant. The authors conclude that dynamic retinoscopy can predict which orthotropic hyperopic infants can be observed without spectacles and are not at risk of developing esotropia, and which are at risk.

Esodeviation without correction for tapering hyperopia in refractive accommodative esotropia

Ha S, Suh Y, Kim S. *Can J Ophthalmol.* October 2018;53(5):453-457.

Full hyperopic correction is typically used to treat refractive accommodative esotropia. There are no standardized protocols for reducing hyperopic correction as children age. The purpose of this study was to investigate the clinical features of children whose hyperopic correction was tapered while maintaining visual acuity and stereoacuity. 106 patients were enrolled with mean follow-up period of 3.1

years. Only those patients with esodeviation within 8 PD in hyperopic correction were included. The medial amount of tapered hyperopia at each visit was 0.5D, with tapering intervals of 4-6 months. Baseline refraction was 7.6 +/- 1.5D. The patients had to maintain alignment within 8PD esodeviation with correction at distance and near at the time of tapering. At the final visit, there was no significant changes in visual acuity, esodeviation with correction, or near stereoacuity. They found a correlation with the amount of tapering with a reduced esodeviation without correction, suggesting that this could be used as a clinical indicator for tapering hyperopia. The authors do note that this was not a controlled study, so caution should be exercised when interpreting results.

The Effect of Prism Adaptation on the Angle of Deviation in Convergence Excess Esotropia and Possible Consequences for Surgical Planning.

Garretty T. *Strabismus.* 2018 Sep;26(3):111-117.

Previous studies by the author demonstrate a poor success rate of strabismus surgery in children with convergence excess esotropia. The author postulates that this is due to a distance deviation that is not revealed by cover testing. Furthermore, monocular occlusion has been found to change the measurement by up to 20 PD at both distance and near. The authors performed a prospective study of 49 children (mean age 7.2 years old, range 4-10 years) with convergence excess who underwent prism adaptation prior to strabismus surgery. The median angle of deviation at near was 25 PD (12-50) and at distance was 6 PD (1-20). This increased to 50 PD (30-70) and 30 PD (8-50) at distance. Twenty-eight (47%) required a change in prism strength during the adaptation period. An increase of 10PD or more was seen in 39 of 49 children at near and 41 of 49 at distance. Forty-six (83.6%) were full binocular post-operatively. The authors conclude that prism adaptation frequently reveals an otherwise masked larger angle of deviation in convergence excess esotropia. They also suggest that convergence excess esotropia can further be divided into two categories: true and simulated, in which the simulated cases will have a distance deviation that approaches the size of the near angle following a period of prism adaptation. This in turn may influence surgical decision-making, as the risk of over-correction is lower.

Infantile exotropia and Developmental delay.

Gregg T.Lueder, Marlo Galli *J of Ped Ophth & Strabismus.*2018; 55(4):225-228

The purpose of this interventional case series was to determine the long-term outcome of surgery in children with infantile exotropia and developmental delay and to assess the need for neurologic evaluations. The records of infants who underwent surgery for the treatment of exotropia with onset during the first year

of life were reviewed. The preoperative ophthalmic and systemic findings, treatment, and developmental and ophthalmic outcomes were reviewed. Surgery was considered successful if the horizontal deviation was less than 10 prism diopters (PD). Developmental assessments were obtained at each visit. Twenty-six patients presented between age 2 and 10 months with exotropia ranging from 20 to 95 PD. Ten (38%) patients had a developmental delay that was recognized at the first visit, 9 of whom had a systemic diagnosis at that time; the other patients remained developmentally normal during a mean follow-up of 7 years. Age at surgery ranged from 4 to 18 months. Surgery was successful in 10 (38%) of 26 patients after 1 surgery and in an additional 13 (50%) of 26 patients after a second surgery. More than half of patients required more than one surgery, but the overall success rate with one or two surgeries was 88%.
The authors concluded that the need for more than 1 surgery was higher in infantile exotropia when compared to other forms of childhood strabismus, but most children achieved good alignment with one or two surgeries. Developmental delay is common in patients with infantile exotropia, but this was usually recognized at the time of the initial evaluation. In the current patients, routine neurologic screening or imaging of these otherwise developmentally normal infants was not required. A limitation of this study is that it included only those patients with early onset exotropia who underwent surgery. Surgery was performed for patients with constant or poorly controlled exotropia. This group would presumably be at greater risk for developmental problems than those with milder forms of intermittent exotropia.

Time and Factors Affecting the Direction of Re-drift in Essential Infantile Esotropia.

Kun-Hoo Na, Yoonae A.Cho, Seung-Hyun Kim *J of Ped Ophth & Strabismus.*2018; 55(2): 93-99

The purpose of this study is to investigate the development pattern of post-operative re-drift in patients with infantile esotropia and identify factors associated with the re-drift. A total of 112 patients with infantile esotropia who underwent surgery before the age of 3 years were included. Surgical outcomes were divided into (1) consecutive exotropia: more than 8 prism diopters (PD)of exodeviation;(2) recurrent esotropia: more than 8 PD of esodeviation; and (3) monofixation syndrome: maintenance of deviations within 8 PD. The occurrence rate, time of onset and associated factors of the re-drift were evaluated. At a mean follow-up of 9.5 years, consecutive exotropia developed in 37 patients (33.0%) and recurrent esotropia in 43 patients (38.4%). Whereas 76.7% of total recurrent esotropia cases were identified within postoperative 1 year, consecutive exotropia occurred constantly over 10 years postoperatively. The mean time to consecutive exotropia development from surgery was 78.6 months, greater than that of recurrent esotropia development (8.9 months) ($P < 0.001$). In multinomial logistic regression using monofixation syndrome as the reference category, fixation preference before surgery (odds ratio [OR]: 6.64, 95% confidence interval [CI]: 2.07 to 21.32) and the rate of myopic progression (OR: 15.07 per −1.00 D/year, 95% CI:

1.23 to 184.86) were associated with consecutive exotropia, whereas increase in the angle of esodeviation on postoperative day 1 (OR: 1.15, 95% CI: 1.04 to 1.26) was correlated with recurrent esotropia. The study showed that re-drift after surgery occurred in more than 70% of patients with infantile esotropia during a long-term observation period. There was a clear difference in the development pattern between exotropic and esotropic drift; most recurrent esotropia cases appeared within postoperative 1 year, whereas consecutive exotropia occurred constantly over a long period of time. Detailed evaluation before surgery and close observation of postoperative deviations and changes in refractive status will help to determine the surgical prognosis in patients with infantile esotropia. The study has several limitations such as retrospective nature and small number of cases. Also there was an interval between the onset of infantile esotropia and the time of operation.

Strabismus – Convergence / Divergence insufficiency

Inconsistent diagnostic criteria for convergence insufficiency.

Lavrich JB, Warner NJK, Hauschild AJ, Thau A et al. *JAAPOS* 2019 Feb;23(1):32. e1-32. e4.

Convergence insufficiency (CI) is a common entity but seems to be an ill-defined diagnosis that incorporates many near-vision symptoms. The current literature often varies in its criteria for diagnosis. Without a clear definition and standardization of the clinical examination, there is the potential for misdiagnosis and/or the inclusion of other diagnoses as CI. The purpose of this retrospective study was to assess the uniformity of diagnostic criteria in a well-defined practice environment. The medical records of 387 individuals diagnosed with CI between June 2007 and November 2014 who were patients of 6 fellowship-trained strabismologists in private practices and at Wills Eye Hospital clinics were reviewed retrospectively. The following data were collected: age, sex, race, age at diagnosis, past medical and family history, relevant symptoms, visual acuity, near point of convergence (NPC), strabismus measurements, and fusional amplitudes at distance with base-out and base-in prisms. Half of the patients were diagnosed with CI with normal NPCs. Only 246 of patients (29.7%) diagnosed with CI had documented fusional amplitudes. This study has demonstrated the variable range of criteria within one group of practitioners to diagnose CI. The authors conclude that no uniformity exists across clinicians in the clinical evaluation and diagnosis of patients with CI. They advocate the need for an evidence-based definition of the disease and its diagnosis. Interestingly, this study describes a group of the patients with CI that have NPCs at 1 cm but are symptomatic. These patients had poor fusional vergence amplitudes. The authors suggest that they may represent a separate subset within this disease or a separate diagnosis.

Postural Patterns of the Subjects with Vergence Disorders: Impact of Orthoptic Re-education, a Pilot Study

Delfosse, G., Bremond-Gignac, D., and Kapoula, Z. *British Orthoptic Journal,* 2018; 14(1), 64-70

Eye movements are essential for body control and equilibrium in addition to vision. The studies goal is to characterize the influence of vergence and orthoptic exercises on postural control. Postural control quality was measured by the Romberg test and was evaluated before and after orthoptic therapy for vergence disorders. Orthotic therapy decreased the amount of body sway with eyes open and at near fixation. There was no change in monocular versus binocular viewing conditions. But there was a small advantage in ocular dominance post-therapy. The authors conclude that orthoptic education and therapy can improve postural control in patients with vergence disorders.

Current Concepts in convergence insufficiency

Lynn H. Trieu and Judith B. Lavrich *Curr Opin Ophthalmol* 2018, 29:401-406 (Sept 2018)

The prevalence of convergence insufficiency (CI) is between 2-17% in the general population, and up to 49% in those suffering from traumatic brain injury. While there is no standardized measurement, using near-point convergence (NPC) and symptomatology is an appropriate screening measure that should be performed by all eye care professionals and those dealing with TBI patients. The most effective treatment for the condition is orthoptic exercises. Office based therapy is the most proven method for treatment. Home based computer therapy can be a good alternative based on some researchers and may be useful in those patients to whom office based therapy is either not practical or not available. Base-in prism glasses were not shown to be more effective than placebo in improving NPC, convergence amplitudes or symptoms. Patients with asymptomatic CI do not require treatment.
The article discussed the screening and diagnostic criteria currently in use for CI as well as the proven treatment methods. It is important given the degree to which vision therapy advances the cause of prism glasses and other unproven treatment techniques.

Near Point of Convergence in Iranian Schoolchildren: Normative Values and Associated Factors.

Hashemi H, Nabovati P, Khabazkhoob M, Yekta A, et al. *Strabismus*. 2018 Sep;26(3):126-132.

The near point of convergence (NPC) is an important diagnostic value, as it can identify conditions such as convergence insufficiency which causes impaired vis-

ual performance at near. The authors performed a cross-sectional study evaluating the NPC of 5444 children age 6-12 years in northern Iran. The mean NPC was 8.08 cm, without differences based on gender or geographic location. However they did find that each year increase in age was associated with a 0.18 cm recession in NPC ($p<0.001$). Myopes had the least remote NPC and hyperopes had the most remote NPC. They note that the NPC is more remote in their population than what is commonly cited in the literature (2.80-3.90 cm), which the authors feel may be attributable to the type of fixation target, racial differences, and age.

Strabismus – Acquired

Spasm of the Near Reflex: Literature Review and Proposed Management Strategy

Hyndman *Journal of Binocular Vision and Ocular Motility*, 2018; 68:3, 78-86

The purpose of the article is to identify, explain, and manage spasm of the near reflex (SNR) by reviewing the literature. SNR includes excessive accommodation leading to pseudomyopia and blurred vision, convergence spasm leading to esotropia and diplopia, and pupil miosis. Other symptoms include headache, eye pain/strain, micropsia, macropsia, and dizziness. A literature review was performed and 44 articles were included. Patients don't always present with all three components at the same time and the condition may be missed because of this. A cycloplegic refraction is essential in the diagnosis to detect pseudomyopia. The presumed etiologies for SNR are most commonly secondary to head trauma, functional/psychogenic, organic/neurologic, or other. Proposed treatments include treating the underlying condition if found, psychiatric evaluation and medication, prolonged cycloplegia and plus lenses to break the cycle, overminusing, orthoptic exercises, miotics, and medial rectus botox. Prognosis is variable, SNR due to psychogenic causes often resolves with therapy and head trauma cases have the poorest prognosis. The authors proposed a treatment algorithm. The authors conclude that SNR has highly variable in presentation, from various causes, and response to treatment is unpredictable.

Double vision in adults

Travis Peck & David Goldberg *Journal of Binocular Vision and Ocular Motility*, 2018; 68:3, 63-69

A retrospective chart review of 125 patients to determine the patient characteristics, presentation patterns and incidences of the various etiologies in adult patients presenting with a chief complaint of double vision. Approximately 4% of adults are diagnosed with new onset strabismus. The majority of patients presented in the 8th and 9th decades of life. The most common type of strabismus was a small angle HT (21%), followed by ET (20%), XT (14%), palsies not includ-

ing trochlear palsy (12%), and trochlear palsy (8%). Of patients with non-paralytic ET 80% had divergence insufficiency. The etiologies of strabismus leading to diplopia were vast, including neurovascular compromise, narcotic use, Lyme disease, dementia, myasthenia gravis, thyroid eye disease, orbital inflammation/mass, neurologic disease, idiopathic, etc. 11% of subjects complaining of diplopia were found not to have strabismus. The author discusses the age-related changes in the EOM pulleys as a cause of ET greater at distance than near in patients over the age of 75.

Adult-onset nonparalytic, small-angle hypertropia

Shah SM, Martinez-Thompson JM, Diehl NN, Mohney BG. *JAAPOS*. Dec 2018;22(6):438-440.

The purpose of this paper is to describe the prevalence and clinical features of a common but underrecognized disorder of adult vertical strabismus. The medical records of all adult (≥19 years of age) residents of Olmsted County, Minnesota, diagnosed with nonparalytic, small-angle hypertropia (NPSAH) from January 1, 1985, through December 31, 2004, were retrospectively reviewed for demographic and clinical features. Of 753 patients diagnosed with adult-onset strabismus, 99 (13.1%) were found to have NPSAH, yielding an annual incidence of 7.50 per 100,000 patients >18 years of age and a cumulative incidence of 1.28%. The median age at diagnosis was 71 years (range, 27-98 years); 63 (64%) of the patients were women. Diplopia was reported at the initial diagnosis in 91 patients (93.8%), with 90 (92.8%) having the diplopia in primary or reading position. The median initial angle of hypertropia was 2^{Δ} (range, 1^{Δ}-22^{Δ}) at near and 2^{Δ} (range, 0^{Δ}-12^{Δ}) at distance. Only 3 patients had an initial deviation of at least 11^{Δ} . After a median follow-up of 10.8 years (range, 6.2 months to 23.7 years), the final median angle of vertical deviation was 4^{Δ} (range, 0^{Δ}-20^{Δ}) at near and 4^{Δ} (range, 0^{Δ}-16^{Δ}) at distance for all 99 patients. 84.8% of the patients received prisms during the follow up period and only one underwent surgery. NPSAH is a relatively common but infrequently recognized disorder among adults. NPSAH was more prevalent among elderly and female patients in this study cohort and the vast majority presented with diplopia and a hypertropia of ≤10^{Δ} that progressed over time.

Strabismus – Misc

Risk factors for strabismus following glaucoma drainage device implantation for refractory childhood glaucoma.

Talsania SD, Nallasamy N, Lee AR, Freedman SF *JAAPOS* 2019 June; 23 (3): 145.e1-145.e6

Strabismus is common in children after glaucoma drainage device (GDD) implantation, but the risk factors for postoperative strabismus remain speculative. The purpose of this retrospective study was to investigate possible risk factors for strabismus following GDD

implantation for refractory childhood glaucoma. A total of 81 consecutive patients (mean age, 7.9 ± 4.8 years) who underwent GDD implantation for refractory childhood glaucoma at Duke Eye Center from 2005 to 2016 were reviewed retrospectively. Pre- and postoperative motility and alignment, best-corrected visual acuity, and demographic and surgical data were extracted from the medical record for analysis. The most common glaucoma type was glaucoma following cataract surgery (GFCS), and the most common GDD was a Baerveldt 250 mm^2 device. Before GDD surgery, 38 patients (47%) had documented strabismus. After GDD implantation, 25 (31%) had new or worsened strabismus, with vertical (16% of new/worsened), horizontal strabismus (exotropia, 48% of new/worsened; esotropia, 12% of new/worsened) and vertical and horizontal (24% of new/worsened) noted. New motility limitation occurred in 32 of 81 (40%) patients. Risk factors including age, type/location/number of GDD, revision, motility limitation, glaucoma type, asymmetric visual acuity, and visual impairment were not significantly associated with new or worsened post-GDD strabismus. The authors conclude that children with refractory childhood glaucoma are at increased risk for strabismus, which increases after GDD implantation; this study identified no clear risk factors for new or worsened post-GDD strabismus. Nonetheless, the families of patients undergoing GDD implantation should be counselled on the substantial risk of strabismus postoperatively.

Measuring attention bias in observers of strabismus subjects.

Raffa LH, Fennell-Al Sayed H, LaRoche R *JAAPOS* 2019 June; 23 (3): 141.e1-143-e5.

Despite the known negative psychosocial impact and the importance of facial aesthetics for individuals with strabismus, the gaze pattern and visual attention to faces with strabismus has not been documented previously. The aim of this study was to determine whether there is any attention bias toward the eye region in individuals with strabismus.Thirty images (15 digitally reconstructed color photographs to show strabismus and 15 photographs of volunteers without strabismus) were viewed in random order by 25 naïve participants (age range, 23-63 years; 15 females). Visual scan paths of participants were recorded using an infrared corneal image eye movement recorder, and the individual parameters of saccades, fixations, and dwell time were assessed using DataViewer software. Viewers primarily tended to fixate on the eyes, the nose was the next most prominent point of focus (both $P < 0.001$). Time to first fixation and the presence of strabismus in the images presented were significantly associated ($P < 0.001$). When presented with photographs of faces with and without strabismus, observers generally spent more time looking at the eye region, and more time was spent looking at the strabismic eye ($P < 0.001$). However, subjects were not more likely to look at the deviated eye before the “fixating” (straight) eye. The authors conclude that the presence of strabismus in the features of the human face draws longer attention from the average viewer to the eye region, and to the strabismic eye specifically. This interesting study used an objective tool to study the

pattern of visual attention to faces with strabismus, it broadens our understanding of how these faces are perceived by orthophoric observers.

Quantitative measurement of horizontal strabismus with digital photography.

Dericioğlu V and Cerman E. *JAAPOS* 2019 Feb;23(1):18. e1-18. e6.

The purpose of this study was to develop a method to calculate the gaze angle in photographs using a smartphone application and to determine its validity and reliability in real strabismus patients. The authors developed an application that provided measurements of the distance from the geometrical center of the cornea to the light reflex (RD) and corneal diameter (CD) based on photographs of the subjects' eyes. Photographs of 15 orthophoric subjects (A total of 1,022 photographs) were taken at different known gaze angles and imaging distances. The RD/CD ratio of each gaze angle was recorded. An equation to determine the best-fit line for the gaze angle data according to each RD/CD ratio was created. In a second clinical analysis, this equation was applied to photographs of strabismus patients (n = 72), and the results were compared with measurements taken by a double-masked strabismus specialist, who assessed the patients using either Krimsky or prism cover testing. A high correlation was found between the real and estimated gaze angles ($r = 0.990$, $P < 0.001$). The mean error of the estimated gaze angle was found to be $0.03^{\Delta} \pm 4.60^{\Delta}$. A high correlation was also documented between the measurements of the smartphone application and the strabismus specialist ($r = 0.966$, $P < 0.001$). The average error was $-0.68^{\Delta} \pm 6.1^{\Delta}$, and the reliability was high (Cronbach's $\alpha = 0.983$). The authors concluded that their application is highly reliable in measuring horizontal strabismus by using photographs.

This application simulates a Krimsky test and relies on corneal reflex for strabismus angle assessment; however, it cannot substitute the prism cover test, which remains the gold standard for quantifying strabismus. Patients with latent strabismus and corneal surface problems could not be assessed using this technique. Imaging was performed, while the patient was fixating on the camera, and thus only strabismus at near fixation was assessed. The concept of an accessible reproducible tool that can easily be used by non-skilled personnel to assess strabismus is very appealing, nonetheless this prototype still has several limitations.

Identification and Correction of Restrictive Strabismus After Pterygium Excision Surgery

Baxter SL, Nguyen BJ, Kinori M, et al. *Am J Ophthalmol.* 2019 June; 202: 6-14.

The authors of this study aimed to describe the clinical characteristics of patients who had restrictive strabismus and double vision after pterygium excision and to describe a successful approach to treat these patients. This was a retrospective interventional case series of fifteen patients at a single academic institution. The authors found a mean time to double vision was 6

months after pterygium surgery, and that all patients had abduction limitation causing a mean esotropia of 18 prism diopters. More than half of the patients this cohort had multiple previous pterygium surgeries, and more than half had amniotic membrane with fibrin glue used at the time of the initial surgery. Surgery to remove the scar tissue was multidisciplinary with a strabismus surgeon and oculoplastic or corneal surgeon. Forced duction testing intraoperatively was used pre and post to make sure that the restriction was relieved. The medial rectus was isolated in all cases using a medial limbal approach and the pseudotendons were excised. All patients received either an amniotic membrane graft (with sutures) or conjunctival autograft. Additionally, the authors used provisc around the muscles, 5-FU, MMC, steroids, and symblepharon rings in some combination depending on the patient's specific situation and surgeon preference but no strict protocol was used. After intervention (follow up average of 24 months), all patients were diplopia free in primary gaze, though 73% still had a small angle esotropia in the abductive, restricted field. Two patients had additional surgery for scar tissue but none had medial rectus recessions. The authors concluded that double vison caused by restrictive strabismus after pterygium surgery is more likely in patients with recurrent pterygium and for those treated with amniotic membrane with glue, but that this is treatable with scar tissue lysis and not eye muscle surgery. The authors point out the main limitation, which was that there was no standard protocol in how these patents were treated, but nonetheless this is an important article sine it demonstrates how removal of scar tissue, and not eye muscle surgery, can be curative in cases of restrictive strabismus after pterygium surgery.

Rectus Extraocular Muscle Paths and Staphylomata in High Myopia

Li Y, Wei Q, Le A, et al. *Am J Ophthalmol.* 2019 May; 201: 37-45.

The authors of this study performed a retrospective case control study over 25 years evaluating the relationship between the displacement of the extraocular muscles (EOMs) and staphylomas in patients with high myopia using magnetic resonance imaging (MRI). Twenty nine patients with high myopia, 11 age matched controls, and 34 patients with sagging eye syndrome underwent an MRI to evaluate the aspect ratio (AR) of the ocular cross section, locations of the EOMs and staphylomata, and the status of the superior rectus to lateral rectus band ligament (SR-LR). High myopia was defined as 5 or more diopters of myopia or axial length greater than 26.5mm. There were 17 patients (29 eyes) with staphyloma, 8 of whom also had strabismus. The authors found that staphylomata tended to be superotemporal, associated with a larger AR in the quasi-coronal plane, more inferior LR displacement, larger LR-globe angle, larger SR-LR displacement. Additionally, there were more SR-LR band ligament ruptures in the highly myopic patients with staphylomas than in those without staphyloma. The authors discuss the possible reasons for the SR-LR band ruptures, but no causality can be determined in this study.

The authors concluded that staphylomata in high myopia is associated with asphericity of the globe, inferior displacement of the LR path, and defect of the LR-R band ligament.

Reevaluation of Current Prism Standards with Recommendations to Increase Accuracy in the Measurement of Strabismus

Freedman K, Ray C, Kirk D. *Am J Ophthalmol.* 2019 Feb; 198:130-135.

This was a reliability and validity analysis of the standards of holding single prisms in measuring of strabismus. The authors calculated effective prism power (EPP) for glass and acrylic prisms held in different positions, specifically in the Prentice position (PP) and the minimum deviation position (MD). The authors nicely plotted the EPP according to rotational angle of the prism and they demonstrated that acrylic prisms held in the frontal plane position had the smallest amount of error induced by rotating the prism. Acrylic prisms had a smaller amount of error compared to glass prisms overall. The authors concluded that the use of glass prisms should be abandoned and reminds the reader to use the frontal plane alignment for minimal calculated error.

Does successful surgical correction of childhood large angle exotropia in adults make any difference to binocularity and quality of life?

Yao J, Qu X, Lin J, Liu H. *Strabismus*. 2019 Jul 23:1-7.

Prior studies have shown that strabismus surgery can have positive effects in adults with large angle exotropia. The authors sought to examine if successful postoperative alignment could significantly improve HRQOL and investigate the relationship between stereopsis and HRQOL in these patients. In this prospective, non-interventional study, the authors enrolled 34 patients (mean age 29.38 ± 8.78 years) with large angle exotropia of either the constant (15) or intermittent (19) subtype who underwent strabismus surgery. Success was achieved in 94.74% of the intermittent group and 73.33% of the constant group. Stereopsis improved in 19 patients and remained unchanged in 10 patients, without any statistically significant difference between the groups. Earlier age of surgery (p=0.05) and smaller preoperative angle of deviation at near (p=0.6) were found to be associated with normal stereopsis. All quality of life scores improved after surgery. The postoperative functional scores had no statistically significant association with the normal stereopsis (AS-20: p=0.07; A&SQ: p=0.16).
The angle of deviation at distance was significantly associated with the functional score of the AS-20 (p=0.02). The results of this study suggest that successful surgical correction of childhood large angle exotropia in adults improves both stereopsis and health related QOL, therefore is not solely for cosmetic purposes.

Global and regional prevalence of strabismus: a comprehensive systematic review and meta-analysis.

Hashemi H, Pakzad R, Heydarian S, Yekta A, et al. *Strabismus.* 2019 Apr 23:1-12.

The authors sought to define the prevalence of strabismus and investigate the affect of patient characteristics on the prevalence. Of the 7980 articles considered, they reviewed 56 articles with a sample size of 229396 patients. They found the pooled prevalence of any strabismus to be 1.93%, exotropia to be 1.23% and esotropia to be 0.77%. Age had a direct effect on the prevalence heterogeneity, as did the WHO region. ET had a higher prevalence in AMRO and EURO while XT was the dominant subtype in Asia, especially WPRO. The authors attribute this to a lower prevalence of hyperopia in these locations. The study is limited by the exclusion criteria which limited the number articles reviewed as well as the limited data sets from some populations. Overall it was helpful in that this study revealed that 1 in every 50 people had strabismus, which is useful in estimating the impact of strabismus.

Diagnostic occlusion test for acquired esotropia

AlAli A, Sherief S, MacNeill K, Quann K, et al. *Can J Ophthalmol.* April 2019;54(2):265-268.

Methods to suspend fusion during strabismus testing include the alternate cover test and prolonged monocular occlusion. The role of occlusion tests for eliminating tonic fusional divergence in esotropia is unclear. This study's aim is to assess the effectiveness 45 minute diagnostic occlusion test (DOT) on decreasing tonic fusional divergence in children with acquired esotropia. Children were randomly assigned to either a patch group or control group. The testing of alignment was done immediately after removing the patch. An increase of 5 prism diopters (PD) or more of esodeviation at distance following the patch test was deemed significant. 67 children were recruited, 37 in the patch group and 30 in the control. The results showed an average increase of esotropia of 6.4 PD in the patch group at distance. 11 subjects showed an increase of >-10 PD. Overall a >5PD increase was seen in 60% of subjects for distance and 70.1% of subjects for near. The differences for the control group were not significant. The authors conclude that the DOT can help determine the maximum angle of deviation present, which could help influence surgical dosing and the risk of surgical undercorrection.

Binocular Function in Subjects with Orthotropic Duane Retraction Syndrome

Lakshmi Marella, Bhagya; Moharana, Ruby; Kekunnaya, Ramesh *Journal of Binocular Vision and Ocular Motility*, 2019; 69:2, 64-68

The purpose of the study was to evaluate binocular vision parameters in subjects with orthotropic Duane retraction syndrome (DRS). The study compared the

near point of accommodation (NPA), near point of convergence (NPC), positive fusional vergence (PFV) reserve, negative fusional vergence (NFV) reserve, and stereopsis between DRS patients and a control cohort. NPA was found to be similar between the groups. NPC, PFV reserve at distance and near, NFV reserve at distance and near, and stereopsis were all significantly reduced in the DRS cohort compared to controls. The authors conclude that DRS subjects have good accommodation, but poor convergence when compared to normal controls.

Postoperative Stereopsis in Adult Patients With Horizontal Comitant Strabismus With Normal Vision Who Are Stereoblind.

Xiaohe Yan, Xiaming Lin.*J Ped ophth &Strabismus.*2018;55(6):407-411

The purpose of this study is to examine the stereopsis in patients with comitant horizontal strabismus who had normal vision and were stereoblind following the strabismus surgery. Twenty patients with primary comitant horizontal strabismus and normal corrected visual acuity were included in this study. The stereoacuity was quantitatively measured by the random dot butterfly stereotest, the Randot Preschool Stereoacuity Test (Stereo Optical, Inc., Chicago, IL), and synoptophore. The average prism deviation was 63.55 ± 18.52 prism diopters (PD) (range: 30 to 90 PD). The mean duration of strabismus was 17.93 ± 7.0 years (range: 5 to 30 years). At 3 days postoperatively, 22.2% (4 of 18) of the patients had improved stereopsis and the mean stereoacuity was 60 ± 28.28 seconds of arc by random dot butterfly stereotest and 150 ± 57.74 seconds of arc by Randot Preschool Stereoacuity Test ($P < .05$). For the fusion and stereopsis at far measured by the synoptophore, 11.1% (2 of 18) of the patients demonstrated recovery of fusion and substantial recovery of stereopsis. The mean stereoacuity (at far) was 200 seconds of arc. At the last follow-up visit (3 to 12 months, average 6.55 ± 3.46 months), 45% (9 of 20) of the patients demonstrated substantial near stereopsis recovery and the median stereoacuity was 53.33 ± 33.17 seconds of arc by random dot butterfly stereotest and 95.56 ± 63.07 seconds of arc by the Randot Preschool Stereoacuity Test ($P < .01$). A total of 25% (5 of 20) of the patients demonstrated recovery of fusion and 15% (3 of 20) of the patients showed substantial recovery of stereopsis at far. The median stereoacuity (at far) was 193.33 ± 179.26 seconds of arc. The study demonstrates that adult patients with comitant strabismus with good vision who are stereoblind benefit from strabismus surgery and the stereopsis significantly recovers in these patients. Strabismus surgery for these patients with comitant strabismus and good vision should not be considered only a cosmetic surgery.

The effect of oral statin therapy on strabismus in patients with thyroid eye disease.

Reynolds AL, Del Monte MA, Archer SM. *J AAPOS*. Oct 2018; 22(5): 340-343.

Statins, known to possess anti-inflammatory characteristics, have recently been identified as potentially reducing the risk of developing thyroid eye disease (TED) in Graves disease patients. The purpose of this retrospective review was to investigate the effect of oral statin therapy on strabismus related to TED. A total of 30 patients with TED and restrictive strabismus (average age, 63.9 years; 50% male; 59% current/former smokers) were included; 12 statin users and 18 nonusers. Both groups were characterized by the following parameters: smoking status, previous radioactive iodine, thyroidectomy, number of decompressions, motility restriction, amount of strabismus, number of surgeries, surgical dose, and number of muscles involved on radiography. Statin users averaged fewer decompressions (1.3 in users vs 2.4 in nonusers [P = 0.04]). Statin users on average had 15 mm of total strabismus surgery compared with 21.4 mm in the nonuser group (P = 0.09) and had fewer muscles involved radiographically (4.3 vs 5.1 [P = 0.08]) The authors concluded that statin users tended to have fewer decompressions, less restriction, fewer surgeries, and fewer muscles involved despite having more current smokers (36% vs 5%), more males, more RAI, and fewer thyroidectomies, all of which are associated with worse TED. In their cohort of patients with TED and strabismus, statin therapy significantly reduced the number of orbital decompressions. Oral statin therapy also trended toward reducing the number and amount of strabismus surgeries as well as radiographic indication of muscle involvement, although these did not meet statistical significance. The study's main limitation is its small sample size; a slightly increased cohort size may have been more conclusive.

Anomalous Vertical Deviations in Attempted Abduction Occur in the Majority of Patients with Esotropic Duane Syndrome

Rhiu S, Michalak S, Phanphruk W, and Hunter D. *Am J Ophthalmol.* 2018 November; 195: 171-175

This is a retrospective, observational case series of patient diagnosed with esotropic Duane syndrome over 13 years. The authors used clinical photographs of the patient's motility to describe the vertical eye position in attempted abduction; they grouped the patients into midline, depression or elevation based on these photos. Three separate ophthalmologists evaluated the photos. Of patients with unilateral esotropic duane syndrome 74/133 patients (66%) had depression in attempted abduction. 18/42 (43%) of the eyes with bilateral esotropic Duane syndrome were also found to have depression on attempted abduction. In the midline group, the limitation in abduction was found to be less severe. In the elevation group, the vertical deviation was more severe. The authors concluded that depression in attempted abduction is present in the majority of patients with esotropic Duane syndrome, yet the description of this is lacking. They speculate that this is likely another form of dysinnervation and that looking for this is important in surgical planning. This paper nicely describes a clinical finding we see often in pediatric ophthalmology practice, but one that has not been described in detail in the literature.

Binocular stereo acuity affects monocular three-dimensional shape perception in patients with strabismus

Sawamura H, Gillebert C, Tood J, Orban G. *Br J Ophthalmol.* October 2018;102:1413-1418.

This study aimed to examine the difference in 3D shape perception between normal subjects and those with strabismus. They did this by enrolling 20 patients with strabismus (mean age 22.3 years) compared to 25 age-matched subjects without strabismus (mean age 21.0 years). The strabismus subjects were further broken down into those with stereo and those without stereo. All participants had normal acuity in both eyes. They were asked to identify certain features of a 3D shape based on shading, texture, or motion cues. Differences in discrimination of texture, motion and luminance did not differ among the groups. Subjects with strabismus without stereo could not discriminate one-dimensional features of binocular disparity. Overall the results showed that patients with strabismus without stereo perceived monocularly defined 3D shapes poorly. This suggest a perceptual benefit of binocular stereopsis in patients with strabismus.

Nonsurgical treatment of diplopia

Michael J. Bartiss *Curr Opin Ophthalmol* 2018, 29:381-384

The author writes about the approach to treatment of diplopia. Monocular diplopia can often be related to improper refractive correction particularly astigmatism. To determine if this is the case a patient should be asked to view the chart through a pinhole. If the diplopia resolves then it is likely an issue in the visual pathway from the cornea to the retina. If a refractive cause is suspected, careful refraction and trial frame evaluation should be undertaken. If there is an anatomic abnormality such as cataract or PCO it should be addressed. The retina should be carefully assessed as well with diagnostic testing. If there is no treatable anatomic abnormality treating the symptoms with various methods of blurring is recommended. In the case where a patient does not wear distance correction inexpensive spectacles can be made to be the “carrier” for the occlusion device used. Binocular diplopia can be treated with many of the same methods as monocular cases such as occlusion or image blur. If the diplopia is not very bothersome and the patient can compensate with a head position no treatment may be an option. Fusional exercises work best when increased fusional convergence amplitudes are required. Prism therapy is the best nonsurgical option in patients with small angle horizontal or vertical deviations. This should be done by careful sensorimotor examination with ductions and versions as well as measuring fusional ranges and vergences after the associated phoria is determined. Once the optimal amount of prism is determined, a press-on prism can be used as initial treatment which is helpful to see if the amount of prism suggested is useful in the patient’s functional needs. If the amount is small enough it can be ground in to spectacles. Horror fusionis continues to be difficult to treat.
The paper discusses options for nonsurgical management of monocular and binocular diplopia.

Parent attitudes toward resident involvement in their child's strabismus surgery

Andrews H, Soni A, Green M, Quillen D. *JAAPOS*. Aug 2018;22(4):262–265.e3

This paper sought to explore patterns in parents' understanding and preferences related to ophthalmology resident participation in their child's strabismus surgery. Over a 4-week period, a survey was distributed at a suburban, academic eye center to English-speaking parents of children with strabismus who have not previously undergone, or were not being scheduled for, strabismus surgery. All of the 64 eligible parents participated in the survey. 80% and 97% of parents, respectively, indicated it was important or extremely important to be asked permission beforehand if a resident was going to assist or perform the surgery; 69% of the patients also indicated the attending surgeon should ask permission for the resident to perform the surgery, whereas only 11% believed a standard written consent was sufficient. Of the 64 respondents, 77% of the patients indicated that they would agree to a resident assisting with their child's operation while 36% of the patients stated they would agree to a resident performing the surgery. Nearly all parents in this study indicated that they would want to be informed of resident involvement by the attending surgeon. The vast majority would consent to having an ophthalmology resident assist in their child's strabismus surgery, and more than one-third would consent to having the resident perform their child's strabismus surgery. The study was small and completed at a single site but emphasizes the importance of communication with the patient regarding resident involvement. Surgeons should keep in mind that obtaining informed consent prior to resident involvement increases transparency and highlights the importance of ophthalmology residency education.

Horizontal deviations in Congenital Brown syndrome.

Gad Dotan, Maya Eiger-Moscovich, Moshe Snir, Miriam Ehrenberg, et al
J of Ped Ophth & Strabismus. 2018; 55(2): 113-116

The purpose of this retrospective study is to report the incidence of horizontal deviations requiring surgical correction in patients with congenital Brown syndrome. Nineteen eyes of sixteen patients were included in this study.
Fourteen patients (88%) had surgery for correction of a compensatory head position, including 8 patients (50%) with a head tilt and 6 patients (38%) with a chin-up position, and 2 patients had surgery for primary position hypotropia. All of them underwent a weakening procedure of the superior oblique tendon, by either Z-tenectomy (81%, n = 13) or suture elongation of the superior oblique tendon (19%, n = 3). Fifty-six percent of patients (n = 9) had primary position horizontal deviation before surgery, including 50% (n = 8) exodeviations, ranging from exophoria of 4 prism diopters (PD) to exotropia of 30 PD, and one esotropia of 14 PD. Fifty percent of patients (n = 8) had surgery to correct the horizontal deviation by a recession of either one (31%, n = 5) or two (19%, n = 3) muscles. Mean preoperative horizontal deviation (9.3 ± 3.4 PD) decreased significantly following

surgery (1.7 ± 1 PD, *P* = .001) (paired *t* test). The authors concluded that significant horizontal misalignment is often present in patients with Brown syndrome, and its correction should be considered at the time of surgery.

The Effect of Childhood Eye Disorders on Social Relationships during School Years and Psychological Functioning as Young Adults

Buckley, CY., et al. *Br Ir Orthopt* J 2018; 14(1): 35-44

To determine the social and psychologic impact of visible eye conditions and their treatments in childhood and young adulthood. The study directly contacted the patients treated as preschoolers, as opposed to previous studies which surveyed the parents, in adulthood to assess the psychosocial effects their eye issues had on them as children and adolescents. Response rate to the on-line survey was only 22.5%. The study found that adults treated for a visible eye condition in pre-school, compared to controls, reported a higher incidence of generalized anxiety and more victimization in school.

10. STRABISMUS SURGERY

Innovative techniques for the treatment of adult strabismus.

Pineles SL, Chang MY, Holmes JM, Kekunnaya R, et al. *JAAPOS* 2019 June; 23 (3): 132-39.

Adult strabismus is often characterized by surgical complexity. In recent years, several innovative techniques for the management of complex strabismus have been developed. Strabismus surgeons should understand the indications for various strabismus surgical techniques in the management of these difficult cases. This workshop describes several new surgical techniques to manage complex strabismus, including small-angle incomitant and very large-angle strabismus, torsional diplopia, and restrictive, paralytic, and secondary strabismus. Because strabismus surgery is an ever-evolving field, it is important to continue to refine our surgical armamentarium. Strabismus surgeons may wish to add these techniques to their surgical repertoire for select cases. A video is also attached to the article.

Management of surgical overcorrections following surgery for Duane syndrome with esotropia in primary position.

JAAPOS 2019 Feb;23(1):2-4. Velez FG and Pineles SL

Surgery for esotropic Duane syndrome may result in overcorrections. Managing these overcorrections can be challenging. Early-onset overcorrection may result from over-recession of the medial rectus muscle or from a tight transposition procedure; late overcorrection, from chronic passive tightening of the transposed muscles or the ipsilateral lateral rectus muscle or from scar tissue formation. The authors believe that a good result is possible if interventions are timely and consider the results of forced duction testing. In this short report they describe the most common over-correction scenarios and recommendations for their surgical management. An algorithm for the management of secondary exotropia after surgery for unilateral Duane syndrome summarizes their approach.

Securing extraocular muscles in strabismus surgery: biomechanical analysis of muscle imbrication and knot tying technique

Brooks SE. *JAAPOS* 2019 Feb;23(1):57-59.

The purpose of this experimental study was to quantitatively evaluate the tensile strength of two important steps in extraocular muscle surgery: muscle imbrication and knot configuration. The study was conducted in a controlled fashion using fresh ex vivo pig eyes with extraocular muscles attached and a precision digital force gauge. Longitudinal tension on the sutures was gradually increased, until rupture occurred.The results suggest that imbrication of the muscle edge is most secure when the suture is looped around itself in a manner that allows it to be tightly cinched and locked, however the two imbrication patterns were sufficient to meet the biomechanical requirements of standard strabismus surgery. No difference was found between granny knots and square knots; both techniques possess similar tensile strength using 6-0 Picryl. The study may provide clinically translatable data to inform optimal surgical technique.

Extraocular and Intraocular Infections Following Strabismus Surgery: A review

MalcomR.Ing, MD; Justin Shortell, MD;Jamie Golez, BS. *J of Ped Ophth & Strabismus* 2019;56(4):214-221

An extensive literature review of various types of infections following strabismus surgery was facilitated by using the search engines PubMed and Google Scholar. In both search engines, the phrases “infection following strabismus surgery, ”infection strabismus surgery, ”complications of strabismus surgery, “endophthalmitis strabismus surgery, and “strabismus scleral perforation” were used for the review. The type of infection, surface involved, and site of the infection determined the type of therapy. Infections involving deeper tissues, such as periocular infection or orbital cellulitis, required systemic therapy. Sub-Tenon’s abscesses required incision and drainage, as well as systemic antibiotics. The development of endophthalmitis following strabismus surgery was rare, but was

usually devastating to the visual result. Symptoms of an adverse intraocular condition began by mean postoperative day 3, but the definitive diagnosis and treatment of endophthalmitis was not made until mean postoperative day 6. Despite early detection of this latter type of infection and early surgical intervention with vitreous paracentesis and intraocular injection of antibiotics, the visual result was extremely poor in more than two-thirds of the reported cases. Although there is no known way to truly prevent all infections following strabismus surgery, several techniques may be prudent for the strabismus surgeon to adopt to decrease the bacterial load and minimize the risk of infection. The surgeon should be encouraged to consider preoperative use of povidone-iodine on the operative field and avoid scleral perforation during surgery. The authors concluded that despite the most meticulous surgery and preparation, an infection following strabismus surgery may still occur. A normal examination early in the postoperative period does not preclude the development of an infection later in the postoperative period. Therefore, an examination or contacting the out-of-town patients or parents by phone and/or requesting photographs later in the postoperative period may be the best way to detect possible infections that jeopardize the visual result. Additionally, families should be made aware of the signs and symptoms of infection and urged to contact the surgeon at the earliest appearance of these possible complications.

Outcomes following surgery for horizontal strabismus in children of lower socioeconomic backgrounds.

Dembinski RL, Collins ME, Kraus CL. *Strabismus*. 2019 Jun 11:1-7.

The authors compared strabismus surgery outcomes in children with lower socioeconomic states to those with private insurance. In total, 69 patients met inclusion criteria and were compared to 34 patients with private insurance. There was no statistically significant difference (p=0.37) between the groups at post-op month 6 (71.0% vs 73.5%). Success (<12 PD) was similar between the groups regardless if the patients were esotropes (73.8% lower SES vs 74.1% private insurance) or exotropes (66.7% vs 71.4%). Success (<12 PD) did not correlate with race, sex, age at time of surgery, and type of strabismus. However, there were correlations between surgical failure and poor compliance with glasses and patching/atropine as well as missed appointments. These results suggest that children of lower socioeconomic status may not expect a decreased chance of satisfactory alignment following surgery, despite poorer outcomes in other surgical specialties.

Long-term outcomes of strabismus surgery in Mobius sequence.

Lueder GT, Galli M. *Strabismus*. 2019 Apr 8:1-4.

The goal of this study was to evaluate the long-term outcomes of medial rectus muscle recessions in patients with Mobius sequence. The authors retrospectively reviewed all children with the condition from 1994-2017 who underwent bilateral

medial rectus recessions. Five patients were included, with age at surgery ranging from 5-14 months. The length of follow up ranged from 4-19.5 years. The deviation was from 20-30 PD pre-operatively and all had a post-operative deviation <8 PD, meeting the criteria for success. The authors conclude that bilateral medial rectus recessions alone can treat moderate angle esotropia in patients with Mobius.

Reduction of oculocardiac reflex with Tetracaine eye drop in strabismus surgery.

Rahimi Varposhti M, Moradi Farsani D, Ghadimi K, Asadi M. *Strabismus*. 2019 Mar;27(1):1-5.

There are limited studies investigating the effect of topical tetracaine on the incidence on the oculo-cardiac reflex. The authors performed a randomized, double-blind prospective study in which tone group was randomized to the tetracaine group and the other was randomized to the placebo group. Seventy patients with similar baseline characteristics were randomized (35 tetracaine, 35 placebo). The investigated the effects at incision and muscle release as well as effects of the duration of surgery, incidence of the oculo-cardiac reflex and time to recovery from the oculo-cardiac reflex. The only statistically significant difference was at the incision stage, as the severity of the reflex was significantly higher in the tetracaine group. However the authors write in the conclusion that topical tetracaine reduces the incidence and severity of the oculo-cardiac reflex in the post-release stage, which seemed to contradict with the data presented in the results.

Strabismus, Strabismus Surgery, and Reoperation Rate in the United States: Analysis from the IRIS Registry

Repka MX, Lum F, Burugapalli B. *Ophthalmology* 125; 10 Oct 2018: 1646-1653.

Recent population-based estimates of the prevalence of strabismus are available for children younger than 6 years of age in the United States, but are lacking for older age groups. Data are even more limited for rates of strabismus surgery in adults. The purpose of this study was to determine the prevalence of strabismus, the rate and types of strabismus surgery and the 1-year reoperation rates among all ages in the US population using the IRIS (Intelligent Research in Sight) Registry. The IRIS Registry is the nation's first comprehensive clinical registry of eye disease. It collects real-world practice patterns from electronic health records of ophthalmology practices across the United States. This study includes encounters from January 1, 2013, to December 31, 2016. As of December 31, 2016, there were 7200 ophthalmologists in 2307 electronic health record-integrated practices participating in the IRIS Registry. Of these, self-designated pediatric ophthalmologist specialists numbered 258. Based on the diagnosis codes and procedures codes, the study identified types and rates of strabismus and strabismus surgery from 2013 to 2016 with subgroups by age, sex, race/ethnicity, and

region of the United States. The 1-year reoperation rate was determined for strabismus surgery performed during 2013–2015 for all age groups. A total of 30,827,185 unique patients were identified; 846,477 (2.75%) had a diagnosis of strabismus: 3.02% of male patients and 2.55% of female patients (difference = 0.47%, 95% confidence interval [CI], 0.46–0.48, $P < 0.0001$). Strabismus surgery was performed in 40,780 (0.13%) unique patients during the 4 years. The rate of surgery decreased from 1.99% for children from birth to 5 years of age to 0.05% for adults 40 years of age and older. Horizontal surgical codes were reported 38, 813 times, vertical surgery codes were reported 9,304 times, and superior oblique codes were reported 711 times. Adjustable sutures were used for 3,027 patients (7.42%). Cases with a code for repeat eye muscle surgery or restrictive myopathy were reported for 6,098 patients (14.9%). Esotropia accounted for 30.06% and exotropia in 21.77% of diagnoses reported for surgery. The rate of reoperation within 1 year of a strabismus surgery was 6.72%, lowest for the group 6 to 9 years of age (3.95%) and increasing with age ($P < 0.001$) to 11.5% for patients 65 years of age and older. Overall, approximately 1 in 750 patients in the IRIS Registry received strabismus surgery (1 in 20 with a strabismus diagnosis) during a 4-year period. Reoperations during the first year after surgery were performed for 1 in 15 patients, increasing with age at surgery. "Big" data from clinical data registries represent real-world care that can be used to develop benchmarks for clinical outcomes and to identify areas for practice improvement and training program design.

Infection following strabismus surgery

Bruce Michael Schnall and Anat Feingold *Curr Opin Ophthal* Sept 2018, 20:407-411

The incidence of infection following strabismus surgery is rare and estimated to be between 1/1100 to 1/1900. Most commonly the causative organisms are MRSA, S. aureus, S. pneumoniae, S. epidermidis, Group A strep, and H. flue. In children, early symptoms may be systemic such as fever and lethargy. Other signs include increasing lid edema, eye redness and pain. Infection usually occurs in the first week and symptoms often begin to appear on postoperative days 1-5. The infections can manifest in a number of ways. Sub-tenon's abscess usually had discharge, painful eye movements and fever associated with it and is often the site of muscle reattachment which can weaken the tendon. IV antibiotics and abscess drainage are used to treat. Orbital cellulitis and abscess usually occurs within 5 days and has systemic symptoms such as fever as well as lid swelling, chemosis, restricted EOMs, and proptosis. Aggressive treatment with IV antibiotics and surgical drainage is warranted if abscess is present. Endophthalmitis occurs in 1:3500 to 1:185,000 cases. Usually visual outcome is poor and can occur with or without globe perforation. It also presents with systemic signs initially in children and then with local pain, redness and swelling. Preoperative measures can reduce the risk of post-operative infection. Preoperative topical antibiotics do not reduce the risk or severity of infection. There may be a role for IV antibiotics as they do achieve adequate levels in the conjunctiva.

Children who have excessive eye rubbing, poor hygiene and are of preschool age have a higher risk of infection. Currently, the most effective method to reduce bacterial colony count prior to surgery is a drop of povidone-iodine 5% in the eye. A second application of two drops after placement of the speculum helps maintain the concentration. And a single dose of povidone-iodine 5% at the conclusion of surgery is as effective as a post-operative course of topical antibiotic/steroids. Soaking sutures in povidone-iodine 5% reduced the suture contamination rate from 28% to 9%. There is NO evidence that postoperative topical antibiotics reduces the incidence of post-op infection.
The authors undertake a review of the frequency of post-operative infection in strabismus surgery and steps to prevent its occurrence. Most notably the use of povidone-iodine 5% before and after surgery is the most effective method of infection prevention.

Efficacy of Botulinum Toxin in the Treatment of Convergence Spasm.

Gupta S, Gan J, Jain S. *Strabismus*. 2018 Sep;26(3):122-125.

Options for the treatment of convergence spasm include long-term cycloplegic drops with plus lenses, base out prisms or botulinum toxin injections to the medial rectus muscles. Currently there is no consensus on the best option. The authors performed a retrospective review of six patients (mean 44 years, range 16-71 years) with an average esotropia of 32.5 PD at near (range 25-45 PD). Five of the six had previously tried and failed conservative therapy with plus lenses and the other patient had failed prism therapy. Three patients received simultaneous injections to both MR muscles and 3 received sequential injections. Four of 6 patients were overcorrected at 2 weeks with an average deviation of 10 PD XT (range 20 PD XT to 25 PD ET). At 3 months after injection, the average deviation was 12.5 PD ET (range 15 PD XT to 35 PD ET). At 9 months after injection, all patients returned to their pre-injection levels. The authors conclude that there is limited benefit from botulinum toxin as the efficacy varies. In addition, repeat injections may be required and overcorrection is a common side effect.

The Globe's Eccentric Rotational Axis: Why Medial Rectus Surgery Is More Potent than Lateral Rectus Surgery.

Clark RA, Demer JL. *Ophthalmology* 2018 Aug;125(8):1234-1238

Surgical tables typically recommend greater lateral rectus (LR) than medial rectus (MR) doses for horizontal strabismus of any given magnitude, a difference unexplained by mechanical models that assume globe rotation about its center. We tested this assumption during horizontal ductions of healthy adult subjects with normal binocular vision. Surface coil magnetic resonance imaging at 390 or 430 μm resolution was obtained using 2-mm-thick contiguous axial planes while subjects fixated targets in central, right, and left gaze. Angular displacements of lines connecting the corneal apex through the minor lens axis to the retina were

measured to approximate clinical ductions. Globe centers were calculated from their area centroids. Apparent lens and globe-optic nerve (ON) junction rotations around the globe center were then compared with clinical ductions. The authors found that the globe-ON junctions appeared to rotate significantly less around globe centers than did lenses for abduction (20.6°±4.7° vs. 27.4°±7.4°, ± standard deviation (SD), $P < 0.001$) and adduction (25.3°±6.7° vs. 31.9°±8.3°, $P < 0.001$). Both rotations differed significantly from clinical adduction (27.9°±8.3°, $P < 0.007$), but only in abduction was globe-ON junction rotation significantly less than clinical abduction (28.6°±9.4°, $P < 0.001$). The true geometric globe rotational center was 2.2±0.5 mm medial and 0.8±1.0 mm posterior to the geometric globe center and was displaced farther medially and posteriorly during adduction. This eccentricity imbues each millimeter of MR recession with approximately 30% more trigonometric rotational effect than equivalent LR recession. The authors concluded that the medial and posterior eccentricities of the normal ocular rotational axis profoundly influence horizontal rectus action. The proximity of the globe's rotational axis to the MR shortens its lever arm relative to the LR, explaining why mechanical effects of smaller MR recessions are equivalent to larger LR recessions.

Challenging Management of Double Vision After Functional Endoscopic Sinus Surgery – A Series of 6 Cases

Artsi EB, Wygnanski-Jaffe T, Shalev B, et al. *Am J Ophthalmol.* 2018; 190: 134-141.

The authors of this study present 6 cases of orbital trauma, double vision and strabismus after functional endoscopic sinus surgery (FESS). This was a retrospective study of patients treated at one institution over 10 years. Five of the 6 patients had medial rectus transection and exotropia. The 6th patient had transient double vision, no evidence of muscle transection, and resolution of symptoms. In all 5 patients with a transected muscle, surgical correction by retrieval of the medial rectus was performed, but in none of the 3 eyes what had primary stump reattachment had resolution of symptoms. Transposition was the only definitive strabismus surgery that resulted in orthotropia, it was temporary in all patients in this case series who had follow up care. All patients who had follow up had recurrent exotropia, demonstrating the poor prognosis in these cases.

The Impact of Strabismus Surgery on Irish Adults

Power, B., et al. *Br Ir Orthopt* J 2018; 14(1): 6-10

The author's objective was to evaluate quality of life (QOL) in Irish adult strabismus patients after strabismus surgery. The psychosocial implications of strabismus on QOL is well documented. Patient undergoing strabismus surgery were given a pre- and post-operative AS-20 QOL questionnaire, addressing both functional and psychosocial factors. The overall average increase in QOL was 14.29, females had lower pre-operative QOL values than males and showed a greater

improvement in QOL than males. The analysis demonstrates a significant improvement in QOL after adult strabismus surgery.

Horizontal muscle surgeries

A modified technique for attaching the lateral rectus muscle to the orbital periosteum through a skin incision over the lateral orbital rim.

Nagasubramanian V, Rajamani M, Dandapani R *JAAPOS* 2019 June; 23 (3): 141.e1-141.e4.

The traditional approach for periosteal fixation of the lateral rectus muscle involves securing the muscle using nonabsorbable sutures by exposing the orbital periosteum 5 mm to the inside of the orbital margin. The authors describe an alternative approach for exposure of the orbital periosteum through a skin incision, providing more room and avoiding extraconal fat manipulation. The technique is described in 2 patients with exotropic Duane retraction syndrome and 1 patient with congenital oculomotor nerve palsy. All 3 patients had satisfactory postoperative alignment, with abduction limitation of 3-. Adduction improved in all patients. The patient with oculomotor nerve palsy had a small overcorrection in primary position that remained stable during follow-up of 18 months. There were no intraoperative complications. The authors conclude that their modified approach to extraocular muscle periosteal fixation may be simpler than the standard approach. However, they acknowledge that further evaluation in a larger series of patients is warranted. A video is enclosed to demonstrate the different stages of surgery.

Botulinum toxin-A injection in esotropic Duane syndrome patients up to 2 years of age.

Sener EC, Yilmaz PT and Fatihoglu ÖU *JAAPOS* 2019 Feb;23(1):25. e1-25. e4

Few studies have evaluated the role of botulinum toxin-A (BTX) in the treatment of Duane Syndrome. This retrospective study evaluated the role of botulinum toxin-A (BTX) injection as the primary treatment for patients with esotropic Duane retraction syndrome in toddlers and infants. A total of 15 patients with esotropic Duane syndrome (14 unilateral, 1 bilateral) who underwent unilateral or bilateral BTX injection to the medial rectus muscle ≤2 years of age were included. Success was defined as permanent resolution of esotropia and head turn in primary position at final follow-up. Before BTX injection the mean primary esotropia at near with full cycloplegic refraction was $29.3^{\Delta} \pm 14.4^{\Delta}$; the mean head turn, 23° ± 11°. Mean duration of follow-up was 37 ± 29 months (range, 7-96 months). Orthotropia and resolution of head turn was achieved in 7 of 15 patients (46.7%). Subgroup analysis demonstrated that the success rate gradually decreased with age: from 100% in patients ≤7 months of age to 33.3% in patients 8-12 months of age,

and 20% in patients >12 months of age. Seven patients (46.7%) eventually required surgery (medial rectus recession and/or superior rectus transposition) because of residual head turn and esodeviation following BTX. Three patients developed mild ptosis that resolved within 3 months of BTX injection. The authors conclude that according to their small cohort, orthophoria in primary position and correction of head turn can be achieved with a single BTX injection in as half of the patients ≤2 years of age with a very high success rate in patients ≤7 months of age. BTX injection early in infancy can obviate the need for surgery in esotropic Duane syndrome. The study is limited by its retrospective nature and small sample size. Age is only implied as a possible risk factor for failure. Nonetheless, the authors experience shows some encouraging results with botulinum toxin injection, which is simple to perform and requires shorter anesthesia time compared with surgery.

Torsional changes after vertical transposition of horizontal recti in V-pattern exotropia without oblique dysfunction.

Sara Maher, MD; Dina El-Fayoumi, MD; Ahmed Awadein, MD; Lobna Khazbak, MD.*J of Ped Ophth & Strabismus*.2019;56(2):107-115

Vertical displacement of the lateral recti alters their scleral attachment relative to the rotation center of the globe, increasing the arc of contact of the transposed muscle in down gaze and decreasing it in up gaze. Thus, the lateral rectus muscles become more effective abductors in down gaze and less effective abductors in up gaze.[2] However, the concern about upward displacement of the lateral recti is that it might induce extorsion of both globes. The extorsion might increase the V-pattern as a result of altering the line of action of both superior and inferior recti. Such extorsion might be more evident with full-tendon transposition, thus negating the useful effect of transposition in pattern collapse. The current study was designed to study the amount of pattern collapse after vertical displacement of the lateral recti and to evaluate whether there would be any torsional changes that might influence the outcome. A prospective study was performed on patients who had V-pattern exotropia and no oblique dysfunction. Lateral recti were transposed upward half-tendon width in V-pattern of 25 prism diopters (PD) or less (n = 14) and full-tendon width in V-pattern of greater than 25 PD (n = 10). Amblyopic patients had unilateral lateral rectus recession with upward transposition and medial rectus resection with downward transposition (n = 8). Ductions, versions, pattern strabismus, disc foveal angle, and astigmatic axis were analyzed before and 6 months after surgery. In the 32 patients (21 females), the mean age was 8.25 ± 1.23 years. Only amblyopic patients showed preoperative fundus extorsion (mean disc foveal angle = 16.9°, $P < .01$). Mean pattern collapse was 13.1 ± 3.8 PD with half-tendon transposition, 35.6 ± 13.7 PD with full-tendon transposition, and 13.8 ± 7.9 PD in the unilateral group. Pattern collapse increased gradually so that pattern normalization occurred after 6 months in most patients. There was a statistically significant correlation between the preoperative V-pattern and the magnitude of pattern collapse after surgery ($r = 0.80$, $P < .01$). There were no significant changes in the mean disc foveal angle (< 0.5°) or axis of astigmatism

(< 0.5°) in all three groups. The study showed that both half- and full-tendon transposition of the lateral rectus muscles are effective in correcting V-pattern exotropia in the absence of oblique dysfunction. The pattern collapse seemed to be related to the preoperative V-pattern, so that the majority of patients had disappearance of the V-pattern irrespective of the preoperative V-pattern value. Pattern collapse was not associated with any significant torsional changes. Limitations of the study include the small sample size, which might be explained by the strict inclusion criteria, and that the authors excluded patients with any evidence of oblique dysfunction. In addition, no subjective tests were used to evaluate the sensory torsion of the patients due to the relatively young age of the studied group.

Surgical Responses and Outcomes of Bilateral Medial rectus recession in Esotropia with Spinocerebellar Ataxia.

Bo Young Chun, Marcelle V.Freire, Dean M.Cestari *J of Ped Ophth & Strabismus*.2019; 56(4): 266-270

The purpose of the surgical responses and outcomes of bilateral medial rectus (BMR) recession in esotropic patients with spinocerebellar ataxia (SCA) and to compare the results with normal controls. The medical records of patients with SCA who underwent strabismus surgery for esotropia between 2006 and 2015 were reviewed retrospectively. Five esotropic patients with SCA (SCA group) and 10 esotropic patients without neurologic disorders (control group) who underwent BMR recession were included. Success rates, surgical responses, and the amount of preoperative and postoperative distance-near disparity were evaluated and compared between the groups. The mean preoperative esodeviation was not different between the SCA and control groups (20 vs 17.3 prism diopters [PD], *P* = .214). However, patients with SCA showed significant undercorrection compared with controls 1 week postoperatively (4.8 vs 1.0 PD, *P* = .048) and at the final follow-up (6.8 vs 1.8 PD, *P* = .032). The surgical success rates for the SCA and control groups were 40% and 80%, respectively (*P* = .095). Patients with SCA demonstrated a significantly reduced surgical response compared with controls (3.15 vs 3.87 PD/mm, *P* = .004), and a greater amount of postoperative distance-near disparity than controls (8.0 vs 1.1 PD, *P* = .001). The authors concluded that a significant undercorrection due to postoperative esodrift after BMR recession in patients with SCA type 3.Accordingly, the y recommend a slight over correction of 5 to 10 pd or adding a slanting procedure, as stated above, in planning strabismus surgery for this distinct group of patients. This study is limited by the small number of patients, mainly due to extremely rare prevalence of SCA type 3, and by the relative short follow-up time, which was approximately 4 months. Because this was a retrospective study, any other factors that could have influenced the surgical response such as the presence of stereopsis or fusional amplitudes were not measured.

A Cluster of Cyclic Esotropia: White matter changes on MRI and Surgical outcomes.

Kimberly Merrill, CO; Jill Anderson, MD; Daniel Watson, MD; Raymond G. Areaux Jr., MD. *J Peds Ophth & Strabismus*.2019;56(3):178-182

The purpose of this retrospective chart review was to report a series of patients with cyclic esotropia, their surgical outcomes, and incidental findings. The medical records of five patients(3 males and 2 females) with cyclic esotropia presenting over 17 months were reviewed. Age at onset, ocular and motility examinations, brain magnetic resonance imaging (MRI), acetylcholine receptor antibodies, thyroid hormone levels and antibodies, calendars documenting phases, surgical treatments, postoperative alignment, and fusion were documented. Typical periodicity followed a 48-hour cycle. Duration of cycling varied from 1 to 9 weeks. Mean maximum deviation was 37 prism diopters (PD) of esotropia (range: 35 to 40 PD of esotropia). All patients had normal laboratory studies. MRIs showed an abnormal white matter signal in the frontal lobes in 2 patients and were normal in the others. Bilateral medial rectus recessions for the maximum angle were successful in 4 patients at a minimum follow-up of 13 months; the other patient required reoperation for a residual esotropia. Fusion was present in 4 patients preoperatively and all postoperatively. Stereopsis was stable or improved in all postoperatively. This is the first report of frontal white matter changes occurring in the setting of cyclic esotropia and the the largest case series of cyclic esotropia reported in North America at a single institution. Future studies may determine whether this is a common finding occurring in association with cyclic esotropia. It is possible that an initial cycling pattern is present with some frequency in later-onset esotropia and may facilitate the family's delay to clinical evaluation until a constant tropia is manifest. MRI with attention to frontal lobe white matter might be considered in the work-up of cyclic esotropia to determine if this is a common finding. Bilateral medial rectus recessions can restore fusion in these patients.This study is limited by the small sample size, retrospective nature, as well as the short follow-up.

Bupivacaine injection combined with recession of antagonist rectus muscle to treat sensory strabismus.

Hopker LM, Modelli R, Allemann N. *Strabismus*. 2019 Mar;27(1):6-10.

In this prospective interventional study, the authors aimed to evaluate the amount of correction with bupivacaine injection combined with recession of the antagonist muscle in patients with sensory strabismus. They enrolled nine patients (6 male, mean age 43.5 ± 12.3 years old) of whom 5 had exotropia (mean deviation 50 ± 6.12 PD) and 4 had esotropia (28.7 ± 14.9 PD). The patients with exotropia had a mean correction
of 23 ± 14.4 PD with a dose-response of 2.6 PD/mm. The patients with esotropia had a mean correction of 21.25 ± 4.8 PD with a dose response of 5 PD/mm. The

follow up time was 180 days for all patients. At that visit, 44% had successful outcome. No toxicity and no significant side effects were noted. The authors did note technical issues with difficulty injecting the posterior 1/3 of the medial rectus muscle and that the volume and concentration of bupivacaine were standardized regardless of the size of the deviation, which may have limited the efficacy. Overall it is possible that bupivacaine can be used in cases where a muscle cannot undergo a resection or plication, such as in cases where there is a risk of anterior segment ischemia.

A Randomized Trial Comparing Bilateral Lateral Rectus Recession versus Unilateral Recess and Resect for Basic-Type Intermittent Exotropia

Sean P. Donahue, Danielle L. Chandler, Jonathan M. Holmes, Brian W. Arthur, et al for the Pediatric Eye Disease Investigator Group *Ophthalmology*. February 2019;126:305-317

Intermittent exotropia is the most common childhood exotropia. This prospective study randomized children with basic intermittent exotropia to receive either recess-resect unilateral surgery or bilateral lateral rectus recession surgery. The sample size was only powered to detect a 25% difference in effect between treatments. Although the enrollment criteria included manifest plus latent deviations, the success criterion was limited to only manifest deviations. Strengths included masked observations and relatively long follow up, while weaknesses included flexibility to allow surgeons to augment recession amounts for non-standardized reasons, variable preoperative treatment with patching and/or orthoptic exercises, and overlapping failure criteria. All treatment outcomes favored unilateral recess/resect surgery except for a slightly higher rate of esotropia, but the probabilities were only strong enough to exclude bilateral recessions as the superior treatment option. Given prior randomized control trials favoring unilateral recess/resect surgery for this condition, this study provides additional evidence that bilateral lateral rectus recessions are not equivalent, as the authors concluded, but rather the inferior treatment option, with a stronger conclusion limited by the power of the study.

Outcomes of bilateral lateral rectus recession in treatment of recurrent exotropia after bilateral medial rectus resection

Elkamshoushy A and Langue MA *EJO* July 2019,29(4) 402–405

The paper aimed to report the results of bilateral lateral rectus muscle recession for recurrent exotropia in cases where the primary surgery was a bilateral medial rectus resection. Retrospective chart review of 15 subjects who completed 6 months of follow-up. Data collected included patients' demographics and pre- and post-operative measurements of ocular alignment and motility. Surgical nomogram used was the same nomogram we use for primary cases of exotropia. At

6-month follow-up, 73.3% of cases had a successful surgical outcome (defined as 8 PD of esotropia to 10 PD of exotropia). In addition, recession of lateral rectus muscles against the previously resected medial recti did not result in a significant increase in the limitation of abduction. Bilateral lateral rectus recession using standard surgical tables is a safe and effective method for treating recurrent exotropia following bilateral medial rectus resection. Even large primary resections up to 12 mm do not seem to affect the results of bilateral lateral rectus recession.

Treatment of Intermittent Exotropia of the Convergence Insufficiency Type with Bupivacaine 0.75%: 5-Year experience and Outcomes

Josephson, Matthew and Mathias, Stephen A. *Journal of Binocular Vision and Ocular Motility,* 2019; 69:1, 3-7

Bupivicaine 0.75% may provide an alternative to orthoptic exercises, prism glasses, and traditional strabismus surgery in patients with convergence insufficiency type exotropia (CIXT). Bupivicaine induces changes in muscle structure and length giving it greater contractile strength and intrinsic stiffness when injected directly into an extraocular muscle. This is a retrospective chart review study of one hundred and twenty-four CIXT patients who underwent unilateral medial rectus bupivacaine injection of varying amounts based on angle. At 6 months post injection 91% of patients had successful resolution of symptoms with or without prism of <5Δ. Thirty patients had 5-year follow-up data, 20 patients (80%) of these had successful resolution of symptoms with 14 (56%) requiring prism glasses. The alignment stability trended towards recurrence but was not found to be statistically significant. The studies data suggests a dose-response effect of 3.1Δ/cc of bupivacaine 0.75%. The maximum angle treated by a single medial rectus injection was 20Δ. The authors conclude that bupivacaine 0.75% injection is a potential alternative treatment for CIXT.

Long-term outcomes After Same Amount of Bilateral Rectus Muscle Recession for Intermittent Exotropia With the Same Angle of Deviation.

Haeng-Jin Lee, Seong-Joon Kim, Young Suk Yu.J *Ped Ophthal & Strabismus.*2018;55(5):319-325

The purpose of this retrospective review is to evaluate the long-term outcomes of homogenous bilateral rectus recession in patients with the same preoperative angle of deviation in intermittent exotropia and investigate factors associated with surgical outcomes. Patients with the same preoperative angle of deviation who underwent bilateral 6-mm lateral rectus recession were observed for 2 or more years. Patients were classified into two groups based on deviation angle: success (orthophoria or exodeviation < 10 prism diopters [PD]) or recurrence (exodeviation ≥ 10 PD). Preoperative and postoperative ophthalmologic factors were

compared between groups. The success and recurrence groups contained 50 and 49 patients, respectively. Preoperative maximum angle of deviation was 29.0 ± 1.8 PD at distance in the success group and 28.9 ± 1.8 PD in the recurrence group. Deviation at the 2-year follow-up was 3.7 ± 3.7 and 18.3 ± 5.3 PD in the success and recurrence groups, respectively ($P < .001$). Preoperative factors were not significantly different between groups except for presence of lateral incomitance; success group patients presented more lateral incomitance ($P = .035$). The success group also presented more esodeviation just after the operation and showed a more stable course during follow-up. Surgical outcomes of patients with 10 PD or more of esodeviation 1 week postoperatively were significantly more favorable than patients with less than 10 PD of esodeviation ($P = .027$, log-rank test). The authors conclude that the presence of lateral incomitance and early postoperative overcorrection were significantly associated with favorable surgical outcome and should be considered when planning intermittent exotropia surgery. There were some limitations in this study. First, this was a retrospective study. Second, the authors assigned groups based on 2-year postoperative deviation values because the final follow-up period was different for all patients. Even if the minimum follow-up was 2 years, a prospective study including a long-term follow-up exceeding 2 years would be necessary to validate the results of the study.

Immediate Postoperative Alignment Following Bimedial Rectus Recession for Esotropia in Children Compared to Adults.

Mohamed B.Hassan, Nancy N.Diehl, Brian G.Mohney.J *Ped Ophth& Strabismus.*2018;55(5):299-305

The purpose of this study is to determine whether the immediate postoperative alignment among patients undergoing successful bilateral weakening surgery for esotropia is different in children compared to adults. The medical records of all patients undergoing surgery for esotropia by a single surgeon at a major academic referral center between January 1, 2002, and July 1, 2014 (n = 544), were retrospectively reviewed. Exclusion criteria included those with prior strabismus surgery, unilateral surgery, strengthening procedures, vertical or superior oblique surgery, and those wearing hyperopic spectacles for accommodative esotropia. Additionally, all patients had to have a 1- and 6-week postoperative examination and 8 prism diopters (PD) or less of deviation at their 6-week examination. Ninety-five (17.5%) of the 544 patients met the inclusion criteria. Surgery was performed at a median age of 3.7 years (range: 7 months to 86 years) for a median esodeviation of 35 PD (range: 12 to 70 PD). Among the 73 patients younger than 11 years, the immediate mean postoperative alignment was 9 PD of exotropia (range: 14 PD esotropia to 30 PD exotropia) compared to 2 PD of exotropia (range: 9 PD esotropia to 30 PD exotropia) in the 22 patients 11 years or older ($P = .001$). Seventy-one percent of successfully aligned patients younger than 11 years were exotropic in the immediate postoperative week compared to

23% of those 11 years or older ($P < .001$). Twenty-four (32.8%) of the younger cohort had an immediate overcorrection of 15 PD or more compared to 1 (4.5%) in the older cohort ($P = .006$. The authors conclude that children younger than 11 years who undergo successful surgery for esotropia are significantly more likely to exhibit overcorrection in the immediate postoperative period when compared to those 11 years or older. Successfully aligned esotropic children were more significantly exotropic, including one-third with 15 PD or more of exotropia, in the first postoperative week compared to adults undergoing the same procedure. There are limitations to the findings of this study. The retrospective nature of this investigation is hindered by incomplete data and irregular follow-up. Moreover, the study cases were drawn from the practice of one surgeon. This study is also restricted by a small sample size, especially the number of patients aged 11 years or older, which limits the conclusions drawn from these findings. However, statistical significance in the postoperative alignment was still observed, and significance was maintained even if the cut-off age for the two groups was increased, leaving even fewer patients in the older cohort. Finally, given the inclusion criteria of requiring both 1- and 6-week postoperative examinations, this was not a consecutive series of patients undergoing surgery for esotropia and may have unexpectedly eliminated some patients with less overcorrection.

The value of Fusional Convergence Amplitudes in Esodeviation Surgery Without Adjustable Sutures.

Anu Maudgil, Naz Raoof, John Burke. *J Ped Ophth & Strabismus*. 2018;55(6):375-381.

The purpose of this study is to explore the application of preoperative fusional convergence amplitudes in the selection of a target angle for non-adjustable suture strabismus surgery with deteriorated intermittent esotropia and diplopia. Thirty-one consecutive cases of presumed acquired non-accommodative, deteriorated intermittent esotropia managed surgically were reviewed retrospectively. For each individual, a target angle (deviation angle for which surgery was based) was selected preoperatively after analysis of fusional convergence amplitudes. Outcomes in patients selected for overcorrection at 6 meters (target angle > angle in primary position at 6 meters) were compared to those who had planned surgery based on a target angle that did not exceed their measured angle (target angle ≤ angle in primary position) at 6 meters. The study showed that all 31 patients achieved binocular single vision in primary position at both near and 6 meters without prisms, orthoptic therapy, or additional surgery at 4 to 6 months postoperatively. Greater mean correction in the target angle > angle in primary position group compared to the target angle ≤ angle in primary position group was observed, but this difference was not statistically significant ($P = .57$).The authors demonstrated a role for using clinically measured motor fusion to select a target angle for this group with esotropia with binocular single vision undergoing lateral rectus resection where target angles could be selected that are larger, similar, or

less than the primary position deviation measured at 6 meters, and with no statistically significant difference in medium-term outcome without resorting to adjustable sutures. The authors recognize the benefits of adjustable sutures in more complex cases, notably strabismus with restrictive and neurological causes, and in those with less robust binocular single vision potential. However, categorizing esodeviations according to their etiology and binocular single vision potential is a seemingly desirable management strategy, allowing some etiological cases to be recommended for non-adjustable suture surgery and achieving clinically successful outcomes by economical and subjectively less stressful means. This study has limitations: a relatively small sample size and retrospective design, an etiological retrieval bias, heterogeneity of surgical approach, and incomplete data set at final follow-up visit. Arguably, combining different etiological groups with varying levels of stereopsis in their analysis could affect the durability of the surgical result.

Comparison of plication and resection in large-angle exotropia.

Sukhija, J. and S. Kaur. *J AAPOS*. Oct 2018; 22(5): 348-351.

Rectus muscle plication has recently attracted attention as an alternative to resection in exotropias of varying degree. In contrast to resection, it is a vessel-sparing procedure that permits simultaneous operations on multiple rectus muscles. The purpose of this small cross-sectional case series was to compare the relative efficacy of plication of rectus muscles to resection in cases of exotropia along with quantitative assessment of ultrasound biomicroscopy (UBM). A total of 28 patients with basic comitant exotropia of 30 PD – 50 PD who had undergone first-time horizontal strabismus surgery were recruited and prospectively underwent UBM evaluation 1 year after surgery; Fifteen patients underwent resection of the medial rectus and 13 underwent plication. Deviation and motility were assessed postoperatively, when UBM was performed. The two groups were matched for age and deviation size preoperatively. The patients undergoing plication and resection fared equally in terms of postoperative deviation ($P = 0.81$) and abduction limitation ($P = 0.169$). UBM could identify and quantify plication in all cases with excellent agreement with the operative data (intraclass correlation coefficient = 0.886; $P = 0.000$). The authors concluded that medial rectus plication or resection performed for similar angles of exotropia produced quantitatively similar results. Plication offered the advantage of being characteristically identifiable and measurable on UBM. This study has several limitations, apart from its small sample size, the UBM was prospectively performed by an unmasked observer. Yet, it expands on a topic of controversy with limited information and demonstrates with imaging that plication of the medial rectus is comparable to resection of this muscle.

Long-term motor and sensory outcomes after surgery for the nonaccommodative component of partially refractive accommodative esotropia.

Mohan, K. and S. K. Sharma. *J AAPOS*. Oct 2018; 22(5): 356-360.

The purpose of this retrospective study was to assess the long-term motor and sensory outcomes after surgery for the nonaccommodative component of partially refractive accommodative esotropia (PRAET). A total of 47 consecutive patients ≤11 years old (median age, 3.0 years) operated for the nonaccommodative component of PRAET and follow-up of at least 10 years, were included in the study. Excluded from the study were patients with high AC/A ratio. The mean cycloplegic refraction was +4.22±1.65 D (range, +1.75 to +9.00 D). Forty patients (85%) underwent unilateral medial rectus recession combined with lateral rectus resection, and 7 (15%) underwent unilateral medial rectus recession alone. The mean postoperative follow-up was 12.15 ± 2.05 years (range, 10.00-17.50 years). Overall, 23 patients (49%) had surgical success (an orthophoria or alignment within 10 PD of esotropia at near and distance); 10 (21%), decompensation (an increase of a previously controlled esotropia to >10 PD at near and distance); and 7 (15%), esotropia with a high ratio of accommodative convergence to accommodation (AC/A) or consecutive exotropia. None of the patients had residual esotropia. Kaplan-Meier survival analysis showed probabilities of surgical success of 57% at 5 years, 51% at 10 years, and 47% at 15 years postoperatively. Surgical success was achieved in 22 of 40 patients (55%) who underwent recession-resection surgery, compared to 1 of 7 patients (14%) with unilateral medial rectus recession alone (P = 0.008). The median age at surgery, mean cycloplegic refraction, median near and distance deviation, presence of binocular vision, and amblyopia did not predict long term outcome (decompensation, a high AC/A ratio esotropia or consecutive exotropia). Eight patients (18%) achieved stereopsis. Patients with an older age at onset (2.87 ± 1.31 years) and a shorter duration of strabismus (≤4 years) achieved better stereopsis. The authors concluded that in their cohort of patients with PRAET nearly half achieved a successful ocular alignment after surgery for the nonaccommodative component. Few patients achieved stereopsis. Older age at onset and a shorter duration of strabismus predicted a better stereopsis outcome. Despite its relatively small sample size, this study provides us with some insights into the of the long-term effects of surgery in partially accommodative esotropia.

Short prism adaptation test in patients with acquired non-accommodative esotropia; clinical findings and surgical outcome.

Akbari, M. R., Mehrabi Bahar MR, Mirmohammadsadeghi A, Bayat R, et al. *J AAPOS*. Oct 2018; 22(5):352-355.

The purpose of this prospective interventional case series was to evaluate the surgical outcomes of patients with acquired nonaccommodative esotropia

(ANAET) operated on based on a short prism adaptation test (PAT). The authors were also keen on characterizing the subgroup of patients most responsive to PAT. Patients with ANAET were enrolled between 2014 and 2016. The PAT was performed prior to surgery as follows: patients wore Fresnel trial lenses based on the results of alternate prism-cover testing. With the Fresnel prism in place, alignment was measured after 20 minutes. If the deviation increased, the power of prism was increased to neutralize this angle. The test was repeated every 20 minutes to achieve motor stability. Patients were classified as either prism *responders* (if the angle of deviation increased by >10 PD compared to the entry angle) or prism *non-responders.* Of the 28 subjects enrolled, 14 (50%) were prism responders and 14 (50%) were classified as prism non-responders. Interestingly, the deviation did not increase after 1 hour in patients who showed motor stability after 20 minutes. After 6 months, 100% of prism responders and 92.9% of non-responders were aligned within 8 PD. The authors concluded that a short PAT of 20-minutes with an endpoint of motor stability, which is less rigorous than previously described techniques, in patients with acquired nonaccommodative esotropia was associated with a good surgical outcome and a low rate of over- and undercorrection. All the responders in this cohort had an angle of deviation at entry that was 30 PD or less, hence the authors concluded that PAT may be unnecessary for patients with an angle of deviation of >30 PD.

Surgical results and factors affecting outcome in adult patients with sensory exotropia.

Jung EH, Kim SJ. *Eye* (Lond). 2018 Aug 28. doi: 10.1038/s41433-018-0189-x.

This retrospective evaluated the results of surgical treatment for sensory exotropia and examined the factors associated with the surgical outcome in patients older than 18 years at the time of surgery. Surgical success was defined as a final deviation of <10 prism diopters (PD) at distance in the primary position. A total of 64 patients were included. Forty patients (62.5%) achieved surgical success. Twenty (31.3%) had a residual exotropia larger than 10 PD. Only the preoperative distant angle of deviation was significantly associated with surgical outcome.

Clinical Research on the efficacy of Modified Surgery for Esotropia Fixus With High Myopia.

Dongmei Qi, Lixia Gao, JingXie, Tao Yu *J of Ped Ophth & Strabismus*.2018; 55(4): 219-224

The purpose of this study is to investigate the efficacy of a modified surgical procedure for esotropia fixus with high myopia. Thirteen patients (15 eyes) with esotropia fixus and high myopia who underwent the Jensen procedure for superior and lateral rectus muscles at Southwest Hospital between February 2014 and December 2015 were retrospectively analyzed. Intraoperatively, the superior rectus and lateral rectus muscles were separated up to 12 to 14 mm posterior to

their respective insertion. A medial rectus large recession or rectus tenotomy was performed based on the degree of fibrosis of the medial rectus muscle. Postoperative examinations were performed at 1 day, 2 weeks, 3 months, and 6 months. The study showed that on the first postoperative day, 12 eyes (10 patients) were in the primary position (80.0%), 2 eyes (2 patients) exhibited 5° to 10° esotropia (13.3%), and 1 eye (1 patient) exhibited 15° esotropia (6.7%). At the 2-week follow up, 1 eye (1 patient) was lost to follow-up, 9 eyes (7 patients) were in the primary position (64.3%), 3 eyes (3 patients) exhibited 10° esotropia (21.4%), and 2 eyes (2 patients) exhibited 15° to 20° esotropia (14.3%). At the 3-month follow-up, the patient whose ocular alignment was 20° esotropia at 2 weeks was found to have developed 30° esotropia; no change was observed in the other patients. A remarkable improvement in ocular motility was observed in all patients. The authors concluded that the Jensen procedure fot the union of the superior rectus and lateral rectus muscles, using two pairs of sutures applied 12 to 14 mm posterior to their respective insertions, yielded favorable outcomes.

Long-term Surgical Outcomes for Large-angle Infantile Esotropia

Wan MJ, Chiu H, Shah AS, and Hunter D. *AJO* 2018; 189: 155-159

This is a two center, retrospective, nonrandomized study of 88 patients with large angle ($\geq$55 prism diopters) infantile esotropia with the goal of reporting the long-term surgical outcomes. The study period was 13 years (2002 to 2015) and patients were followed for a minimum of 3 years post op. The authors excluded patients with other ocular comorbidities, those with developmental delays, or eyes without full motility. Success was defined as postoperative deviation of $\leq$10 prism diopters without need for more surgery. Treatment was bilateral medial rectus recession in 70 patients, botulinum toxin-augmented surgery in 15 patients, 3-muscle surgery in 3 patients. The mean follow up was 40 months and of those 23% had a successful outcome. Of the treatment failures, 59/68 patients had recurrent esotropia and 9 had consecutive exotropia. Patients with botulinum toxin augmented surgery were more likely to have successful outcomes compared to those with bilateral medial rectus recessions only (47% vs. 17%). Of those who had retreatment, the mean number of procedures was 2.1 and 27% of those 97 patients had a deviation of 10 or fewer prism diopters at final follow up. The authors also looked at some secondary outcomes. Of the patients who had BMRc, 21 of the 70 developed inferior oblique overaction and 44% developed dissociated vertical deviation. In the botulinum group, 20% (3/15) had IOOA, 5 developed DVD. Of those with 3 muscle surgery (3 patients), none developed IOOA or DVD. At the end of the final follow up, 24 patients (27%) had evidence of some stereo acuity, though that was not well defined in the methods section. The authors concluded that success rates for large angle infantile esotropia were poor, most children had recurrent esotropia, and that botox augmented surgery had better outcomes at the 3 year follow up. The nonstandardized approach due to retrospective nature of the study was discussed by the authors. Additionally,

longer term studies in the future will be helpful for the clinician to decide which surgical approach is best.

The effect of Botulinum Toxin Augmentation on Strabismus Surgery for Large-Angle Infantile Esotropia

Wan MJ, Gilbert A, Kazlas M, Wu C et al. *AJO* 2018; 189: 160-165

This is a retrospective comparative case series of 30 patients from one center with large angle infantile esotropia. The authors compared the effect of botulinum toxin augmented surgery with traditional bilateral medial rectus recessions with the goal of creating dosing table. There were 14 patients who had botulinum augmentation and 16 patients who had surgery only. The authors looked at ocular alignment at 4 months and calculated the change in prism diopters per millimeter of surgery. Alignment was measured by a certified orthoptist using prism alternate cover testing or Krimsky if needed. Secondary outcome was eye alignment at 1 year and the change of alignment between 4 months and a year. The mean recession for the surgery only group was 5.5mm in the augmented surgery group and 6.1mm in the surgery-only group. The median dose of botulinum used was 3.9 units in each medial rectus. 86% of patients in the botulinum augmented group had a transient overcorrection and 50% had transient ptosis, all resolved within 3 months. Patients who had botulinum augmentation had a larger mean effect at 4 months and at 1 year. At 4 months the botulinum augmented group had a deviation of 5.7mm per mm and the surgery-only group had a rate of effect of 4.0PD/mm (prism diopters per millimeter). At one year, the botulinum group had a rate of effect of 5.4PD/mm and the surgery-only group was 3.7PD/mm. There was a trend toward improved effect with the botulinum augmentation, but it was not statistically significant. The authors used this mathematical formula to create a dosing table for botulinum augmented medial rectus recessions for infantile esotropia. The authors point out some of the limitations, one being the lack of standardization of the botulinum dose. The number of patients in this study and nonstandardized botulinum dosing and concentration makes creating a dosing table a step too far, but certainly a good starting point since there are no other papers looking at this to guide clinicians who want to start using this technique.

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

Soon Young Cho, Se youp Lee *J of Ped Ophth & Strabismus*.2018; 55(1):53-58

The purpose of this study is to compare the surgical outcomes of modified (surgical dose reduction by 5 PD compared to conventional surgical dose) and conventional contralateral lateral rectus recession and medial rectus resection for exotropia after unilateral lateral rectus recession and medial rectus resection. A total of 36 patients were included in this retrospective study. As a primary surgery

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

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

Seung Pil Bang, Dong Cheol Lee, Se Youp Lee *J of Ped Ophth & Strabismus*.2018; 55(1):59-64

In this study the authors evaluated the effect of improved control with part-time occlusion therapy on the final postoperative outcome in patients with intermittent exotropia. Control of intermittent exotropia was graded as good, fair, or poor in 89 consecutive patients with intermittent exotropia during their first visit. The patients were reevaluated after part-time preoperative occlusion therapy and divided into two groups (improvement and no improvement) according to whether they showed improvement in control grade. The surgical success rate was compared retrospectively between the two groups. The mean angle of deviation on the first visit was 27.61 ± 5.40 prism diopters (PD) at distance and 29.82 ± 5.28 PD at near. There were significant improvements in the angles of deviation for distance (26.17 ± 5.09 PD) and near (27.26 ± 5.56 PD) after part-time occlusion (both $P < .001$). The 49 patients who had a significantly improved control grade had a significantly better surgical success rate (77.6%) than the 40 patients who

did not (50%; *P* = .007). The final success rate of surgery was better in the improvement group than in the no improvement group (77.6% vs 50.0%), without any other contributing factors that might have caused a statistically significant difference between the two groups. This suggests that patients with intermittent exotropia who achieve improved control with part-time occlusion therapy could expect better surgical outcomes than their counterparts who did not. There are some limitations to this study. First, its retrospective nature meant that it was difficult to confirm the exact degree of compliance with occlusion therapy. Second, the sample size was relatively small, and the larger size of the improvement group might have led to an overestimation of the success rate in this group. Third, it was not possible to perform fusion and stereoacuity tests at distance or near, so we could not determine the relationship between control, fusion, and stereoacuity. Fourth, the follow-up period was only 1 year, so a study incorporating a longer follow-up evaluation might be necessary in the future.
The authors conclude that improving the control grade of intermittent exotropia through the implementation of part-time preoperative occlusion therapy may lead to a better surgical success rate than that achieved by surgery alone. Part-time occlusion therapy improves the control grade, which affects the surgical outcome in addition to decreasing the angles of deviation for distance and near.

Vertical muscle surgeries

Simple Horizontal muscle (medial or lateral rectus) transposition and Inferior rectus recession in Monocular Elevation Deficit: A novel Surgical Technique

Uppal Gandhi, DNB; Ramesh Kekunnaya, MD, FRCS. *J Peds Ophth & Strabismus.*2019;56(3):183-187

The purpose of this article is to describe a novel surgical technique for the treatment of monocular elevation deficit and report its short-term outcomes. In this prospective interventional case series of five patients with monocular elevation deficit, a single horizontal rectus muscle was transposed to 2 mm from the insertion of the superior rectus muscle along the spiral of Tillaux, augmenting it with a non-absorbable suture taken 8 mm behind its insertion. The main outcome measures were primary position hypotropia and elevation deficit at 8 months postoperatively. The mean age was 12.4 years (range: 6 to 26 years). Four patients underwent lateral rectus transposition and one underwent medial rectus transposition. Inferior rectus recession was done in all patients. The mean follow-up period was 8 months (range: 6 to 12 months). The mean hypotropia reduced from 34.6 prism diopters (PD) (range: 20 to 48 PD) preoperatively to 0.8 PD (range: −4 to 8 PD) at 8 months postoperatively. Additionally, 3 patients had exotropia with a mean of 12 PD (range: 2 to 20 PD) and 2 had esotropia with a mean

of 28.5 PD (range: 12 to 40 PD); 1 underwent lateral rectus recession and 1 medial rectus recession. Three patients did not require any horizontal muscle surgery. The mean elevation deficit in abduction, straight up gaze, and adduction improved from 4.4, 3.2, and 2.8 to 2.0, 2.0, and 1.8, respectively. The mean depression deficit was 0.5. No adverse effects were noted. The authors concluded that single horizontal muscle transposition (lateral rectus or medial rectus) along with augmentation by a non-absorbable suture at 8 mm from the insertion of superior rectus muscle and simultaneous inferior rectus recession achieves good correction of hypotropia in the primary position along with good improvement of elevation. An ipsilateral horizontal muscle surgery can be done simultaneously when needed. There were no torsional changes and over-corrections up to 8 months of follow-up. This novel procedure can be considered as a primary procedure in cases of monocular elevation deficit with or without coexisting horizontal deviation as an alternative to the classic Knapp's procedure.

Superior oblique tuck: evaluation of surgical outcomes.

Dwivedi R, Marsh IB. *Strabismus*. 2019 Mar;27(1):11-15.

A variety of techniques exist to surgically manage superior oblique palsy. The authors performed a retrospective chart review of 162 patients who underwent a superior oblique tuck from 1992-2016 to compare surgical success. Of the cases of superior oblique palsy, 110 patients had a congenital palsy. Pre-operatively the mean angle of deviation was 15.88 PD (range 4-35 PD) and the mean post-operative angle was 5.09 PD (range 0-20 PD). The mean overall reduction was 10.79 PD (range 0-34 PD). A significant difference was observed between those patients who had pre-operative angles of deviation >15 PD and those with <15 PD (14.85 PD vs. 6.83 PD; $p < 0.0001$). 54 patients (33.33%) required additional extraocular muscle surgery. 24 patients (14.82%) experienced post-operative iatrogenic Brown’s syndrome but only two of these required further corrective surgery. Patients with acquired superior oblique palsy tended to have worse clinical outcomes with a greater incidence of post-operative diplopia and the requirement for further surgery. There was no linear relationship between the amount of the tuck and surgical outcomes. Overall, a superior oblique tuck seems to be an effective manner of surgically managing superior oblique palsy, although there appears to be a somewhat unpredictable amount of correction.

The efficacy of superior rectus recession with simultaneous inferior oblique disinsertion on superior oblique palsy with superior rectus contracture.

Özkan SB, Akyuz Unsal AI, Kagnici DB. *Strabismus*. 2019 Mar;27(1):16-23.

Ipsilateral superior rectus contracture may develop in cases of long-standing superior oblique palsy. The authors sought to evaluate the efficacy of superior rectus recession with simultaneous inferior oblique weakening in these patients. The

records of 145 patients were reviewed retrospectively and 15 patients met the inclusion criteria. Of these the superior oblique palsy was congenital in 12 patients and traumatic in 3 patients. SR contracture was confirmed intraoperatively by forced ductions in all patients. The SR was recessed 4.86±1.18 mm. The mean post-operative vertical deviation was -3.0±4.3 PD. Postoperative overcorrection occurred in 3 of 15 cases. All three overcorrected patients received Botox. Two resolved and one was determined to have a masked bilateral superior oblique palsy. The results of our study suggested that SR recession in combination with IO disinsertion is an effective procedure in long-standing SOP with SR contracture. However, we have found 20% risk of overcorrection despite adjustable suture surgery.

Effect of inferior oblique anterior transposition in correcting vertical hyperdeviation in primary position

Gunduz A, Firat M, Ozsoy E, and Cankaya C. *Can J Ophthalmol.* February 2019;54(1):75-82.

This retrospective study aimed to evaluate the effectiveness of inferior oblique anterior transposition (IOAT) on the improvement of vertical hyperdeviations. 33 patients from 2010 to 2016 were included in the analysis. The patients underwent IOAT due to either primary inferior oblique overaction (15) or unilateral superior oblique palsy (18). Mean follow-up time was 11.43 months after surgery. The eyes were divided into 5 groups according to the amount of transposition done. Mean pre-operative primary position vertical hyperdeviation was 16.52 PD, and mean posterior hyperdeviation was 0.97 PD. The mean improvement ranged from 11.0 PD in the first group (muscle placed 2mm posterior to the inferior rectus insertion) to 25.5 PD in the last group (muscle placed 2mm anterior to the inferior rectus insertion). The improvement was significant in all groups. In the two groups were the muscle was moved anterior to the insertion of the inferior rectus, a total of 4 patients developed post-operative upgaze limitation, but did not develop hypotropia or abnormal head posture. Overall the results suggest that IOAT is effective to correct vertical hyperdeviation in this group of patients, although larger studies are warranted.

Superior Oblique Palsy: Efficacy of Isolated Inferior Oblique recession in Cases with Ipsilateral Hypertropia in Abduction

Torrado, Laura A. and Brodsky, Michael C. *Journal of Binocular Vision and Ocular Motility*, 2019; 69:1, 8-12

The purpose of this retrospective review is to evaluate the effects of single inferior oblique (IO) recession in superior oblique palsy (SOP) patients with persistent hypertropia in abduction. Numerous studies have illustrated the effect of isolated IO weakening in patients with SOP with a hypertropia in primary position of 15Δ or less. Secondary superior rectus (SR) contraction can lead to spread of

comitance and persistent hypertropia of the paretic eye in abduction, and due to frequent overcorrections SR recessions are inadvisable in these patients. Patients with a SOP and hypertropia of < 20Δ in primary position with persistent hypertropia of > 3Δ in abduction were included. Seven patients were identified and they underwent a 14mm IO recession. All patients had a decrease in hypertropia in primary position, contralateral hypertropia, ipsilateral hypertropia, lateral incomitance, and subjective intorsion. The authors conclude that an isolated maximal IO recession is effective in the treatment of unilateral SOP that is accompanied by a modest hypertropia of the paretic eye in abduction.

Surgical Outcome of Single Inferior Oblique Myectomy in Small and Large Hypertropia of Unilateral Superior Oblique Palsy.

Mohammad Reza Akbari, Samira Sadrkhanlou, Arash Mirmohammadsadeghi. *J Ped Ophth & Strabismus.*2019;56(1):23-27

The purpose of this study is To determine the efficacy of isolated inferior oblique myectomy on hypertropia in primary position, side gazes, and tilts, and its effect on comitancy and abnormal head posture in unilateral superior oblique palsy. Thirty-nine patients with unilateral superior oblique palsy who had inferior oblique overaction underwent inferior oblique myectomy. The hypertropia was measured in primary position, side gazes, and tilts preoperatively and postoperatively. Abnormal head posture was also assessed. Success was defined as primary position hypertropia of 5 prism diopters (PD) or less. The mean distance hypertropia was 15.7 ± 7.7 PD (range: 3 to 30 PD) preoperatively and 1.5 ± 3.3 PD (range: 0 to 16 PD) postoperatively ($P < .001$). The mean reduction of distance hypertropia postoperatively was 14.2 ± 7.8 PD (range: 3 to 30 PD). The contralateral gaze hypertropia decreased from 21.7 ± 9.0 PD (range: 5 to 45 PD) preoperatively to 3.6 ± 5.1 PD postoperatively (range: 0 to 20 PD) and ipsilateral head tilt hypertropia decreased from 21.9 ± 8.4 PD (range: 8 to 40 PD) preoperatively to 5.0 ± 5.9 PD (range: 0 to 24 PD) postoperatively ($P < .000$ for both). Incomitance (contralateral ipsilateral gaze hypertropia) decreased from 15.0 ± 7.4 PD (range: 3 to 35 PD) preoperatively to 2.8 ± 4.1 PD (range: 0 to 16 PD) postoperatively ($P < .001$). The success rate between the two groups of patients who had hypertropia of 15 PD or less and greater than 15 PD in primary position was not statistically different (94.7% vs 85%). Two patients underwent a second operation for residual hypertropia. There was no overcorrection. Thirty-two patients had abnormal head posture, which resolved postoperatively in 29 cases. The authors conclude that isolated inferior oblique myectomy is a simple and effective procedure in improving hypertropia due to superior oblique palsy. It can resolve large amounts of hypertropia with low risk of undercorrection and overcorrection. It is effective in resolving abnormal head posture and concurrent small amounts of horizontal deviation. In addition, inferior oblique myectomy is a self-adjusting measure that also decreases incomitancy. It is recommended that isolated inferior oblique myectomy be the first procedure for every patient with hypertropia of 30 PD or less

due to unilateral superior oblique palsy with negligible superior oblique under action. This study has some limitations. The traumatic superior oblique palsy group is small and there is no quantification for abnormal head posture. In addition, objective torsion was not measured in this study.

Surgical Mangement in Type 1 Monocular Elevation Deficiency.

Osman Bulut Ocak, Asli Inal, Ebru Demet Aygit, Selcen Celik et al. *J Ped Ophth & Strabismus.*2018;55(6):369-374

The purpose of this retrospective chart review is to evaluate the outcome of surgical treatment in patients with type 1 monocular elevation deficiency who were diagnosed as having type 1 monocular elevation deficiency by forced duction test and exaggerated traction test. Epidemiologic and clinical features of the patients were noted. The efficacy of ipsilateral inferior rectus recession to vertical misalignments and limitation of elevation were evaluated. The clinical features of the patients who did not achieve surgical success after inferior rectus recession were determined. The surgical and functional results of contralateral superior rectus recession were evaluated for patients who had residual hypotropia under inferior rectus recession. Thirty-nine patients were included in the study. Preoperatively, vertical deviations were 20.53 ± 4.50 prism diopters (PD) for near and 22.21 ± 5.12 PD for distance. After inferior rectus recession, the amount of vertical deviation corrected was 15 ± 1.14 PD for near and 17.01 ± 2.00 PD for distance. Ten (25.64%) patients did not achieve surgical success (> 6 PD residual hypotropia). Nine patients (preoperative inferior rectus recession measurements = 28.77 ± 7.25 PD for near and 27 ± 7.44 PD for distance) underwent contralateral superior rectus recession as a second surgery. After contralateral superior rectus recession, 7 of 9 (77.78%) patients achieved surgical success. The limitation of elevation significantly improved after both surgeries (Wilcoxon test, $P < .05$). No diplopia or other complications after surgeries were reported. The authors concluded that inferior rectus recession is the first surgical option for inferior rectus restriction in patients with type 1 monocular elevation deficiency. It is an effective procedure to decrease vertical misalignments but can be insufficient for large vertical deviations. After inferior rectus recession, contralateral superior rectus recession was effective for decreasing large vertical deviations. Contra-lateral superior rectus recession is a suitable alternative treatment option because it is relatively easy to perform and avoids the potential risks of tendon transposition surgery, such as anterior segment ischemia. The main limitations of this study were the relatively small sample size and no comparison with other surgical options, such as tendon transposition surgery, due to the retrospective design.

Consecutive superior oblique palsy after adjustable suture spacer surgery for Brown syndrome: incidence and predicting risk.

Sharma M, MacKinnon S, Zurakowski D, Dagi LR. *J AAPOS.* Oct 2018; 22(5): 335-339.e332.

The aim of this retrospective study was to determine the incidence of significant superior oblique palsy (SOP) after adjustable superior oblique suture spacer surgery for treatment of Brown syndrome and to identify characteristics predicting its development. A total of 19 patients treated for unilateral Brown syndrome with adjustable suture spacers (2005-2016) were reviewed to identify possible association of age at surgery, spacer length, surgeon performing procedure, severity of Brown syndrome, preoperative hypotropia in primary position and affected side gaze, and reduction in Brown restriction on postoperative superior oblique function. "Good" postoperative superior oblique function was defined as absence of hypertropia and diplopia in primary position and no more than intermittent diplopia in downgaze comfortably fused with ≤4 PD base-down or head tilt of <10°. Of 19 patients, 16 (84%) achieved sufficient resolution of Brown syndrome (defined as Brown restriction of ≤-2), but 6 (32%) developed significant SOP. Using logistic regression modelling, preoperative minimal hypotropia on contralateral gaze was shown as the only predictor of significant SOP (likelihood ratio test =7.11; P= 0.008). The authors concluded that suture spacer surgery can result in significant SOP. Risk may be predicted by magnitude of preoperative contralateral side gaze hypotropia. In their discussion the authors suggest that given the potential for spontaneous resolution of Brown syndrome and the high risk of SOP associated with minimal preoperative hypotropia in affected side gaze, conservative management would have been preferable for these patients. On the other hand, patients with >16PD of hypotropia in affected side gaze have ≥80% estimated probability of retaining good postoperative superior oblique function. These patients benefit the most from surgery. This study makes an important observation regarding adjustable suture spacers in Brown. The discussion outlines the possible approach to patients with Brown drawn from this study’s data.

Anterior superior oblique tuck: an alternate treatment for excyclotorsion.

Pineles, S. L. and F. G. Velez. *J AAPOS*. Oct 2018; 22(5): 393-393.e391.

Excyclotorsion is typically treated with surgical procedures such as the Harada-Ito, rectus muscle transposition, and inferior oblique weakening. The authors describe in this short report an alternative technique, the anterior superior oblique tuck. Their report includes 5 consecutive patients with a symptomatic excyclotropia of at least 5°. The patients ranged in age from 47 to 67 years. Preoperative torsion measured with the Maddox rods ranged from 7° to 15° (mean, 10± 3°), decreasing significantly to 2.5±2 ° (P = 0.009). Postoperative follow up ranged from 20 to 113 days (mean, 69± 34 days). The effect on torsion was stable in all but 1 patient, who had developed non-symptomatic excyclotorsion of 5 ° by final follow-up. The authors conclude that this procedure is technically simpler than the Harada-Ito and provides similar results. A demonstrative video is included.

Modified anterior transposition of the inferior oblique muscle.

Jeon H, Kwon H, Choi HY. *J AAPOS*. Oct 2018; 22(5): 361-365.e361.

The purpose of this retrospective case series was to introduce a modified method of anterior transposition of inferior oblique (ATIO) and to compare it with the traditional method in terms of efficacy and complications. A total of 31 patients who had undergone unilateral ATIO and were followed for at least 6 months were included in the study. The patients were divided into two groups according to surgical method: modified ATIO (modified group, n = 16) and traditional ATIO (traditional group, n = 15). In modified ATIO, the anterior nasal fibers of the inferior oblique muscle were anchored to the sclera and the posterior temporal fibers were folded and buried under the fixed anterior nasal fiber of inferior oblique muscle. In the traditional method, both the anterior and posterior fibers were fixed with individual suturing. Postoperative change in vertical deviation and grade of inferior oblique overaction (IOOA) were analyzed. Complications, including anti-elevation syndrome, fat adherence syndrome, and lower lid deformity were assessed. Both modified and traditional methods effectively weakened the action of the inferior oblique muscle. The efficacy of the two methods did not differ in terms of change in vertical deviation (P = 0.225) and grade of IOOA (P = 0.169). Anti-elevation syndrome occurred more frequently in the traditional group than in the modified group (8/15 vs 2/16, resp. [P = 0.019]). Incidences of fat adherence syndrome (0/15 vs 0/16 [P = 1.0]) and lid deformity (3/15 vs 1/15 [P = 0.678]) were not different. The authors concluded that modified ATIO was comparable to traditional ATIO in correcting vertical deviation and IOOA and had a lower risk of anti-elevation syndrome compared with traditional ATIO. Despite its retrospective nature and small sample size, this study demonstrates nicely the advantages of this technique.

Dose Effect and Stability of Postoperative Cyclodeviation After Adjustable Harada-Ito Surgery

Liebermann L, Leske DA, Holmes JM, et al. *Am J Ophthalmol.* 2018 December; 196: 91-95.

A retrospective cohort study of one surgeon's patients over a 20-year period was performed with the goal of reporting the dose-response relationship of the adjustable Harada-Ito surgery. The secondary goals of this study were to report the changes in the cyclodeviation over time and to recommend a target angle in the immediate postoperative period (adjustment target). There were 20 patients who underwent a unilateral adjustable advancement of the anterior fibers of the superior oblique tendon. Double Maddox rod was use to measure the cyclodeviation. The pre op measurements were compared to the 1 day and 6-week post op measurements in all patients and to the in 1- and 5- year measurements when available. The authors found that there was a dose effect of 1.3 degrees per mm of advancement ($\pm$ resection). There was a regression towards excyclodeviation between adjustment and the 6 week post op of 6.5 $\pm$ 2.6 degrees, and to a lesser extent after that. The authors recommend an initial overcorrection target of 7

degrees of incyclotorsion after adjustment. The authors point out the limitations, which include lack of complete follow up data in all patients and continued debate about the need for an adjustable procedure for torsion. This paper's most important contributions are the reminder of the cyclodeviation regression with time and the dose effect calculations.

Superior oblique tuck: evaluation of surgical outcomes.

Dwivedi R, Marsh IB. *Strabismus.* 2018 Dec 7:1-6.

A variety of techniques exist to surgically manage superior oblique palsy. The authors performed a retrospective chart review of 162 patients who underwent a superior oblique tuck from 1992-2016 to compare surgical success. Of the cases of superior oblique palsy, 110 patients had a congenital palsy. Pre-operatively the mean angle of deviation was 15.88 PD (range 4-35 PD) and the mean post-operative angle was 5.09 PD (range 0-20 PD). The mean overall reduction was 10.79 PD (range 0-34 PD). A significant difference was observed between those patients who had pre-operative angles of deviation >15 PD and those with <15 PD (14.85 PD vs. 6.83 PD; $p < 0.0001$). 54 patients (33.33%) required additional extraocular muscle surgery. 24 patients (14.82%) experienced post-operative iatrogenic Brown's syndrome but only two of these required further corrective surgery. Patients with acquired superior oblique palsy tended to have worse clinical outcomes with a greater incidence of post-operative diplopia and the requirement for further surgery. There was no linear relationship between the amount of the tuck and surgical outcomes. Overall, a superior oblique tuck seems to be an effective manner of surgically managing superior oblique palsy, although there appears to be a somewhat unpredictable amount of correction.

Vertical rectus muscle recession versus combined vertical and horizontal rectus muscle recession in patients with thyroid eye disease and hypotropia

Cestari DM, Friere MV, Chun BY. *JAAPOS*. **Aug 2018;22(4):257-261.**

This paper compares the postoperative vertical drift in patients with thyroid eye disease (TED) with hypotropia who underwent vertical rectus recession alone versus vertical rectus recession combined with horizontal rectus recession. The study was a retrospective review of the medical records of patients with TED who underwent strabismus surgery for hypotropia between 2006 and 2015 were reviewed retrospectively. Patients were divided into two groups: group 1 underwent vertical rectus recession only; group 2 underwent vertical rectus recession plus horizontal rectus recession. Data collection included pre- and postoperative deviation measurements and amount of surgical recession performed. The amount of postoperative vertical drift between groups was compared. Of 67 patients who underwent surgery during the study period, 9 in each group met inclusion criteria for a total of 18 included in the study. In the study, the mean postoperative hypotropia was 24.2^{Δ} in group 1 and 24.5^{Δ} in group 2 ($P = 0.82$). The mean vertical

deviations were 0.3Δ and −2.2Δ (P = 0.134) on postoperative day 1; −0.9Δ and −8.0Δ (P = 0.043) at final follow-up for groups 1 and 2. The mean postoperative vertical drift toward hypertropia was 1.2Δ in group 1 and 6.8Δ in group 2 (P = 0.048). The authors found that the surgical success rate for group 1 was superior to that for group 2 (89% vs 67% [P = 0.024]). The paper is limited by the short average follow up of 4 months and small number of patients. The authors conclude that there was a significantly larger postoperative vertical drift in TED patients with hypotropia who had combined vertical rectus and horizontal rectus recessions compared with those who underwent vertical rectus recession alone; this is important to consider in approaching these patient surgically.

The efficacy of superior rectus recession with simultaneous inferior oblique disinsertion on superior oblique palsy with superior rectus contracture.

Özkan SB, Akyuz Unsal AI, Kagnici DB. *Strabismus. 2*018 Dec 7:1-8.

Ipsilateral superior rectus contracture may develop in cases of long-standing superior oblique palsy. The authors sought to evaluate the efficacy of superior rectus recession with simultaneous inferior oblique weakening in these patients. The records of 145 patients were reviewed retrospectively and 15 patients met the inclusion criteria. Of these the superior oblique palsy was congenital in 12 patients and traumatic in 3 patients. SR contracture was confirmed intraoperatively by forced ductions in all patients. The SR was recessed 4.86±1.18 mm. The mean post-operative vertical deviation was -3.0±4.3 PD. Postoperative overcorrection occurred in 3 of 15 cases. All three overcorrected patients received Botox. Two resolved and one was determined to have a masked bilateral superior oblique palsy. The results of our study suggested that SR recession in combination with IO disinsertion is an effective procedure in long-standing SOP with SR contracture. However, we have found 20% risk of overcorrection despite adjustable suture surgery.

Long-term follow-up after vertical extraocular muscle surgery to correct abnormal vertical head posture.

Kumar P, Lambert SR. *Strabismus.* 2018 Sep;26(3):150-154.

There is a lack of studies looking at the results of extraocular muscle surgery to address chin up or chin down head positions in nystagmus. The existing studies are limited by short followup, heterogenous patient populations and a variety of surgical techniques. The authors report a case series of 7 patients who underwent vertical extraocular muscle surgery to address a chin up or chin down head position. The patients ranged in age from 19-96 months and were all categorized as infantile nystagmus syndrome. Five of 7 underwent combined vertical recti and oblique surgery, and 2 underwent vertical recti muscle recessions only. Six patients improved post-operatively, of which 3 had complete resolution of the anomalous head position. One patient was overcorrected, however the family

opted to defer further surgery. Overall the authors conclude that combining the procedures resulted in smaller surgical doses, which avoids other complications such as eyelid malposition and restricted range of ductions. Additionally the combination lowers the risk of inducing torsion, which improves the chances of maintaining binocularity in patients capable of perceiving diplopia.

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

Shiqiang Yang, Xin Guo, David Robbins Tien *J of Ped Ophthal & Strabismus.*2018;55(1):43-46

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

Transposition surgeries

Transposition procedures in Duane retraction syndrome.

Doyle JJ and Hunter DG. *JAAPOS* 2019 Feb; 23(1):5-14.

Duane retraction syndrome, or Duane syndrome (DS), is one of several congenital cranial dysinnervation disorders. Patients present with limited horizontal eye movement(s) and globe retraction with eyelid fissure narrowing on attempted adduction due to co-contraction of the lateral and medial rectus muscles in one or both eyes. Various surgical approaches have been proposed to improve binocular alignment, reduce head turn, and minimize undesirable up- or downshoots in DS.

Transposition procedures are one such approach, and several techniques have been described. These may involve one or both vertical rectus muscles and may or may not include full or partial disinsertion of the rectus muscle(s) from the insertion. Different options are discussed in this review including the following procedures: transposition of both vertical rectus muscles such as the full vertical rectus transposition (VRT), partial VRT, rectus muscle union, and other modifications; transposition of one vertical rectus muscle, such as the superior rectus transposition (SRT) and inferior rectus transposition (IRT). The effectiveness of any transposition procedure may be enhanced with augmentation (posterior fixation) sutures, resection of the transposed muscle(s), and/or simultaneous weakening of the ipsilateral medial rectus muscle. The indications, strengths, weaknesses, and other considerations of these approaches within the context of DS are discussed in this review.

Postoperative correction and drift after vertical rectus muscle transposition for total sixth cranial nerve palsy.

Lindsay Rothfield, KaraM.Cavuoto, Daniela P.Reyes-Capo, Elizabeth A.Vanner et al. *J of Ped Ophth & Strabismus*.2019; 56(4): 238-242

The purpose of this retrospective review was to determine the magnitude of change between the preoperative and postoperative alignment and amount of postoperative drift for two vertical rectus muscle transpositions (VTRs). Twenty-seven patients with total sixth nerve palsy were included in the study. Sixteen had full tendon transposition with Foster augmentation (FTT+FA) and 11 had partial tendon transposition with resection and simultaneous medial rectus recession (PTT+R+MRR). A larger correction was obtained with PTT+R+MRR (mean ± standard deviation [SD]: 52 ± 19 PD; range: 27 to 87 PD) when compared to FTT+FA (mean: 40 ± 13 PD; range: 15 to 68 PD). At postoperative month 2, a greater esotropic drift was noted in the PTT+R+MRR group (16 PD) than the FTT+FA group (6 PD). Although the difference in the amount of correction was not statistically significant (P = .071), the difference in the amount of drift was statistically significant (P = .009). The authors concluded that if surgical success is defined as less than 10 PD of horizontal deviation, the success rate of PTT+R+MRR was 73% and that of FTT+FA was 44%. We identified that PTT+R+MRR had a larger correction despite a greater postoperative esotropic drift when compared to FTT+FA. With this in mind, targeting a small immediate postoperative overcorrection may be desirable in PTT procedures. This study had several limitations, including the retrospective nature of chart review, a relatively small patient population, and a different number of patients in each surgical group. The authors did not have complete preoperative and postoperative data regarding the limitation to abduction or ocular torticollis. A wide range of correction was obtained for each group, which could be due to multiple surgeons with

differing techniques. This might also have resulted from patients with a −4 duction deficit being compared to those with −5 or worse deficits. It is also possible that some patients may have had only a partial palsy and a tight medial rectus muscle that masked some of the abducting capability. A final discrepancy could lie in the fact that there were different examiners assessing and measuring alignment, thus introducing another source of variability. Additionally, there was a wide range in the postoperative drift and it is possible that additional changes in alignment could occur at postoperative time intervals longer than 2 months. Despite these limitations, the study provides valuable information because it directly compares two VRT procedures by evaluating not only the postoperative correction, but also the immediate postoperative drift, which has not been reported to this extent in prior studies.

Lateral rectus-medial rectus union: A new Surgical Technique for Treatment of Complete Third Nerve Palsy.

Abbas Bagheri, Mohadeseh Feizi, Ramin Sahebghalam, Shahin Yazdani. *J of Ped Ophth & Strabismus*.2018;56(1):10-18

The purpose of this article is to describe a new surgical technique for the treatment of complete third nerve palsy. The lateral rectus muscle was split, followed by disinsertion of the superior and inferior halves, which were passed between the sclera and superior and inferior rectus muscles, respectively. Then the medial rectus muscle was sutured as posteriorly as possible from its insertion and cut. Next, the distal stump of the medial rectus muscle was split into two halves and united with the superior and inferior halves of the lateral rectus muscle. Finally, the proximal portion of the medial rectus muscle was sutured back to its original insertion. In cases with hypotropia and a functional superior oblique muscle, superior oblique tenectomy was also performed. Success was defined as postoperative horizontal deviation of 10 prism diopters (PD) or less and vertical deviation of 5 PD or less. Ten patients with a mean age of 32.4 ± 18.4 years had surgery using this technique; 2 of them had a history of strabismus surgery. Mean exotropia was 84 ± 14.9 PD, which reduced to 6.5 ± 8.2 PD. Mean vertical deviation was 16.5 ± 10 PD, which reduced to 2.5 ± 3.5 PD. Mean follow-up was 13.2 ± 7.9 months, and the success rate was 70% and 90% for horizontal and vertical deviations, respectively. The patients were followed for 3 months. One should note that, with this method, the sequence of actions during the operation must be precisely followed for the procedure to be successful and this requires a long learning curve. It is also predictable that reoperation may be difficult after this procedure; however, reoperation was performed in two of the authors' cases successfully. One limitation of all types of surgeries for correction of strabismus associated with complete third nerve palsy is the inability to address aesthetics by ptosis surgery in most cases; in this study, ptosis correction could be performed in

only 30% of cases. Another limitation of this study is the small sample size requiring further evaluation to show its efficacy and safety and the short follow-up. The authors conclude that transposition and union of a split lateral rectus muscle with the stump of a resected medial rectus muscle, together with superior oblique tenectomy in hypotropic cases, is a dynamic procedure that improves alignment in primary position and can help balance ocular movements in a paralytic eye. This technique can be used as a reoperation procedure and in children without using any autogenous or exogenous material.

Dual-Augmented Transposition of Vertical Recti in Chronic Abducens Palsy

Farid MF *Am J Ophthalmol.* 2019 January; 197: 59-64.

This retrospective case series of 14 patients with abducens palsy aims to report the results of dual-augmentation of a partial tendon transposition. The author of this paper collected pre and post surgical data including alignment, head position, limitation in eye motility, and demographic data. The author uses a combination of posterior scleral fixation (Foster modification) and a suturing the transposed vertical recti to the lateral rectus (Wright modification) to augment the effect of the partial tendon transposition in the treatment of abducens nerve palsy. A partial transposition was performed in all patients and eyes with positive intraoperative forced duction testing an ipsilateral weakening of the medial rectus muscle was also performed. The dual augmented partial tendon transposition procedure provided a mean of 31.3 prism diopters of correction. Head position and limitation in abduction was also improved with this procedure. The author had no cases of anterior segment ischemia, and 3 cases did have a small angle vertical deviation (hypertropia) post operatively, but none requiring surgical intervention. This paper does a good job providing the reader with another option in the treatment of abducens palsy. The small sample size is a main limitation. The discussion section has a good review of other options for treating this difficult condition. The title should reflect that this is a partial tendon transposition.

A modified vertical muscle transposition for the treatment of large-angle esotropia due to sixth nerve palsy.

Sabermoghadam A, Etezad Razavi M, Sharifi M, Kiarudi MY, et al. *Strabismus*. 2018 Sep;26(3):145-149.

Non-resolving sixth nerve palsies can be treated by a variety of surgical procedures, of which the augmented Hummelsheim has become the most popular. However alternatives to this procedure, such as the Nishida procedure, are emerging. The authors performed a prospective study in which they enrolled 10 patients with complete sixth nerve palsy who underwent a modified Nishida procedure. In the procedure, the authors used 6-0 Mersilene through the temporal margin of each vertical rectus muscle 1/3 of the width from the edge 10mm behind in the insertion and then transposed the vertical muscles without tenotomy

or splitting, inserting them 16mm from the limbus in the superotemporal and inferotemporal quadrants. A medial rectus recession was performed in conjunction with the transposition. The mean correction was 49 PD. The post-operative deviation ranged from ortho to 12PD ET at final followup. Two patients had a slight overcorrection at POM 1 but this resolved. All patients had some abduction to at least midline. There were no cases of anterior ischemia syndrome. This procedure may be an option to consider when surgical treatment for complete CN 6 palsy is planned.

Sutures / Adjustables

Outcomes of medial rectus recession with adjustable suture with acute concomitant esotropia of Adulthood.

Ignacio García-Basterra; José Maria Rodríguez Del Valle; Antonio García-Ben; José María Rodríguez Sánchez et al. *J of Ped Ophthal & Strabismus.*2019;56(2):101-106

The purpose of this study is to review and analyze the surgical outcomes of bilateral medial rectus recession with adjustable suture in acute concomitant esotropia of adulthood (ACEA).The charts of all adults diagnosed as having ACEA between 2004 and 2017 were reviewed. Best corrected visual acuity, refractive error, ocular alignment measured in prism diopters (PD), and stereopsis were examined at presentation, 1 day postoperatively, and final follow-up visit (median: 10 months; range: 4 to 144 months). All patients underwent bilateral medial rectus recession using adjustable suture surgery and topical anesthesia. Statistical analysis was used to calculate surgical dose-responses and to study possible correlations with clinical parameters. Fifteen patients diagnosed as having ACEA were included. The mean age was 39.2 ± 10.7 years, and the mean refractive errors in the right and left eyes were −3.97 ± 2.87 and −3.60 ± 2.74 diopters (D), respectively. Average esotropia deviations at near and distance were 22.7 ± 7.2 and 23.0 ± 7.5 PD. All patients improved with medial rectus recession (mean: 12.0 ± 2.2 mm) with a final mean deviation of 0.7 ± 1.8 PD. The mean dose-responses at 1 day postoperatively and final visit were 1.86 ± 0.58 and 1.83 ± 0.43 PD/mm, respectively. There was a significant positive correlation between surgical dose-responses at 1 day postoperatively and final visit and preoperative deviation (R^2 = 0.55; P < .001; R^2 = 0.66; P < .001), whereas there were no significant correlations with age, sex, refractive error, BCVA, or stereopsis (all P > .05). The authors concluded that a larger surgical dose than conventionally used may be necessary to achieve orthophoria in ACEA. The use of adjustable sutures allows for the appropriate adjustment of surgical dose with good clinical results. More preoperative deviation predicts more surgical dose-response soon after surgery and at several months of follow-up. This study has the following limitations: first, this study did not use a control group of esotropias to compare the response to surgery in different kinds of convergent strabismus or the effectiveness of different surgical techniques. Second, a relatively small sample was studied

and consequently it may have limited the possibility of obtaining significant associations between variables. Further studies comparing different esodeviations and surgical techniques may be useful to identify the best approach to this disorder.

Topical Anesthesia in Children with Intraoperative Adjustable Strabismus Surgery.

Filippo Franco, MD; Elena Bolletta, MD; Silvia Mancioppi, MD; Elena Franco, CO; Alberto Migliorelli, MD; Paolo Perri, MD *J Peds Ophth & Strabismus*.2019-56(3):173-177

The purpose of this study was to evaluate strabismus surgery with intraoperative adjustment of sutures under topical anesthesia in children. Nineteen children with horizontal deviation underwent a one-stage surgical technique performed under topical anesthesia. Surgery consisted of unilateral or bilateral recession and/or resection of horizontal muscles or the medial or lateral rectus muscles, with intraoperative adjustment of sutures based on alternate prism cover test. The adjustment target was to leave patients with esotropia within 4 prism diopters (PD) of straight in cases of fusion potential and undercorrect by +8 to +10 PD at distance in cases of no fusion potential, whereas patients with exotropia were overcorrected (esotropia) in distance by +2 to +6 PD. The amount of surgery was adjusted until target correction was reached and no diplopia was present on the APCT in primary position and down gaze. The topical anesthesia protocol consisted of sublingual or intranasal midazolam 0.25 mg/kg from 20 to 30 minutes before the child entered the operating room, followed by instillation of lidocaine 4% eye drops in the conjunctival sac before beginning surgery. The use of topical benoxinate 4 mg/mL eye drops before lidocaine reduced a burning sensation, whereas additional lidocaine 4% eye drops were instilled if the patient complained of discomfort during surgery Follow-up was done at 1 day and 1, 3, and 6 months postoperatively. Mean age at surgery was 12.68 ± 2.50 years (range: 8 to 16 years). Mean preoperative angle of deviation was 24.21 ± 11.20 prism diopters (PD) (range: −50 to +30 PD) at distance. Mean postoperative angle of deviation at 6 months was 4.11 ± 2.87 PD (range: −10 to +10 PD) at distance. The study showed that in esotropic patients, the average angle of deviation decreased from +23.80 ± 5.89 PD preoperatively to +4.80 ± 3.35 PD at 6 months, whereas in exotropic patients it decreased from −24.36 ± 12.76 to −3.86 ± 2.77 PD. Seventeen of 19 patients (89%) remained comfortable during surgery, whereas 2 needed an intravenous injection of propofol. The success rate, defined by a postoperative residual angle of deviation of ±8 PD or less, was 89% at 6 months. All patients reported no pain during conjunctival limbal incision and tissue dissection. Greater discomfort was reported during muscle isolation due to the hooking maneuver. No pain was reported during muscle reattachment or suture adjustment. Intraoperative cardiac monitoring did not record positive oculocardiac reflex in any patients. No patients experienced side effects after sublingual administration of midazolam or after intravenous injection of propofol, when

provided. Strabismus surgery with intraoperative suture adjustment under topical anesthesia in children is a tolerable procedure with encouraging outcomes, representing an alternative to general anesthesia in well-selected children. Clinical evaluation of both the child and parents is fundamental in predicting a likely poor collaboration of the child during surgery, which, if present, would require surgery under general anesthesia. The limitations of this study are the relatively small number of patients, the short postoperative observation period, the non-masked observer for preoperative and postoperative examination, the need for an orthoptist in the operating room, and the effect of midazolam and propofol on deviation. Studies are needed to elucidate further the patients who are eligible for this procedure and to compare this procedure with conventional techniques.

Retrobulbar anaesthesia for adjustable strabismus surgery in adults: a prospective observational study

Modabber M, Dan A, Coussa R, Flanders M. *Can J Ophthalmol.* December 2018;53(6):621-626

Retrobulbar anesthesia allows for patients with significant comorbidities to undergo surgery without the risk of general anesthesia. There is limited data on the utility of retrobulbar anesthesia in adjustable strabismus surgery. Concerns about how long it takes for the anesthesia to wear off prior to same day adjustments as well as injection complications may limit its use. This observation study attempted to characterize ocular responses to retrobulbar anesthesia and its efficacy for adjustable strabismus surgery. 33 patients were included in the study. Two of these were excluded from data analysis due to complications – perioperative retrobulbar hemorrhage and postoperative suprachoroidal hemorrhage (both of which recovered to baseline). Of the 31 patients included in analysis, surgery outcome was satisfactory (within 10PD of orthotropia for horizontal surgery, 5 PD for vertical surgery) in 30/31 at first post-operative visit and in 15/19 at last follow-up visit (mean 6.1 months). Visual impairment due to the anesthesia resolved to pre-operative levels within mean of 3.7 hours. Pain returned at 4.1 hours, ptosis resolved at 4.3 hours, and pupils returned to normal reactivity at 6.1 hours. Extraocular motility returned to normal within 5.7 hours. These data allowed the authors to conclude that retrobulbar anesthesia is relatively safe and effective, and allows for same day suture adjustments to be performed.

Strabismus surgery - Misc

The incidence and clinical outcome of complications in 4,000 consecutive strabismus operations.

Ritchie AE and Ali N *JAAPOS* 2019 June; 23 (3): 140.e1-140.e6

The British Ophthalmic Surveillance Unit (BOSU) estimated in 2013 the incidence of severe complications in strabismus surgery at 1 in 400 operations, with a poor or very poor outcome in 1 in 2,400 cases. This landmark study provided a benchmark for audit and an evidence-base for discussing the risks of strabismus surgery with patients. The study, however, relied on anonymous surgeons volunteering to take part and remembering to return questionnaires; thus, complications may have been underreported. The purpose of this prospective audit was to test the validity of the British Ophthalmic Surveillance Unit (BOSU) study's incidence figure of severe complications following strabismus surgery and to determine the incidence, type, risk factors, and outcome of all strabismus surgery complications at a single institution. Patient diagnosis, age, sex, surgical details, complications, and outcome were recorded from hospital records. Complications were classified as minor, moderate, or severe. The outcome was graded using the Bradbury and Taylor grading system (I to IV), with a poor or very poor outcome meaning loss of corrected visual acuity or unexpected primary position diplopia. A total of 4,076 consecutive strabismus operations were performed during the study period. There were 46 (1.13%) complications, of which 28 (0.69%) were minor, 7 (0.17%) were moderate, and 9 (0.22%) were severe. The incidence rate of 0.07% (3 patients) for globe perforations in this study is comparable with the BOSU study rate of 0.08%. Two patients had pulled-in-two syndrome (PITS) intraoperatively (0.05%). Only 1 patient (0.02%) had a poor visual outcome. Optical coherence tomography (OCT) imaging was in keeping with paracentral acute middle maculopathy. It is most likely that cilioretinal artery territory infarction occurred during the perioperative period. Two patients had non-ocular postoperative complications (0.05%). Interestingly, of the patients who underwent surgery during the study period, 84% were adults (>16 years of age); 16% were children. The rate of severe complications was 0.23% for adults and 0.16% for children, a difference that was not statistically significant.
The authors conclude that in this large, prospective series, the rate of severe complications of strabismus surgery was found to be 1 in 455 cases. Their results validate the findings of the BOSU study. This seminal study might be the largest prospective series of consecutive cases reporting on the full range of complications of strabismus surgery and can be used as an evidence-base for discussing the risks of strabismus surgery with patients.

Intratrochlear steroid injections in acquired Brown syndrome-a case series.

Ravilla ST, Shetty S and Perumalsamy V. *JAAPOS* 2019 Feb;23(1):23. e1-23. e5
In this short case-series the authors describe their experience in the treatment of children with acquired Brown syndrome by means of intratrochlear injection of betamethasonein. A total of 5 patients (1.5-15 years of age), who were treated with intratrochlear betamethasone in 2016 at the Aravind Eye Hospital, Madurai were included. Betamethasone injection was administered 2-8 weeks following onset of symptoms. During the postoperative period, abnormal head posture and elevation in adduction improved in 4 subjects but did not resolve completely. The median vertical deviation was

11.5$^{\Delta}$ preoperatively and reduced to 3.5$^{\Delta}$ postoperatively. A significant reduction in deviation was demonstrable on Hess charting in 2 of the older children. One patient, who did not improve after injection, was prescribed prism glasses and became diplopia free. The authors conclude that in this case-series, children with acquired Brown syndrome of idiopathic or presumed inflammatory etiology showed significant reduction in deviation and symptoms following intratrochlear injection of betamethasone. They suggest that this treatment be considered for children affected by acquired Brown syndrome. This study is limited by its retrospective nature, small sample size and short follow-up.

Changes in refractive error and axial length after horizontal muscle surgery for strabismus.

Lee D, Kim M, Kim WJ and Kim MM. *JAAPOS* 2019 Feb;23(1):20. e1-20. e5.

Previous reports have documented transient changes in refractive error after horizontal muscle surgery. The aim of this prospective cross-sectional study was to investigate changes in refractive error following horizontal muscle surgery and to analyse the relationship between these changes and axial length. Patients with intermittent exotropia who underwent bilateral lateral rectus recession (LR group) or unilateral lateral rectus recession with medial rectus resection (RR group) were enrolled prospectively. A total of 64 eyes of 47 patients were included-34 eyes in the LR group and 30 eyes in the RR group. The patients were followed for at least 3 months postoperatively; refractive error, axial length, mean corneal astigmatism, anterior chamber depth, corneal thickness, and intraocular pressure were evaluated at each examination. In both groups refractive error, axial length, and mean corneal astigmatism significantly increased 1 day postoperatively, although the changes in all three parameters returned to their preoperative values within 1 month of surgery and remained stable thereafter for the duration of the follow-up period. There was a negative correlation between changes in axial length and refractive error toward myopia in the 64 eyes on postoperative day 1 (partial correlation coefficient $r = -0.637$; $P < 0.001$). Changes in refractive error and axial length were significantly larger in the RR than in the LR group 1 day postoperatively ($P < 0.001$ and $P < 0.001$, resp.). The authors conclude that horizontal muscle surgery induces a transient myopic shift. Their results indicate that this may be due to axial length elongation as well as changes in corneal astigmatism.

Partial scleral buckle removal during strabismus surgery after retinal detachment repair.

Kumar P, Hoover DL and Lambert SR. *JAAPOS* 2019 Feb;23(1):16. e1-16. e4.

The benefit of scleral buckle removal in treating buckle associated strabismus has been controversial. The aim of this retrospective case series was to describe outcomes of strabismus surgery after partial scleral buckle removal at the time of surgery. The medical

records of 12 consecutive patients (mean age, 51 years; range, 14-71 years) with symptomatic diplopia who underwent strabismus surgery after scleral buckling by two surgeons were reviewed retrospectively. All patients underwent forced duction testing and had a segment of the scleral buckle removed intraoperatively. Pre- and postoperative ocular motility and alignment were compared. The outcome was considered successful if residual horizontal deviation was ≤8$^{\Delta}$, vertical deviation ≤2$^{\Delta}$, and cyclotropia <5°. Mean pre-operative horizontal deviation of 16$^{\Delta}$ (range, 2$^{\Delta}$-40$^{\Delta}$) and mean vertical deviation of 10$^{\Delta}$ (range, 2$^{\Delta}$-20$^{\Delta}$) was recorded. Three patients underwent 2 strabismus surgeries. An adjustable suture technique was used in 13 of 15 surgeries (86%). Orthotropia was achieved in 7 patients (58%); surgical success, in 11 (92%). Subjective resolution of diplopia was achieved in all patients, in 2 with the aid of prisms. Mean follow-up was 12.4 months (range, 1-75). No patient had retinal redetachment. The authors conclude that in this case series, removal of a segment of the scleral buckle facilitated advancement or recession of a rectus muscle and was associated with good outcomes without retinal redetachment. The results of this study are limited by its retrospective nature, the small sample size, and the short follow-up. Some reports in the literature show good results without scleral buckle removal; Nonetheless, the technique described in this article may enhance surgical outcome in cases, where the buckle or scar tissue formation is deemed likely to create a physical barrier that could hinder the formation of a firm muscle insertion–sclera attachment.

Postoperative infection following strabismus surgery: case series and increased incidence in a single referral center.

House RJ, Rotruck JC, Enyedi LB, Wallace DK, et al. *JAAPOS* 2019 Feb;23(1):26. e1-26. e7

Postoperative infection following strabismus surgery remains uncommon, with reported incidence ranging from 1 in 1100 to 1 in 1900 cases. Over the last decade, surveys and case reports have described postoperative infections. The purpose of this retrospective study was to identify and analyse cases of postoperative infection following strabismus surgery at a large referral center and to report the incidence, risk factors, and outcomes. An electronic database search identified strabismus procedures at Duke Eye Center from July 1996 to October 2017. Diagnosis codes for periocular infections were used to further identify patients with possible infections following strabismus surgery. Of 9,111 strabismus surgeries, 13 (0.14%) met criteria for probable infection, all occurring since October 2012 (0/6580 before vs 13/2531 [0.51%] after; P < 0.0001). Clinical evidence of infection developed 1-20 days (median, 3; mean, 7.2) following surgery. Mean age of infection cases was 11.4 years; 11 patients (85%) were under 18 years of age. Associated previous diagnoses were genetic abnormalities with associated developmental delay (n = 5 [38%]), previous skin or ear infection (n = 4 [31%]), and acute or chronic rhinitis (n = 3 [23%]). Infection site cultures revealed methicillin-resistant Staphylococcus aureus (n = 3 [23%]), methicillin-sensitive S. aureus (n = 3 [23%]), and Streptococcus pyogenes/group-A Streptococcus (n = 2

[15%]). Only 1 case had bilateral infection that occurred in a child with *Down syndrome* and a history of acute myeloid leukemia in remission. Infection remained extraocular in all cases, but one eye lost light perception secondary to optic atrophy. No common surgeon/procedure/preparation-related risks were identified. The authors could not identify a unifying explanation for the increase in post-strabismus surgery infections at Duke Eye Center, nonetheless they conclude that potential risk factors include age <18 years, developmental delay, immune compromise, preceding nonocular infection, and bacterial colonization. This descriptive study raises an important topic. However, its risk factor analysis was limited. Logistic regression was not applied to assess the potential risk factors that may have been associated with postoperative infection, possibly due to small sample size.

The management of large-angle esotropia in Graves ophthalmopathy with combined medial rectus recession and lateral rectus resection.

Garrity JA, Greninger DA, Ekdawi NS, Steele EA. *JAAPOS* 2019 Feb;23(1):15. e1-15. e5.

There are a multitude of surgical approaches to strabismus in Graves ophthalmopathy, including adjustable sutures, matching the restriction of ductions, and intraoperative relaxed muscle positioning. The purpose of this retrospective study was to describe surgical management and outcomes for large-angle esotropia of ≥50$^{\Delta}$ secondary to Graves ophthalmopathy using combined initial nonadjustable medial rectus recessions and lateral rectus resections. The medical records of 38 consecutive patients undergoing strabismus surgery for large-angle esotropia secondary to Graves ophthalmopathy from 1995 to 2012 by a single surgeon were reviewed. The technique and surgical dosing are further described in the article. Of the 38 eligible patients, 36 had bilateral nonadjustable medial rectus recessions and lateral rectus resections as initial treatment for esotropia, and 6 patients underwent simultaneous vertical muscle surgery. Mean preoperative horizontal deviation was 60$^{\Delta}$ (range 50$^{\Delta}$ -95$^{\Delta}$) and mean preoperative vertical deviation was 10$^{\Delta}$ (range 0 -65$^{\Delta}$). A modified Gorman diplopia scale was used to assess outcome. Satisfactory outcome was defined as absence of constant diplopia in primary or reading position within the central 30^{o}, and unsatisfactory outcome was defined as presence of constant diplopia in primary and/or reading position. A total of 19 patients (50%) reached the primary outcome after one surgery, including 5 of 6 (85%) who had no preoperative vertical strabismus. A total of 21 patients (55%) required repeated surgery. The indications for reoperation were vertical strabismus in 13 of 21 patients (62%), residual esotropia in 7 of 21 (33%), and consecutive exotropia in 1 of 21 (5%). With a median follow-up of 13.2 months, 32 of 38 patients (84%) reached the satisfactory results after consecutive surgery.The authors conclude that combined nonadjustable medial rectus recessions with lateral rectus resections can be beneficial as a primary treatment for large-angle esotropia in patients with Graves ophthalmopathy. The

study is limited by its retrospective nature and relatively short follow-up, nonetheless it offers yet another alternative for these difficult cases with comparable success rate to other techniques.

Optical Coherence Tomography Angiography: Are there any changes in measurements after strabismus surgery?

Asli Inal, MD; Ihsan Yilmaz, MD; Osman Bulut Ocak, MD; Ebru Demet Aygit, MD et al. *J of Ped Ophth & Strabismus*.2019;56(2):95-100

The purpose of this study is to evaluate the possible hemodynamic changes following strabismus surgery via optical coherence tomography angiography. Thirty-two eyes of 16 patients who underwent strabismus surgery in one eye were included in the study. Fellow eyes were used as a control group. The vessel densities of the superficial and deep capillary plexus and superficial and deep foveal avascular zones were measured preoperatively and 3 months postoperatively. The mean superficial and deep foveal avascular zones measurements were 0.84 ± 0.09 and 0.76 ± 1.13 mm^2, respectively. The mean vessel density of the superficial capillary plexus was 1.23 ± 0.12 and 11.13 ± 1.04 mm^2 preoperatively in the 1- and 3-mm zones, respectively, whereas the mean vessel density of the deep capillary plexus was 1.13 ± 0.16 and 10.11 ± 1.28 mm^2 preoperatively. Postoperatively, the mean superficial and deep foveal avascular zones changed to 0.20 ± 0.13 and 0.23 ± 0.12 mm^2, respectively. Postoperatively, the mean vessel density of the superficial capillary plexus changed to 1.47 ± 0.11 and 12.75 ± 1.10 mm^2, and the mean vessel density of the deep capillary plexus changed to 1.56 ± 0.12 and 13.91 ± 1.35 mm^2 in 1- and 3-mm zones, respectively. There was a statistically significant increase in vessel density measurements of the superficial and deep capillary plexus, and a statistically significant decrease in measurements of the superficial and deep foveal avascular zone postoperatively ($P < .05$). In the fellow eyes, there was no statistically significant change in any of the measurements ($P > .05$). The authors concluded that strabismus surgery seems to affect the vessel density of the macula in the short term. OCTA is a non-invasive technology that allows physicians to evaluate the macular circulation. According to OCTA, vessel density measurements may increase and foveal avascular zone measurements may decrease after strabismus surgery. Further studies are needed to confirm these data, and long-term results should be evaluated. Limitations of this study are the small sample size and lack of long-term follow-up. Because this is the first study to present OCTA measurements from patients who underwent strabismus surgery, we could not compare our results to other studies. This study is the first to use OCTA to present the changes in the superficial and deep capillary plexus and superficial and deep foveal avascular zone measurements after strabismus surgery.

Postoperative nausea and vomiting and Phase 1 post-anesthesia Recovery after Strabismus operations.

Kathleen M. Kratt, RN, CCRN; Erick D. Bothun, MD; Sree Chandralek Kruthiventi, MD; Erica R. Portner, RRT; Juraj Sprung, MD, PhD; Toby N. Weingarten, MD *J Peds Ophth & Strabismus*.2019;56(3):151-156

The purpose of this retrospective observational study is to ascertain postoperative nausea and vomiting (PONV) rates in adult patients after strabismus operations and assess causes for prolonged post-anesthesia recovery. The anesthetic records of 479 patients were abstracted and PONV rates were ascertained. On the basis of the cohort's 75th percentile of anesthesia recovery duration, patients were categorized into goal recovery (lower three quartiles) and prolonged recovery (upper quartile). Multivariable logistic regression analyses were performed to assess associations between clinical characteristics and prolonged recovery. The study showed that PONV was present in 31 (3.9%) patients. The median (interquartile range) post-anesthesia recovery was 45 minutes (range: 33 to 63 minutes). Prolonged recovery was associated with long-term benzodiazepine use (odds ratio [OR]: 3.07; 95% CI [confidence interval]: 1.23 to 7.80; *P* = .02). Patients with prolonged recovery had higher rates of PONV (15 [7.2%] vs 16 [2.7%], *P* = .007), oversedation (107 [51.4%] vs 226 [38.6%], *P* = .001), and postoperative analgesic administration (138 [66.4%] vs 222 [37.9%], *P* < .001). Inverse associations were found between desflurane and oversedation (OR: 0.63; 95% CI: 0.45 to 0.86; *P* = .004) and between acetaminophen administration and postoperative analgesic administration (OR: 0.57; 95% CI: 0.38 to 0.86; *P* = .007). The authors conclude that adult patients undergoing general anesthesia for strabismus surgery had a low PONV rate. However, the presence of PONV was associated with delayed recovery room discharge. Other factors associated with prolonged Phase I recovery were long-term benzodiazepine use and longer operations, which likely resulted in an increased need for anesthetic agents and therefore more intense postoperative sedation. The current study was limited by its retrospective research design.

Population trends in adult strabismus surgery

Szigiato A, Caldwell M, Buys Y, Kraft S, et al. *Can J Ophthalmol.* August 2019;54(4):501-508

The purpose of this study was to analyze the current trends in adult strabismus surgery in Ontario, Canada. They performed a retrospective study using data from a centralized database of health care in Ontario. All patients 18 or older who underwent strabismus procedures between 2000 and 2013 were included. The authors found that over the time period studies, the number of surgeons performing adult strabismus surgery decreased 30% (60 to 42 surgeons). As the population increased as well, the number of surgeons per million adult population decreased, and the number of cases per surgeon performed annually increased. A total of 861 procedures were performed in 2000, increasing to 1321 in 2013. The number of adjustable procedures increased 30.3%. Adjustable procedures repre-

sented 44.9% of all strabismus surgeries over the study period. Repeat procedures increased 19.1%. Overall the total number of surgeries increased 26.0%, with the largest increase in 2-muscle surgery. The authors speculate that the overall increase is likely due to health care funding changes and increased awareness of the functional and psychosocial impacts of strabismus surgery.

An analysis of strabismus reoperations in Northern Alberta, Canada from 1995 to 2015

Benson M, Wozniak J, and MacDonald I. *Can J Ophthalmol.* February 2019;54(1):94-97.

The authors of this study conducted a retrospective review of all strabismus surgery patients at a single center in Canada from 1995 to 2015. Over this long 21 year period of study, 6177 strabismus surgeries were performed on 5125 patients. The overall cumulative reoperation rate was 15.7%. A total of 1050 reoperations were performed on 806 patients. 108 of these reoperations occurred within 12 weeks of the previous surgery. Overall 77.7% of reoperation cases required a single reoperation surgery. 17.1% required two, and 5.2% required 3 or more. The average age at time of initial surgery was 26.5 years with a mean time between surgeries for those undergoing reoperation 2.3 years (median 1.0 years). This study did note that the cohort of patients was heterogeneous and included pediatric and adult patients, adjustable and non-adjustable cases, different types of strabismus and different approaches to surgery. However the authors state that the information obtained can still be useful especially with pre-operative counseling of patients regarding the risk of needing reoperation.

Improvement in psychiatric symptoms after strabismus surgery in adolescent patients in long-term follow-up

Ozates S, Ozates M, Can C, Polat S, et al. *Br J* Ophthalmol. July 2019;103:966-970

Strabismus has been shown to affect quality of life in affected patients, and can be associated with depression, anxiety, low self-esteem, communication problems, and overall decreased functionality. Although several studies have shown beneficial psychological effect so strabismus correction, the pre-operative primary eye position and its psychological impacts has not been fully elucidated. This study, conducted in Turkey, included 83 adolescent (age 14-21) patients with manifest intermittent exotropia who underwent strabismus surgery. All patients were scored using scales for social appearance, depression, and anxiety before and 1 year after surgery. Two groups were analyzed, including a manifest group (those that had manifest exotropia), and a latent group (those with orthophoria with minus lenses but recently increased Newcastle Control Scores). The scores on the psychosocial scares were all significantly higher in the manifest

group compared to the latent group. All scores improved after surgery in the manifest group. Scores for social appearance anxiety, depression, and fear of negative evaluation did no significant improve in the latent group. Overall the results suggest that a visible eye deviation caused by strabismus was a strong indicator of psychological distress in adolescent patients.

The use of Botulinum Toxin in Strabismus Treatment

Gomez de Liano, Rosario *Journal of Binocular Vision and Ocular Motility*, 2019; 69:1, 51-60

The use of Botulinum Toxin type A (BoNT-A) has proven to be a useful technique in the treatment of strabismus and oculomotor paralysis, but the frequency of its use varies depending on the country and institution. BoNT-A produces a transient paralysis of the injected extraocular muscle which leads to a transient (1-4 months) overcorrection of the strabismus followed by stable alignment between 3- and 12-months post-injection. The permanent correction of the deviation is due to mechanical, binocular, and proprioceptive factors. The muscle should be injected in the posterior 1/3rd close to the neuromuscular junction. Electromyographic (EMG) devices can aid in injection. The most frequently used doses used at 2.5 and 5 Units of Botox or 2.5 Units of Dysport per muscle in children. The dosage depends on the age of the patients, type of strabismus, and magnitude of strabismus. BoNT-A has been demonstrated to be effective in comitant strabismus, including infantile esotropia, late decompensated esotropia, partially accommodative esotropia, sensory esotropia. BoNT-A is less effective in esotropia than esotropia and requires higher dosage. It is also used to potentiate the effect of a recession in the cases of large deviations. Other uses include residual and consecutive deviations, oculomotor paralysis, restrictive strabismus, and nystagmus. The authors note that there are very few contraindications to the use of BoNT-A injection for ophthalmic conditions. The most frequent complication is ptosis. An induced vertical deviation may occur after injection of the horizontal muscles. Other complications reported include diplopia, dry eye, accommodation deficit, tonic pupil, retrobulbar hemorrhage, and ocular perforation. The author concludes that there is long-term experience using BoNT-A in the treatment of strabismus.

Surgery option in the management of delayed diplopia after radiation therapy for nasopharyngeal carcinoma

Zou L, Wu S, Liu Y, Wang S, Wen W, Liu H *Eur J Ophthalmol.* Sep 2018;28(5):547-551.

The authors in this study retrospectively evaluate outcomes of strabismus surgery for patients with 6th nerve palsy after radiation treatment for nasopharyngeal carcinoma. In this study, all patients underwent unilateral lateral rectus resection for a mean reduction in horizontal strabismus from 16 PD to 1.5 PD. Outcomes were favorable at 1 year with no recurrence of diplopia in the cohort.

Spontaneous reattachment of medial rectus after free tenotomy.

Daniel L.Adams, Brittany C. Rapone, John R.Economides, Jonathan C. Horton.J *Ped Ophth & Strabismus*.2018;55(5):335-338

The purpose of this study is to assess the outcome of free tenotomy of the medial rectus muscle in post-natal monkeys. The medial rectus muscle was disinserted in both eyes of 6 macaques at age 4 weeks to induce an alternating exotropia. After the impact on the visual cortex and superior colliculus was investigated, the animals were examined post-mortem to assess the anatomy of the medial rectus muscles. The study showed that after tenotomy, the monkeys eventually recovered partial adduction. Necropsy revealed that all 12 medial rectus muscles had reattached to the globe. They were firmly connected via an abnormally long tendon, but at the native insertion site. The authors conclude that the medial rectus muscles are able to reattach spontaneously to the eye following free tenotomy in post-natal macaques. The early timing of surgery and the large size of the globe relative to the orbit may explain why reinsertion occurs more readily in monkeys than in children with a lost muscle after strabismus surgery.

A randomized controlled trial comparing the efficacy of topical antibiotic steroid combination versus no treatment after fornix-incision strabismus surgery.

Elkamshoushy AA, Soni A, Alsanousy A. *J AAPOS.* Oct 2018; 22(5): 344-347.

The purpose of this prospective, randomized single-masked study was to compare comfort and inflammation in patients treated with postoperative topical antibiotic-steroid combination in one eye versus no treatment in the other eye. The study included all patients with planned symmetrical strabismus surgery via fornix incision. One eye was randomly assigned to topical postoperative tobramycin-dexamethasone and the other eye was used as control and was not treated. Patient and parent questionnaires were administered, and two masked observers assessed conjunctival injection over the muscle and wound site. A total of 70 patients completed at least 1 postoperative visit and were included. There was no statistically significant difference between the treated eye and the untreated eye in any of the studied parameters. The authors concluded that post-operative topical antibiotic steroid was not superior to no treatment in uncomplicated fornix surgery regarding patient comfort and inflammation. The authors suggest that in uncomplicated fornix strabismus surgery, consideration should be given to sparing the patient the inconvenience, cost, and potential complications of the topical medication.

The study was not designed to draw any conclusions regarding the possible risk of infections, when antibiotic drops are avoided post-operatively.

Investigation of factors associated with the success of adult strabismus surgery from the patient's perspective

Sim PY, Cleland C, Dominic J, Jain S. *JAAPOS*. Aug 2018;22(4):266–271.e3

This paper seeks to explore factors that influence the success of adult strabismus surgery based on health-related quality of life (HRQOL) criteria. The HRQOL aspect of strabismus surgery was assessed using the Adult Strabismus 20 (AS-20) questionnaire. Adult patients (≥16 years of age) undergoing strabismus surgery between 2014 and 2016 were identified using a treatment register. In this study, pre- and postoperative AS-20 scores were calculated. The HRQOL surgical success was defined as a pre- to postoperative change in AS-20 score exceeding previously published 95% limits of agreement. In addition, the relationship between surgical success and demographic factors (sex, age, and socioeconomic status), presence or absence of diplopia, type and magnitude of deviation, and change in deviation size with HRQOL success was investigated. In this study, a total of 87 patients were included (mean age, 47 years; 53% female). The authors found that nondiplopic patients showed significantly lower pre- and postoperative scores on the AS-20 psychosocial subscale compared to diplopic patients. Of the total of 87 surgeries, 54 cases (62%) were classified as successful based on HRQOL criteria. The multiple logistic regression analysis showed the only lower socioeconomic status was significantly associated with a higher rate of HRQOL success (P = 0.04). The authors conclude that strabismic patients with a lower socioeconomic status are more likely to achieve HRQOL success following surgery. The authors also show that nondiplopic patients have more psychosocial concerns than those with diplopia and that this disparity persists even after strabismus surgery. These factors should be considered in assessing patients for adult strabismus surgery.

Surgical outcome of a new modification to muscle belly union surgery in heavy eye syndrome.

Akbari MR, Bayat R, Mirmohammadsadeghi A, Inanloo B, et al.*Strabismus*. 2018 Dec;26(4):198-202.

Several surgical techniques have been described to treat ocular misalignment due to heavy eye syndrome. The authors presented a modified technique in which the muscle bellies of the superior rectus muscle and lateral rectus muscle were united with two 5-0 Mersilene sutures 15 mm posterior to the insertion. The authors used two sutures to join the muscles as they observed inadequate muscle approximation with only one suture in prior cases. They did not include scleral fixation due to the risk of scleral perforation in high myopes. They performed a medial rectus recession if restriction was noted on forced duction testing. Of the 24 eyes of 16 patients, the mean deviation improved from 93.71 ± 23.1 PD (range 45 to 104 PD) to 11.53 ± 15.59 PD (range 0 to 25 PD). There were no overcorrections and no patients required additional surgery. The authors conclude that their modification is comparable and perhaps easier than other surgical options to treat heavy eye syndrome.

Immediate postoperative alignment Measurements as a Predictor of Alignment stability in fixed Suture Strabismus Surgery.

Charlene S. Boente, Griffin J.Jardine, Tina G.Damarjian, Derek T. Sprunger et al
*J of Ped Ophth & Strabismus.*2018; 55(4):240-244

The purpose of this study is to evaluate the use of immediate postoperative alignment measurements as a predictor of future alignment stability in fixed suture strabismus surgery. Forty-seven patients were prospectively evaluated after undergoing horizontal or vertical rectus muscle surgery using a fixed suture technique. Alignment measurements were taken approximately 1 hour, 1 to 3 weeks, and 2 to 3 months postoperatively. A Spearman correlation coefficient was used to compare measurements from the immediate postoperative period to the 2- to 3-month postoperative period. Patients with dissociated strabismus, only oblique muscle surgery, or poor vision in one or both eyes precluding precise alternate cover test were excluded.
Mean age of all patients was 46.7 years (range: 12 to 86 years). Twenty-two patients underwent surgery for exotropia: 19 for esotropia and 6 for hypertropia. Mean alignment for all surgeries was 2 prism diopters (PD) undercorrection in the immediate postoperative period, which was similar to the mean of 4.6 PD undercorrection at 2 to 3 months postoperatively. However, the Spearman correlation between the immediate postoperative and 2- to 3-month postoperative measurements was 0.18 for all surgeries, 0.03 for exotropia, 0.56 for esotropia, and 0.40 for hypertropia. The overall success rate, defined as 8 PD or less of horizontal deviation and 4 PD or less of vertical deviation, was 77% at 2 to 3 months postoperatively.
The relationship between immediate postoperative alignment and future alignment stability in fixed suture strabismus surgery has not been previously defined. The current study demonstrated that although the surgical success rate was reasonably good, poor correlation occurred between the alignment immediately postoperatively and 2 to 3 months postoperatively. Limitations of the current study include the relative small amount of patients in each subgroup, the variability of surgical technique by each surgeon, and the follow-up time limited to postoperative month 2 and 3 although it seems reasonable that the alignment at 2 to 3 months postoperatively is an adequate time frame to assess the result of the surgery.

The efficacy of Bilateral lateral Rectus Recession According to Secondary Deviation Measurements in Unilateral Exotropic Duane Retraction Syndrome.

Daphna Mexad-Koursh, Ari Leshno, Ainat Klein, Chaim Stolovich
*J of Ped Ophthalmology & Strabismus.*2018;55(1):47-52

The purpose of this retrospective chart review study is to evaluate the surgical results of asymmetric bilateral lateral rectus recession in exotropic Duane retraction

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

Postoperative Muscle Migration Through Stretched Scar Formation After Superior Rectus Muscle Nonscleral Sutures Resection in Rabbit eyes.

Won Yeol Ryu, Sun Tae Kim, Mee Sook Roh. J of Ped Ophthalm & Strabismus.2019; 56(4): 254-260

The purpose of this study is to determine whether suturing to the residual muscle stump induces postoperative muscle migration after superior rectus muscle (SRM) resection in rabbit eyes. Twenty-four eyes in 12 rabbits were randomly divided into two groups. Each group underwent a 3-mm SRM resection. The muscle stump was not removed in one randomly assigned eye in each rabbit and the resected muscle was sutured to the residual muscle stump (residual muscle stump group). In the other eye, the muscle stump was completely removed and the resected muscle was sutured to the original insertion site (control group). At postoperative weeks 1, 2, and 4, the distances between the most anterior aspect of the reattached muscle and the corneal limbus were measured. Histopathologic differences at the new attachment sites were assessed between the two groups

at postoperative week 4. The study showed that the mean distance between the corneal limbus and SRM was 2.97 ± 1.00 mm in the residual muscle stump group and 1.99 ± 0.40 mm in the control group at postoperative week 2 (*P* = .026) and 3.14 ± 0.78 mm in the residual muscle stump group and 1.81 ± 0.44 mm in the control group at postoperative week 4 (*P* = .002). Connective tissue, fibrosis, and myofibroblast proliferation in the front of the SRM were identified based on histopathologic findings. The authors concluded that postoperative loosening associated with a stretched scar frequently occurred when the residual muscle stump was sutured at the original insertion during SRM resection in a rabbit model. These conclusions are based on the finding that proliferation was observed in the fibrous connective tissue at the muscle reattachment site observed in histopathologic examinations. The authors also concluded that their results support the view that secure reattachment between the muscle and sclera is important for increasing the success rate of strabismus surgery. Therefore, we believe that the complete removal of the muscle stump and accurate scleral suturing are critical for decreasing errors during rectus muscle resection.

11. ANTERIOR SEGMENT

Monotherapy of topical tacrolimus 0.03% in the treatment of vernal keratoconjunctivitis in the pediatric population.

Samyukta SK, Pawar N, Ravindran M, et al *JAAPOS* 2019 Feb;23(1):36. e1-36. e5.

The successful off-label use of tacrolimus in VKC has been previously reported, however some conflicting results have been shown. The aim of this prospective, nonrandomized observational study was to report the results of treating children with vernal keratoconjunctivitis (VKC) using a monotherapy of topical tacrolimus 0.03%. The severity of the disease was graded on a 4-point scale of symptoms and signs. Patients were treated with tacrolimus 0.03% ointment and were followed for 8 months according to a schedule based on the severity of the disease. The primary measure of treatment efficacy was the change in the score of objective signs. The incidence and severity of adverse events, if any, were recorded. A total of 60 children aged 5-15 years were enrolled, only 45 (37 males [82%]) were available for analysis. The mean composite *symptom* score was 6.84 ± 2.26 at baseline and 0.71 ± 1.62 at 8 months, a statistically significant reduction (P < 0.001). The mean composite *sign* score was 9.6 ± 3.14 at baseline and 1.16 ± 1.28 at 8 months, also a statistically significant reduction (P < 0.001). Four patients had to be started on steroids within the first month of treatment and were considered treatment failures. Thus, 89% of patients showed significant improvement. No participant experienced adverse effects, although some reported a transient stinging sensation. In this cohort topical tacrolimus ointment 0.03% as a monotherapy for VKC was successful in the majority of subjects, and there was no adverse effect. The study was limited by its small sample size and its short follow-up. It is also biased by high rate of loss to follow-up.

Nevertheless, the results indicate that early inclusion of low-strength tacrolimus (0.03%) in the management of pediatric patients with VKC can prevent the development of blinding sequelae of the disease.

Single-piece femtosecond-assisted mushroom keratoplasty in children.

Elkamshoushy A, Gonnah R, Madi S and Beltz J. *JAAPOS* 2019 Feb;23(1):28. e1-28. e5.

Penetrating keratoplasty (PKP) has long been the standard treatment for full-thickness corneal opacities in children. Visual outcomes of PKP in children are guarded due to increased incidence of rejections, failure, and suture-related complications. Previous reports indicated that the mushroom keratoplasty technique compared favourably to conventional PKP regarding visual and refractive outcomes. The purpose of this case series was to report the outcomes of femtosecond-assisted single-piece mushroom keratoplasty for the treatment of full-thickness corneal disease in pediatric patients with healthy endothelium. The authors present their one-year experience with this procedure in 8 patients (age range, 8-17 years) with central full-thickness corneal opacity. The single-piece mushroom-shaped graft consisted of a large anterior portion (9 mm in diameter; 250 μm in thickness) and a small posterior portion (6-6.5 mm). Donor and recipient corneas were prepared using the WaveLight FS200 laser (Alcon Laboratories, Fort Worth, TX). The donor cornea was oversized by 0.2 mm. All patients completed 12-months of follow-up. Mean best spectacle-corrected visual acuity at 1, 3, 6, and 12 months was 0.28, 0.16, 0.13, and 0.10 logMAR; all patients achieved logMAR of at least 0.4 at 1, 3, 6, and 12 months. The mean refractive cylinder was 2.6 D and mean endothelial cell loss was 13.3% at 12 months postoperatively. Two eyes had immunologic rejection episodes that were reversed with topical steroids. All corneas remained clear at final follow-up. The authors conclude that the single-piece femtosecond laser-assisted mushroom keratoplasty may be appropriate for older pediatric patients with full-thickness corneal opacity and healthy endothelium. Results of this technique for the younger children (<8 years of age) is yet to be tested. This technique combines the refractive advantage of a large corneal transplant with the improved survival and endothelial preservation of a small corneal transplant. Single-piece femtosecond-assisted mushroom keratoplasty may have a mechanical advantage over regular penetrating keratoplasty. The limitation of the technique is mainly the availability of the femtosecond laser and its cost. This is further discussed in the article.

Prosthetic Replacement of the Ocular Surface Ecosystem Treatment for Ocular Surface Disease in Pediatric Patients with Stevens-Johnson Syndrome

Wang Y, Rao R, Jacobs DS et al. *Am J Ophthalmol.* 2019 May; 201: 1-8.

This was a retrospective, interventional case series of 49 pediatric patients (27 female) over a 24-year period who used the prosthetic replacement of the

ocular surface ecosystem (PROSE) treatment after chronic ocular surface disease associated with Stevens-Johnson Syndrome (SJS). The mean age of onset of disease was 6.4 years and of initial presentation was 9.3 years. The mean follow up was 5.5 years. Visual acuity at presentation was a median of LogMAR 0.6 (20/80) and improved to 0.18 (20/30) with the PROSE. Fifteen patients (30%) failed PROSE treatment. The authors concluded that PROSE treatment was possible in over 2/3 of pediatric patients with OSD related to SJS/TEN and resulted in improved and durable visual acuity improvement. The limitation of selection bias related to excluding patients lost to follow up was discussed by the authors. This article's importance lies in its reminder to the ophthalmologist that a scleral contact lens to treat OSD related to SJS is often successful in the pediatric patient and can provide improvement in the visual acuity.

Corneal Limbal Stem Cell Deficiency in Children with Stevens-Johnson Syndrome.

Choi SH, Kim MK, and Oh JY. *Am J Ophthalmol.* 2019 March; 199: 1-8.

The purpose of this study was to determine the incidence of corneal limbal stem cell deficiency (LSCD) as a chronic ocular morbidity in patients with Steven Johnson syndrome (SJS) / Toxic Epidermal Necrolysis (TEN) and to better understand the risk factors for developing LSCD. This was a retrospective case series of 19 children from a single institution over a 14-year time period. The authors found 6/19 (32%) of patients developed LSCD a mean of 12+/-21 months after the onset of their disease. Patients who received an LSCD did worse in terms of visual acuity, and those who received penetrating keratoplasty with limbal autograft did poorly. Patients were treated at the time of the illness with a protocol involving artificial tears, levofloxacin drops, prednisolone acetate, mechanical lysis of adhesions, bandage lenses in cases with epithelial defects, and amniotic membrane transplantation within 10 days in patients with persistent epithelial defects and/or formation of symblepharon. The authors highlight a few important points of this paper – the first being that this disease can cause severe long-term ocular morbidity and blindness and these patients require long term follow up. Secondly, that earlier amniotic membrane transplantation and a more current and more aggressive treatment of these patients may prevent or at least lessen the severity of LSCD in pediatric patients with SJS/TEN. Overall this paper does a good job highlighting the morbidity of SJS/TEN but might not be an accurate reflection of current outcomes since standard of care now involves earlier and more aggressive amntiotic membrane grafting than was used in this study.

Keratoconus Natural Progression *A Systematic Review a Meta-analysis of 11529 Eyes*

Alex C Ferdi, Vuong Nguyen, Daniel M Gore, Bruce D Allan, et al
Ophthalmology. July 2019;126(7): 935-945.

The purpose of this study was to describe the natural history of keratoconus through systematic review and meta-analysis. Interventions including corneal cross-linking, intracorneal ring segments, refractive laser, and grafting are utilized to stabilize disease or improve vision but they carry risks. Detailed knowledge of the natural history keratoconus is fundamental in make informed decisions. Their search yielded 3950 publication titles, of which 41 were included in their systematic review and 23 were incorporated into the meta-analysis. The meta-analysis of 12-month outcomes found that younger patients progress more aggressively: patients younger than 17 years old are likely to have more than 1.5 diopters (D) of maximum keratometry (Kmax) progression. Patients with steeper Kmax demonstrated more severe progression: patients is greater than 55 D K max are likely to progress by at least 1.5 D Kmax. Middle eastern patient also experienced more progression. They conclude that closer follow-up and a lower threshold for cross-linking should be adopted in patients less than 17 years with steeper than 55 D Kmax.

A Randomized, Controlled Trial of Cyclosporine A Cationic Emulsion in Pediatric Vernal Keratoconjunctivitis

Andrea Leonardi, Serge Doan, Mourad Amrane, Dahlia Ismail, et al
Ophthalmology. May 2019;126(5): 671-681.

The purpose of the VErnal KeratoconjunctivTIs Study (VEKTIS) was to evaluate the safety and efficacy of an investigational therapy, cyclosporine A (CsA) cationic emulsion (CE) for severe vernal keratoconjunctivitis (VKC). CsA is practically insoluble in water and must be delivered topically in a lipid-based system. With CsA CE, there is increased residence time at the ocular surface due to attraction between positively charged nanodroplets and the negatively charged cell membranes thereby providing improved ocular bioavailability. VEKTIS is a phase 3, multicenter, double-masked, vehicle-controlled trial. Participants included pediatric patients ages 4 to 18 years with active severe VKC (Grade 3 or 4 on Bonini severity scale) and severe keratitis (corneal fluorescein staining [CFS] score of 4 or 5 on modified Oxford scale). One hundred sixty-nine patients were randomized to CsA CE 0.1% (1mg/ml) eyedrops 4 times per day (high-dose), CsA CE twice daily (low dose) plus vehicle twice daily, or vehicle 4 times daily for 4 months. Dexamethasone 0.1% 4 times daily for up to 5 days served as the rescue medication. Study visits occurred every four weeks, and efficacy was evaluated utilizing 3 primary criteria: (1) keratitis assessed by CFS, (2) need for rescue medication, and (3) occurrence of corneal ulceration. Results showed statistically significant improvement for both the high-dose (0.76; P=0.007) and low-dose (0.67; P=0.010) groups versus the vehicle group with treatment effect driven largely by CFS score. Significant differences were found between both active treatment groups and vehicle for use of rescue medication. VKC symptoms and patient quality-of-life improved in all three groups with significant improvement for high-dose CsA CE versus vehicle. The greatest improvement in the composite

efficacy score was achieved from baseline to month one, indicating that treatment benefits occurred rapidly. The safety data were consistent with the known safety profile of topically applied CsA and no unexpected safety findings were identified. Instillation site pain was noted in all three groups, but it was slightly more in the high-dose group. One limitation of the study was lack of a true placebo but any topical products including eyewash will potentially have an effect due to dilution of allergens and mediators. In addition, the authors note it is not ethically acceptable to have children with severe VKC receiving placebo and a clinical trial. The other limitation was a four-month comparative period. The effects of continued treatment with CsA CE at an eight-month safety follow-up will be reported in a subsequent publication.

Conjunctival Retention Cysts: Outcomes of Aspiration and Sclerotherapy With Sodium Tetradecyl Sulfate

Tarjani Dave, Shikha Taneja, Sweety Tiple, et. al. *Ophthalmic Plast Reconstr Surg* Mar/Apr 2019;35:165–169

This study aimed to assess the outcome of aspiration and sclerotherapy with sodium tetradecyl sulfate in the management of conjunctival inclusion cysts. This was a retrospective interventional case series of 6 patients with clinical diagnosis of conjunctival inclusion cysts treated with cyst aspiration and foam sclerotherapy with 3% sodium tetradecyl sulfate. The volume of the sclerosant was 20% of the aspirated cyst volume. Four patients had an inclusion cyst in anophthalmic sockets and 2 patients in sighted eyes. Average time lag between primary surgery and cyst formation was 14.6 months (range 2–30 months). Average amount of fluid aspirated from cyst was 3.07ml (range 1–9ml). Average volume of sclerosant injected was (20% of the aspirated volume) 0.55ml (range 0.2–1.1ml). All 6 patients showed complete resolution of cyst at a mean follow-up period of 15.6 months (range 9–24 months). All but one showed complete resolution of cyst with single injection sclerosant. Only 1 patient required a second sclerosant injection. There was no ocular surface or implant-related complications in this cohort. Cyst aspiration and sodium tetradecyl sulfate foam sclerotherapy is a minimally invasive procedure for the management of conjunctival inclusion cysts in anophthalmic sockets and sighted eyes. The injection of sodium tetradecyl sulfate in a dose of 20% of the aspirate is effective in the management of conjunctival inclusion cysts over a follow-up period of 13 months. The procedure is safe, with insignificant inflammation and without ocular surface or implant complications.

Femtosecond Lasers for Ophthalmic Surgery Enabled by Chirped-Pulse Amplification

Daniel Palanker, Ph.D. *NEJM* 379:2267-2269. 2018

In this report about the clinical implications of basic research, we learn that Donna Strickland and Gerard Mourour were awarded the 2018 Nobel Prize in

Physics for their work leading to the development of femtosecond lasers. Femtosecond lasers precisely deliver small amounts of energy in very short duration, allowing precise cutting of tissues without damage to collateral tissues. Their ophthalmological applications include those in corneal surgery: the creation of corneal flaps for LASIK, cutting the corneal tissue required for SMILE (small incision lenticule extraction) refractive surgery, creating various types of corneal incisions for full and partial thickness corneal transplantation, and creating limbal relaxing incisions. They have additional applications in cataract surgery: cutting precise capsulotomies for cataract surgery, and performing lens fragmentation without ultrasound energy induced collateral endothelial damage. Femtosecond lasers are also being investigated in the treatment of floaters. Knowledge about this technology /Nobel Prize is of relevance to pediatric ophthalmologists because these lasers may become more widely used in pediatric anterior segment surgery in the future.

Prevalence of keratoconus in paediatric patients in Riyadh, Saudi Arabia

Netto E, Al-Otaibi W, Hafezi N, Kling S, et al. *Br J* Ophthalmol. October 2018;102:1436-1441.

Keratoconus (KC) prevalence estimates show significant geographic variation. The study looked at the prevalence of KC using Scheimpflug imaging in pediatric patients in Riyadh, Saudi Arabia. This was a prospective multicenter study of subjects 6 to 21 years old seen at emergency rooms (for non-ophthalmic reasons) at 4 different locations. Corneal measurements were obtained with a Scheimpflug corneal tomography system. Two masked examiners were used to make the diagnosis of KC. 522 patients (1044 eyes) were evaluated. Prevalence for KC was 5.56% for the first examiner and 3.83% for the second. There was discrepancy in the diagnosis in 9 cases. After consensus obtained, final prevalence was 4.79% (1:21 patients). This prevalence is higher than numbers from other studies in other countries. The authors state this might be due to geographical variations or improved screening technology.

Rigid Gas Permeable Contact Lens as a vision-sparing tool In Children After Traumatic Corneal Laceration

Rabab Mohamed Elseht, Khaled Ahmed Nagy *J of Ped Ophth & Strabismus*.2018;55(3):178-181

The purposed of this comparative study is to evaluate the clinical value of rigid gas permeable contact lenses in children after traumatic corneal scarring. Fifteen children (age range: 5.7 to 14 years; mean ± standard deviation = 9.4 ± 2.9 years) with corneal scars and best-corrected visual acuity (BCVA) of worse than 20/20, history of penetrating ocular trauma, and/or cataract extraction were included in the study. All children were advised to wear spherical rigid gas permea-

ble contact lenses for 6 months with a special regimen. Visual acuity was compared before and after fitting. The total and anterior surface aberrations of all children were measured using a corneal topographer before and after treatment. There was a significant improvement in the BCVA after wearing rigid gas permeable contact lenses compared to spectacle visual acuity (P = .001). There was also significant improvement of the keratometric astigmatism (P = .001) and corneal aberrations such as higher order aberrations (P = .008), lower order aberrations, root mean square, and point spread function (P = .001). The authors conclude that the optical performance of rigid gas permeable contact lenses has been demonstrated to be effective in the visual rehabilitation of children with traumatic corneal lacerations and prevention of amblyopia. The study regimen of rigid gas permeable contact lenses use was effective in wearing lenses for 6 months of follow-up. Corneal topography was an objective tool for detecting optical disorders compared to visual acuity tests.

Chronic Ocular Sequelae of Steven-Johnson Syndrome in Children: Long-term Impact of Appropriate Therapy on Natural History of Disease

Basu S, Shanbhag SS, Gokani A, et *Am J Ophthalmol.* 2018; 189: 17-28.

This is a retrospective comparative case series of 568 eyes of 284 children who had Steven-Johnson Syndrome (SJS) with eye involvement between 1990 and 2015. The goal was to look at the visual outcomes of children, the associated ocular morbidities and chronic sequelae of SJS. The primary outcome of the study was best-corrected visual acuity. Two thirds of patients presented over a year after they had acute SJS. Patients who were under 8 at presentation tended to have worse outcomes. At 5 years of follow up, it was clear that definitive therapy (mucous membrane grafts, limbal stem cell grafting, PROSE lenses, etc) significantly altered the natural history of disease. Patients with definitive therapy had better best corrected visual acuities and did not have continued progression of keratopathy when compared to patients who only had conservative treatment. The authors were mainly looking at a large early cohort that was treated conservatively before the advent of AMT for this disease, to compare them with the more modern cohort that was treated more aggressively. This paper highlights the importance of definitive treatment for SJS. However, this paper does not provide insight into which patients to treat since the patients in this study were managed after their acute disease in the outpatient setting thus the results may not be generalizable to all populations.

Mechanical versus transepithelial phototherapeutic keratectomy epithelial removal followed by accelerated corneal crosslinking for pediatric keratoconus: Long-term results

Ozge Sarac, Pinar Kosekahya, Mehtap Caglayan, Burak Tanriverdi, et al. *Journal of Cataract and Refractive Surgery*;2018;44(7):827-835.

In this retrospective Turkish study of 40 eyes of 35 consecutive keratoconus patients younger than 18 years, transepithelial phototherapeutic keratectomy (PTK) epithelial removal was as effective and safe as mechanical epithelial removal followed by accelerated corneal crosslinking (CXL). While initial visual and topographic outcomes of transepithelial PTK ablation were better than those of mechanical epithelial removal before accelerated CXL when comparing the two patient groups (mechanical=15 patients vs. transepithelial PTK=20 patients), results were similar at 36 months. This article is important to pediatric ophthalmologists in that the Global Consensus on Keratoconus and Ectatic Diseases recommended that pediatric patients with keratoconus receive CXL as soon as the diagnosis is confirmed because of faster progression of corneal ectasia. However, I am not sure how relevant this article would be to the AAPOS audience given that 1) most pediatric ophthalmologists are not performing corneal collagen crosslinking and 2) the accelerated CXL protocol is not yet approved in the United States.

Anterior segment disorders - surgical procedures

Anterior segment disorders – nonsurgical management

Anterior segment biometry and refraction

12. CATARACT

Spectacle Adherence Among Four-Year-Old Children in the Infant Aphakia Treatment Study

Lambert SR, Dubois L, Cotsonis G, et al from the IATS study group
Am J Ophthalmol. 2019 April; 200: 26-33.

This retrospective cohort analysis aimed to evaluate the spectacle adherence of 4-year-old children in the infant aphakia treatment study. Both the contact lens group and the intraocular lens group from IATS were included in this cohort analysis. The authors reviewed annual diaries kept during the study and the telephone interviews conducted every 3 months during the study to assess adherence to spectacle treatment. The visual acuities were assessed at age 4.5 years. There were 114 children in the IATS and of those 101 were included in this analysis. The authors found that children with 20/40 vision (assessed by ATS-HOTV test) or better in the affected eye were more likely to have excellent (greater than 80% of the time) adherence to spectacle treatment. The adherence correlated to the reported patching but did not corelate with refractive error or type of healthcare insurance. The adherence was not

different in the IOL vs. the contact lens groups. The authors concluded that it is possible to achieve excellent adherence to spectacles in this age group and that those who needed the eye protection the most had the worst adherence. The authors note that in this study the spectacles were replaced for no charge, which may overestimate the spectacle compliance in a more real-world setting. The major limitations were discussed, which were the sample size and parental reporting of adherence. They speculated that their main conclusion, that patients with better vision had better compliance with spectacles, was either due to being a more adherent family overall or perhaps that those with better vision noted an improved visual benefit from wearing the glasses. This article reinforces the ability of the monocular patient to adhere to spectacle correction and perhaps the pediatric ophthalmologists' role in reinforcing the importance of wearing protection in this patient population.

Persistent Fetal Vasculature With Elongated Ciliary Processes in Children.

Warren N, Trivedi RH, and Wilson *Am J Ophthalmol.* 2019 Feb;198: 25-29.

This was a retrospective case series of eleven eyes of 22 patients at a single institution who had surgery for unilateral persistent fetal vasculature before 7 months of age and had elongated or stretched ciliary processes on exam. Patients with retinal involvement and those without at least 6 months of follow up were excluded. All patients had lensectomy, posterior capsulotomy and vitrectomy. The purpose of the study was to evaluate the outcomes, complications, and reoperation rates in this specific patient population. The most important finding was that only two patients had a visual acuity better than 20/200. The authors also found a high (60%) rate of post-operative visual axis opacification and 2/11 patients (18%) developed glaucoma. One patient developed glaucoma and retinal detachment and the eye was enucleated. Ten of the 11 patients were initially left aphakic and three patients later received a secondary IOL. Three patients developed strabismus. The authors nicely summarize previous papers on PFV cataract outcomes and point out that no other papers focus on these more severe cases. This paper highlights the poor visual outcomes and high rate of reoperation in patients with PFV and elongated ciliary processes.

Long-term treatment effect in cerebrotendinous xanthomatosis depends on age at treatment start.

Stelten BML, Huidekoper HH, van de Warrenburg BPC, Brilstra EH et al. *Neurology.* Jan 2019;92(2):e83-e95.

The authors in this retrospective study examine the outcomes of patients with a rare condition CTX which is associated with the presence of pediatric cataracts. Outcomes on 56 Dutch patients with CTX were collated with respect to time of diagnosis. Neurologic symptoms were reversed and eliminated in all patients for

whom an early diagnosis and treatment were initiated prior to 24 months in contrast to patients whose neurologic function deteriorated with later diagnosis. This study emphasized the importance of early diagnosis. Because childhood cataracts may be the first insight into this diagnosis in the setting of chronic, infantile diarrhea, pediatric ophthalmologists must be aware of the condition and recognize the importance of early diagnosis and its impact on long term neurologic outcomes.

Medical Management of Children With Congenital/Infantile Cataract Associated with Microphthalmia, Microcornea, or Persistent Fetal Vasculature.

Moritz Claudius Daniel, Gillian G.W.Adams, Annegret Dahlmann-Noor.*J Ped Ophthal & Strabismus*.2019;56(1):43-49

The purpose of this study is to report the surgical outcomes of children with cataract associated with microphthalmia, microcornea, or persistent fetal vasculature (MMP) and children with isolated cataract. It included 111 children (cataract associated with MMP: n = 25) who underwent cataract surgery at younger than 16 years. Exclusion criteria were duration of follow-up less than 5 years, intraindividual differences in age at surgery, eye disorders other than MMP, secondary cataract, and syndromal diseases. Main outcome measures were proportion of eyes with glaucoma and best corrected visual acuity (BCVA). Both groups were dichotomized by age at surgery (early intervention group: ≤ 48 days). Descriptive analysis was performed throughout. It showed that the Median age at surgery was 3.9 months for cataract associated with MMP and 23.3 months for isolated cataract. The median (interquartile range [IQR]) duration of follow-up was 95.9 months (range: 76.0 to 154.5 months). In children with bilateral cataract associated with MMP, the proportion of eyes with final BCVA worse than 0.3 logMAR was similar regardless of age at surgery (early intervention: 80%, later intervention: 78%). In bilateral isolated cataract, the proportions were 56% and 33%, respectively. Children with cataract associated with MMP had a high prevalence of glaucoma (28%). Glaucoma prevalence was lower in the later intervention group. The authors concluded that surgery for congenital/infantile cataract is associated with a high risk of secondary aphakic or pseudophakic glaucoma, especially in eyes with cataract associated with MMP. Due to the lower prevalence of glaucoma, these children might profit from surgery at older ages. Randomized controlled trials on this vulnerable group of children are unlikely to be carried out. A sufficiently powered (potentially multicenter), prospective, non-randomized study, taking into account the anatomical situation at the time of diagnosis, the high variability and wide spectrum of potentially coexisting eye conditions, and the burden of children with glaucoma, might help to optimize the care of children with cataract associated with MMP.

Contact Lens Correction of Aphakia in Children: A Report by the American Academy of Ophthalmology

Lambert SR, Kraker RT, Pineles SL, Hutchinson AK, et al. *Ophthalmology* September. 125(9): 1452-1458.

In this review, the authors evaluated the use of 2 most commonly used contact lenses for treating aphakia in children (silicone elastomer and rigid gas permeable) to assess the visual outcome and adverse events associated with these lenses. Literature searches were conducted in January 2018 in the PubMed, Cochrane Library, and ClinicalTrials.gov databases with no date or language restrictions. These combined searches yielded 167 citations, 27 of which were reviewed in full text. Of these, 10 articles were deemed appropriate for inclusion in this assessment and subsequently assigned a level of evidence rating by the panel methodologist. The literature search identified 4 level II studies and 6 level III studies. There were insufficient data to compare visual outcomes for eyes treated using SE lenses versus RGP lenses. Silicone elastomer lenses have the advantage that they can be worn on an extended-wear basis, but they were associated with more adverse events than RGP lenses. These adverse events included microbial keratitis, corneal infiltrates, corneal edema, corneal scars, lenses adhering to the cornea, superficial punctate keratopathy, lid swelling, and conjunctival hyperemia. The lens replacement rate was approximately 50% higher for RGP lenses in the only study that directly compared SE and RGP lenses. The authors concluded that there is limited evidence in the literature on this topic. Both silicone elastomer and RGP contact lenses were found to be effective for treating aphakia in children. Silicone elastomer lenses are easier to fit and may be worn on an extended-wear basis. Rigid gas permeable lenses must be removed every night and require a more customized fit, but they are associated with fewer adverse events. The choice of which lens a practitioner prescribes should be based on the particular needs of each patient.

Association of Pediatric Atopic Dermatitis and Cataract Development and Surgery.

Hyun Sun Jeon, Mira Choi, Seong Jun Byun, Joon Young Hyon, et al. *JAMA Ophthalmology*. August 2018; 136(8):912-918.

This was a retrospective population-based longitudinal cohort study in Korea from 2002 to 2013 to analyze the association of Atopic Dermatitis (AD) and cataract development and cataract surgery. Incident AD cases were matched to 4 controls each using a propensity score derived from age, gender, residential area, and household income. Of note, the patient analysis was from the nationally representative data from the Korean National Health Insurance Service database. Approximately 85% of all AD cases begin before 5 years old. AD has been associated with ocular complications including anterior subcapsular cataract and posterior subcapsular cataract. The authors found 34,375 patients with incident AD (47% girls with mean age of 3.47years) and there were 3,734 patients with severe AD cases (10.9%) with 137,500 matched controls for analysis.

The development of cataracts was not significantly different between the AD patients and the matched controls. Results indicated that the incidence probability of cataract was 0.216% in patients with AD and 0.520% in patients with severe AD at 10-year follow up. The authors also report that only a small number of patients with AD underwent cataract surgery (0.075% in patients with and 0.221% in patients with severe AD at 10-year follow up). Therefore, the authors conclude that the threat of cataract and visually significant cataract in children with severe AD is rare, even after 10-year follow up with severe disease. This longitudinal study helps put in perspective the rarity of cataracts associated with severe AD after 10-year follow up and. However rare, the authors suggest that monitoring closely for the development of cataracts in pediatric patients with severe AD is important.

Preoperative biometry data of eyes with unilateral congenital cataract.

Lidia Kun, Andrea Szigeti, Maria Bausz, Zoltan Zsolt Nagy, et al. *JCRS* Oct 2018;44(10):1198-1202

In this retrospective, Hungarian study of 42 infants with unilateral congenital cataracts, data collected from each eye at the time of surgery including central corneal thickness (CCT), corneal refractive power (keratometry [K]), horizontal corneal diameter, and axial lengths was recorded and analyzed. In the eyes with unilateral congenital cataract, a greater CCT (p=.1330), higher average K (p=.00243) and smaller corneal diameter (p=.0010) were found. There was no significant difference in AL when compared with the unaffected contralateral eyes. The collected data showed that biometric characteristics of the eyes with unilateral congenital cataract differ from those of the fellow, normal eye before cataract surgery. The authors state that it is essential to use this biometric data in intraocular lens power calculation and to take it into account in long-term care when screening for secondary glaucoma. Overall, I found the quality of this article to be pretty poor. I am not sure that the authors present much new information, but there is some interesting discussion about the abnormal parameters of the cataractous eye resulting from congenital cataract hindering the formation of a normal anterior segment.

Correlation of monocular grating acuity at age 12 months with recognition acuity at age 4.5 years: findings from the Infant Aphakia Treatment Study

Hartman EE, Drews-Botsch C, Dubois LG, Cotsonis G, et al. *JAAPOS*. Aug 2018;22(4):299-303.e2.

This paper's purpose is to determine whether grating acuity at age 12 months can be used to predict recognition acuity at age 4.5 years in children treated for unilateral congenital cataract enrolled in the Infant Aphakia Treatment Study (IATS). Traveling testers assessed monocular grating acuity at 12 months of age

(Teller Acuity Card Test [TACT]) and recognition acuity at 4.5 years of age (Amblyopia Treatment Study Electronic Visual Acuity Testing, HOTV) in children treated for visually significant monocular cataract in the IATS. Spearman rank correlation was used to evaluate the relationship between visual acuities at the two ages in the treated eyes. Visual acuity data at both ages were available for 109 of 114 children (96%). Grating acuity at 12 months of age and recognition acuity at 4.5 years of age were significantly correlated for the treated eyes ($r_{spearman}$ = 0.45; P = 0.001). At age 4.5 years, 67% of the subjects who had grating acuity at 12 months of age within the 95% predictive limits in their treated eye demonstrated recognition acuity better than 20/200. Similarly, at age 4.5 years 67% of the subjects who had grating acuity at age 12 months below the 95% predictive limits in their treated eye demonstrated recognition acuity of 20/200 or worse. The authors conclude that a single grating acuity assessment at age 12 months predicts recognition acuity in a child treated for unilateral congenital cataract in only two-thirds of cases and therefore provides limited utility in predicting the long-term visual outcomes of these eyes. Clinicians should consider other factors, such as patching compliance and age at surgery, when using an early grating acuity assessment to modify treatment.

Frequency of pediatric traumatic cataract and simultaneous retinal detachment

Qui H, Fischer NA, Patnaik JL, Lung JL., et al. *JAAPOS*. Dec 2018;22(6):429-432.

Traumatic cataract in children is a treatable cause of vision loss. In cases of simultaneous retinal detachment, the prognosis for visual recovery is often poor. The purpose of this study was to investigate risk factors for concurrent retinal detachment in patients with traumatic cataract. In this study, a retrospective review of patients diagnosed with traumatic cataract at Children's Hospital Colorado between 2005 and 2014 was conducted. Demographics, mechanism of injury, and incidence of retinal detachment were recorded. Logistic modeling with generalized estimating equations to account for correlation of eyes within patients was used to analyze associations between potential risk factors and retinal detachment. A total of 62 total eyes with traumatic cataract were included: 52 patients presented with unilateral cataract; 5 presented with bilateral cataracts. Mean patient age was 8.4 ± 4.1 years (range, 0-16 years), and 83% of patients were male. A total of 9 eyes (14.5%) had comorbid retinal detachment. Traumatic cataracts caused by self-injurious hitting were more likely to present with simultaneous retinal detachment than those caused by other mechanisms of injury (OR = 24.0; 95% CI, 3.8-153.3; P = 0.0010). Patients with traumatic cataract who display self-injurious behavior are at higher risk for concurrent retinal detachment. These patients can often only be examined under sedation and often have associated developmental delay or intellectual disability. Ophthalmologists should counsel families of high-risk patients and consider involving retinal specialists in surgical planning.

Association of Pediatric Atopic Dermatitis and Cataract Development and Surgery

HS Jeon, M Choi, SJ Byun, et al. *JAMA Ophthalmol.* August 2018; 136(8):912-18.

This population-based retrospective longitudinal cohort study from the Korean National Health Insurance Service database from 2002 to 2013. Patients younger that 20 years old with incident atopic dermatitis (AD) were matched to 4 controls each using propensity score derived from age, sex, residential area, and household income. Statistical analysis included incidence probabilities of cataract development and cataract surgery between the AD group and controls were compared using Kaplan-Meier methods and log-rank tests. Cox proportional hazard models were fitted for cataract and cataract surgery to determine the risk factors in the matched cohort.
Of 34 375 patients with incident AD (16 159 girls [47%]; mean [SD] age, 3.47 [4.96] years), there were 3734 severe AD cases (10.9%) with 137 500 matched controls. Development of cataracts was not different between the AD and control groups, (0.216% vs 0.227%; 95% CI, -0.041% to 0.063%; P = .32) or between the severe AD cohort and their controls (0.520% vs 0.276%; 95% CI, -0.073% to 0.561%; P = .06). Cataract surgery was performed more frequently in the AD cohort than in the control group (0.075% vs 0.041%; 95% CI, 0.017%-0.050%; P = .02) and in the severe AD cohort compared with their controls (0.221% vs 0.070%; 95% CI, 0.021%-0.279%; P = .03). Severe AD was associated with both development of cataract (adjusted hazard ratio, 1.94; 95% CI, 1.06-3.58, P = .03) and requirement for cataract surgery (adjusted hazard ratio, 5.48; 95% CI, 1.90-15.79, P = .002). In summary, this study showed that the absolute risk of cataract was rare, with or without AD, even after 10 years of observation. However, AD disease severity may increase the risk for cataract development and cataract surgery.

Unilateral Congenital Cataract: Clinical Profile and Presentation.

Sudarshan Khokhar, Cijin P.Jose, Ramanjit Sihota, Neha Midha
J of Ped Ophth & Strabismus.2018; 55(2): 107-112

The purpose of this study is to identify the clinical profile and presentation of children with unilateral cataract. In this hospital-based, observational, cross-sectional study, patients 15 years of age or younger who presented with unilateral cataract were recruited. Cases of cataract secondary to causes such as trauma or uveitis were excluded. Age at detection and presentation, distance from the treatment center, presenting complaints, cataract morphology, and biometry were noted for each case. A total of 76 patients were recruited. Most patients presented with complaints of leukocoria. Persistent fetal vasculature accounted for 27.6% of cases and was the most common identifiable cause of cataract in this study. Subsequently, patients were divided into two groups: no persistent fetal vasculature (control) and persistent fetal vasculature. A male predominance was noted in both groups. The mean age at detection was 27.58 ± 37.02 and 6.17 ± 8.42

months and the mean age at presentation was 55.613 ± 45.21 and 14.83 ± 17.75 months in the control and persistent fetal vasculature groups, respectively. In the persistent fetal vasculature group, a significant difference was noted in the axial length, keratometry, and corneal diameter between the affected and normal eyes (*P* = .027, .00176, and .0114, respectively). In the control group, this difference was observed only in keratometry readings (*P* = .0464). The mean distance traveled by patients to reach the treatment center was 211 km. The study concluded that it is imperative to increase awareness among parents, pediatricians, and ophthalmologists about disease and its potential to cause an irreversible loss of vision.

Morphological and biometric features of preexisting posterior capsule defect in congenital cataract

Zhangliang Li, Pingjun Chang, Dandan Wang, Yinying Zhao, et al.
Journal of Cataract and Refractive Surgery;2018;44(7):871-877.

This Chinese study reviewed the cases of 81 eyes of 53 patients less than 1 year of age to identify a series of diagnostic signs that were preoperative predictors of a preexisting posterior capsule defect in eyes with congenital cataract. Clinical signs indicative of a preexisting posterior capsule defect in the study group (42 eyes) are described as are biometric characteristics of preexisting posterior capsule defect. The lens was significantly thinner and the vitreous chamber significantly deeper in the study group than in the control group. Also, corneal diameters were significantly smaller in the control group. Multivariate analysis identified lens thickness as an independent risk factor for preexisting posterior capsular defect. While many pediatric cataract surgeons may be familiar with the characteristic morphological clues associated with preexisting posterior capsular defects, awareness that lens thickness and corneal diameter may be decreased in this setting may aid in the preoperative detection of posterior capsule defects and facilitate preoperative planning permitting avoidance of complications during surgery for congenital cataract.

13.CATARACT SURGERY

Pediatric cataract surgery outcomes

Visual Acuity and Ophthalmic Outcomes in the Year After Cataract Surgery Among Children Younger Than 13 Years

Writing Committee for the Pediatric Eye Disease Investigator Group (PEDIG)
JAMA Ophthalmology. July 2019;137(7):817-824.

This a cohort study of 880 children younger than 13 years old who underwent cataract surgery in a prospective observational PEDIG study from 2012 to 2015

at sixty one pediatric eye care practices. The goal of this report was to describe the visual acuity and refractive error outcomes as well as the rates of amblyopia, glaucoma, and additional eye surgery during the first year after lensectomy in children. Among the 880 children, there were 432 girls and 448 boys with a mean age at annual follow-up of 4.9 years old. Lens surgery was bilateral in 362 children and unilateral in 518 children. An intraocular lens was implanted in 654 of 1132 eyes (60.2%). Amblyopia was identified in 449 children. In children who were age 3 years or older, mean visual acuity was 0.30 logMAR (about 20/40) in 153 bilateral pseudophakic eyes, 0.49 logMAR (about 20/63) in 141 unilateral pseudophakic eyes, 0.47 logMAR (about 20/63) in 21 bilateral aphakic eyes, and 0.61 logMAR (about 20/80) in 17 unilateral aphakic eyes. Mean visual acuity improved with older age at surgery in eyes with bilateral pseudophakia by 0.2 logMAR line ($P = .005$) and by 0.3 logMAR line ($P = .004$) in eyes with unilateral pseudophakia. A new diagnosis of glaucoma or suspected glaucoma was made in 67 of 1064 eyes that did not have glaucoma prior to lensectomy (5.9%); 36 of 273 eyes with bilateral aphakia (13.2%), 5 of 308 eyes with bilateral pseudophakia (1.5%), 14 of 178 eyes with unilateral aphakia (7.9%), and 12 of 305 eyes with unilateral pseudophakia (3.9%). Additional intraocular surgery, most commonly vitrectomy or membranectomy to clear the visual axis, was performed in 189 of 1132 eyes (17.0%). In summary, amblyopia was frequently observed during the first year after lensectomy in this cohort of children younger than 13 years. For children age 2 years or older at the time of initial surgery, visual acuity was typically less than normal and was worse with unilateral cataract. The authors note that management of visual axis obscuration was the most common complication requiring surgical intervention during the first year after surgery.

Outcomes of Unilateral Cataracts in Infants and Toddlers 7 to 24 Months of Age: Toddler Aphakia and Pseudophakia Study (TAPS)

Erick D. Bothun, M. Edward Wilson, Elias I. Traboulsi, Nancy N. Diehl, et al for the Toddler Aphakia and Pseudophakia Study Group (TAPS)
Ophthalmology. August 2019;126:1189-1195

Intraocular lens implantation after lensectomy in children younger than 2 years of age is becoming more commonplace. This study retrospectively reports long-term visual outcomes in children ages 7 to 24 months originally enrolled in the Toddler Aphakia and Pseudophakia Treatment Study between 2004-2010. The primary treatment outcomes were determined at the eye examination closest to age 5. The average age at surgery was 14 months and average treatment follow up was 4 years. The average final vision in the operated eye was 20/125; only 11% of subjects demonstrating 20/40 or better vision, all older than 13 months at time of surgery. Visual axis opacification occurred in 14% of children, resulting in unplanned surgeries. Only one child was considered a glaucoma suspect. Only 32% of subjects did not manifest strabismus; stereopsis was only detectable in 3 children. Compared with intraocular lens implantation in children less than 7

months, this older study cohort had dramatically fewer adverse events and unplanned surgeries. In addition, the range of refractive outcomes at age 5 was much narrower, implying that the expected myopic postoperative shift in refraction is much more predictable in the older patients. The data provides strong support to lower the standard of care age for intraocular lens implantation after lensectomy to 13 months or less.

Intraocular lens implantation in children with unilateral congenital cataract in the first 4 years of life

Yangzes S, Kaur S, Gupta PC, Sharma M, et al. *EJO,* May 2019, 29(3) 304–308

The paper aimed to describe the outcome of phacoaspiration with intraocular lens implantation in children with unilateral congenital cataract in the first 4 years of life. A retrospective chart review of children with visually significant unilateral congenital cataract presenting in the first 4 years of life was done. Children with a minimum postsurgical follow-up of 1 year were included. Outcome measures were mean spherical equivalent, visual axis clarity, visual acuity and complications till the last follow-up. Ninety-three children met the inclusion criteria. The mean age of surgery was 13.23 ± 11.89 months and the mean follow-up period was 24.37 ± 17.35 months. Nearly 40% of children presented during their first year of life. No difference was noted between the subgroups in terms of age (p = 0.310), sex (p = 0.475) or laterality (p = 0.349). Surgical membranectomy was performed in 22 eyes (23.6%) after an average period of 4.85 ± 2.58 months after surgery. One eye underwent piggy back intraocular lens and four eyes underwent intraocular lens exchange after a mean duration of 50 months (range 40–60 months). The mean visual acuity was 0.79 ± 0.11 (log MAR chart). A total of 60.7% of these children (n = 31) achieved best corrected visual acuity or 20/80 or better. The results of our study suggest that primary intraocular lens implantation in children with unilateral congenital cataract gives good structural and functional results. Besides a meticulous surgery, visual outcome is affected by the time of presentation and postoperative compliance to amblyopia therapy.

Visual outcomes of pediatric traumatic cataracts

Jinagal J, Gupta G, Gupta PC, Yangzes S, et al. *Eur J Ophthalmol.* Jan 2019.

The authors retrospectively evaluated 147 children with a history of traumatic cataract to identify risk factors and outcomes. Penetrating injury comprised the majority of cases. The authors analyzed whether outcomes were impacted by placement of PCIOL and by primary posterior capsulotomy. Overall both factors contributed positively to good surgical outcomes in these patients and this superceded the type of injury. Therefore the authors advocate for PCIOL placement and primary posterior capsulotomy when performing surgery for traumatic pediatric cataract.

Outcome of pediatric cataract surgery with intraocular injection of triamcinolone acetonide: Randomized controlled trial.

Allam G, Ellakkany R, Ellayeh A, Mohsen T, et al. *Eur J Ophthalmol.* Nov 2018 Nov;28(6):633-638.

The authors performed a randomized controlled trial evaluating the impact of intraocular injection of triamcinolone acetonide during pediatric cataract surgery in 44 eyes of 22 children. Their hypothesis was that this agent would serve to highlight vitreous as a "vitreous dye" and facilitate better anterior vitrectomy during surgery thereby reducing post operative complication. Outcomes evaluated included IOP, post op inflammation, development of PCO and post op infection. The main difference in outcome was with respect to PCO where it was noted in 1 eye which had triamcinolone and 9 eyes without injection. The authors suggest that this agent is a useful tool and should be considered in pediatric cataract surgery to improve inflammation and reduce PCO formation.

Long-term results of secondary intraocular lens implantation in children under 30 months of age

Koch CR, Kara-Junior N, Serra A, and Morales M. *Eye*. Dec 2018;32:1858-63.

This study reports the long-term outcome of early secondary intraocular lens (IOL) implantation following congenital cataract extraction in a large number of eyes. Data of aphakic children under 30 months of age who underwent secondary IOL implantation and had at least one year of follow-up after the surgery was reviewed. In all of the patients, a foldable three-piece acrylic IOL was implanted in the ciliary sulcus by the same surgeon using the same technique. Fifty patients (75 eyes) were included. The average age at the time of cataract extraction was 94.20 ± 44.94 days and 20.7 ± 6.0 months in the secondary IOL implantation. After 82.32 ± 48.91 months, the VA was 0.58 ± 0.35 LogMAR and the spherical equivalent was −2.20 ± 4.19 D. There was a negative correlation between a longer follow-up period and myopia at the SE measured (P = 0.001). The most frequent complications included glaucoma and corectopia. Performing the secondary IOL implantation ≤ 20 months of age was not a risk factor for glaucoma development (P = 0.095). Secondary IOL implantation under 30 months of age is an option for children who do not adapt well to contact lenses. A predictable IOL power calculation and satisfactory visual outcomes compared to results of later secondary IOL implantation are possible. This study was limited by its retrospective design, the fact that more than one type of IOL was implanted, and the fact that effective lens position was not calculated.

Five-Year Postoperative Outcomes of Bilateral Aphakia and Pseudophakia in Children up to 2 years of Age: A Randomized Clinical Trial

Vasavada BR, Vasavada V, Shah SK, et al. *Am J Ophthalmol.* 2018 September;193: 33-44.

This is a randomized clinical trial of 60 children (120 eyes) undergoing bilateral congenital cataract surgery. Half of the patients were randomized to receive intraocular lens (IOL) implantation and the other half were randomized to aphakia (n=30 in each group). The authors compared the outcomes of visual acuity, glaucoma, visual axis obscuration requiring surgery, and inflammation. The median age of surgery was 5 months in the aphakic group and 6 months in the pseudophakic group (p=0.56). At 5 years, the incidence of glaucoma was not different between the groups: 16% in the aphakic group and 13.8% in the pseudophakic group (p=0.82). Visually significant obscuration requiring surgery was also not different between the two groups (p= 0.79) with 10.3% of eyes in the pseudophakic group and 8% of eyes in the aphakic group needing surgery. The one significant difference was the incidence of posterior synechiae, which was significantly higher in the pseudophakic group (27.6% vs. 8%; p=0.004). In regards to vision, mean LogMAR acuity was 0.59 +/- 0.33 and 0.5 +/- 0.23 (p=0.79) with a trend toward better vision in the pseudophakic group, and more eyes in that group giving documentable vision earlier in their postoperative course. The authors point out one of the major limitations, which was that the aphakic group had very poor compliance with contact lenses and aphakic spectacle correction vs IOL may not be a fair comparison. There is a letter to the editor from the authors of the Infant Aphakia Treatment Study (IATS) highlighting some of the differences between this study and IATS, which is an important corollary to this paper.

Outcome of paediatric cataract surgery in Northwest Ethiopia: a retrospective case series

Asferaw M, Mekonen S, Woodruff G, Gilbert C, et al. *Br J Ophthalmol.* January 2019;103:112-118.

Up to one third of childhood blindness in sub-Saharan Africa is due to congenital or developmental cataract. In Ethiopia the prevalence of blindness in children is estimated to be 1 in 1000 children. This retrospective study evaluated the medical records of children less than 16 years old who had cataract surgery between 2010 and 2014. 143 children (176 eyes) were included. Mean age was 7.9 years, with 66% male. 25% were bilateral. 63% were unilateral traumatic cataracts, and 13% were unilateral non-traumatic cataracts. 93% had an intraocular lens implant. At last follow-up, visual acuity was >=6/18 or fix/follow in the better eye in over ½ of bilateral cases. Children with bilateral cataracts had worse outcomes if they had preoperative nystagmus or strabismus. In unilateral non-traumatic cases, only 1/3 achieved a good outcome (>=6/18) with half having poor visual outcome (<6/60). 39% with traumatic cataract had VA 6/18 or better. The authors did note, however, that overall follow-up was poor, which could have skewed visual acuity results.

Koch CR, Kara-Junior N, Serra A, Morales M. Long-term results of secondary intraocular lens implantation in children under 30 months of age.

Eye (Lond). 2018 Aug 28. doi: 10.1038/s41433-018-0191-3.

This study reported the long-term refractive and visual acuity (VA) outcomes and complications of early secondary intraocular lens (IOL) implantation in aphakic patients implanted under the age of 30 months. All patients underwent sulcus implantation of a foldable three-piece acrylic IOL. Fifty patients (75 eyes) were included. Patients under went lensectomy At the age of 94.2 ± 44.9 days and secondary IOL implantation at the age of 20.7 ± 6 months. Postoperative follow up was 82.3 ± 48.9 months. Authors found a negative correlation between a longer follow-up period and myopia (P = .001). Secondary IOL implantation did not increase the risk for glaucoma development.

Visual and Refractive Outcomes of Children After Secondary Cataract Extraction Following Wound Repair for Penetrating Ocular Trauma.

Kamaldeep Arora, Priyanka Arora, Suma Ganesh, Shriya Gupta et al
J of Ped Ophth & Strabismus.2018; 55(2): 122-127

The purpose of this retrospective, non-comparative case series is to evaluate the visual and refractive outcomes in children 8 years of age or younger with corneal laceration and cataract following penetrating ocular injuries who underwent primary corneal tear repair followed within 1 to 8 weeks by early secondary cataract extraction. The participants were followed for a period of 6 months postoperatively. The main outcomes were best -corrected visual acuity (BCVA) and refractive error as spherical equivalent at the final follow-up visit. A total of 47 children (33 boys, 14 girls) were included. The mean age at the time of injury was 5.9 ± 2.2 years (range: 3 to 8 years). Follow-up periods ranged from 6 months to 3 years (median: 18 months). The mean time gap between the wound repair and cataract extraction was 5 weeks (range: 1 to 8 weeks). Approximately 36 (77%) eyes obtained BCVA better than 6/18. All but one eye achieved BCVA better than 6/60. The deviation from emmetropia was less than 1.00 diopter (D) in 23 (54%) eyes, 1.00 to 3.00 D in 15 (35%) eyes, and more than 3.00 D in 5 (12%) eyes. Early removal of cataract with implantation of an IOL after primary wound repair in young children with penetrating corneal injury and traumatic cataract and no other associated ocular damage can result in excellent visual outcomes. In children of amblyogenic ages, visual outcomes comparable to older children can be achieved with early cataract surgery, a limited period of visual deprivation of less than 8 weeks, visual rehabilitation with an IOL, and elective primary posterior capsulotomy with anterior vitrectomy followed by aggressive amblyopia therapy. The study is limited by its retrospective nature and the small sample size.

Long-term outcomes for pediatric patients having transscleral fixation of the capsular bag with intraocular lens for ectopia lentis

Julia M. Byrd, Marielle P. Young, Wei Liu, Yue Zhang, et al. *Journal of Cataract and Refractive Surgery*; 2018;44(5):603-609.

This study from the Moran Eye Center in Utah of 37 patients (67 eyes) with atraumatic ectopia lentis having transscleral fixation of the capsular bag using a capsular tension ring fixated with 9-0 or 10-0 polypropylene, 8-0 polytetrafluoroethylene, or 9-0 nylon found a 78.5% improvement in corrected distance visual acuity at a mean follow up time of 35.3 months (0.25-120 months). The mean age at time of surgery was 7.25 years (2-18 years). The range of resulting refractive error was similar to that seen with traditional IOL placement. Short-term complications included hyphema in 1 eye and IOL repositioning at 3 months in 1 eye and long-term complications included posterior capsule opacification in 35 eyes (52%), uveitis-glaucoma-hyphema syndrome in 1 eye (1.5%), and spontaneous IOL dislocation in 3 eyes (4.4%) requiring IOL repositioning. As 7 patients who were initially considered for transscleral CTR suturing were unable to receive the procedure for various reasons determined intraoperatively, the authors note that the technique presented may not be appropriate for all cases. Nevertheless, this is an important article for pediatric ophthalmologists given the paucity of data regarding long-term outcomes in pediatric patients having surgical intervention for visually significant ectopia lentis.

Surgical Outcome of Congenital Cataract in Eyes With Microcornea.

Jyoti Matalia, Sheetal Shirke, Bhujang Shetty, Himanshu Matalia *J of Ped Ophthal & Strabismus.*2018;55(1):30-36

In this retrospective, interventional, comparative case series, the authors reviewed 47 eyes of 26 children with microcornea and congenital cataract who underwent lens aspiration with primary posterior capsulectomy and anterior vitrectomy between 2008 and 2014 with a minimum follow-up period of 6 months. Demographic profiles and systemic and ocular features were documented. Intraoperative and postoperative complications were studied separately for bilateral and unilateral cases. Patients were also divided into two groups on the basis of their ages at surgery (early surgery group: 3 months or younger; late surgery group: older than 3 months) and postoperative complications were compared. Visual outcome was analyzed in those with a follow-up period of more than 1 year. Early surgery was performed in 24 eyes of 13 patients (11 bilateral and 2 unilateral) and late surgery in 23 eyes of 13 patients (10 bilateral and 3 unilateral). Intraoperatively, all eyes had poor pupillary dilatation and 6 (12.8%) eyes needed iris hooks. Postoperatively, the most common early complication was transient corneal edema observed in 22 (46.8%) eyes (13 and 8 eyes in the early and late surgery groups, respectively). Late complications included visual axis opacification in 6 (12.76%) eyes (3 in each group), and secondary glaucoma in 5

(10.64%) eyes (2 and 3 eyes in the early and late surgery groups, respectively). Vision was normal for age in 18 (60%) of the bilateral cases with a follow-up period of more than 1 year. The study shows that we can expect favorable postoperative outcomes after early surgery for congenital cataract in microcornea. Meticulous surgery with adequate capsulectomy and complete anterior vitrectomy, as well as regular follow-up with early identification and timely judicious management of postoperative complications, especially visual axis opacification and glaucoma, is crucial for a successful outcome. Furthermore, good visual rehabilitation with the appropriate use of amblyopia therapy and vision stimulation maximizes the visual outcome for these children. Although this study has the limitations of being retrospective in design and having a relatively shorter follow-up period for some patients, it adds to the limited literature on cataract surgery in microcornea in the pediatric age group.

Modified technique of endocapsular lens aspiration for severely subluxated lenses

Khokhar S, Aron N, Yadav N, Pillay G, Agarwal E. *Eye* (2018) 32, 128–135

Authors describe an endocapsular technique to remove the lens material in patients with subluxated lenses. Authors include patients between 5-15 years who underwent a standard surgical technique. An MVR was used to create two paracentesis and to open two small incisions on the lens capsule. A vitrector and an irrigation with a 27 canula. The lens material was removed using the cut I/A vitrector. After the remaining capsules were also removed. An AC IOL was placed.Thirty-two eyes of 16 patients were included. Out of 16 patients, 9 patients (56.2%, 9/16) were diagnosed as having Marfan's syndrome, 4 patients (25%, 4/16) had a marfanoid habitus, and 3 patients (18.7%, 3/16) had bilateral microspherophakia with anterior subluxation of lens.
The mean age was 9.375 ± 3.16 years (range 5–15 years). All surgeries were uneventful. ACIOL were inserted safely in 22 eyes and 10 eyes were left aphakic. Out of these 10 eyes, 8 eyes had a large W–W diameter (412.5 mm) in which the ACIOL if placed may be small for the eye resulting in undue mobility. The rest of the 2 eyes of the same patient had microspherophakia out of which one eye had an anterior dislocated lens with pupillary block glaucoma (IOP = 30 mm Hg) and corneal edema (CCT = 640 µm), The mean endothelial cell loss at 3 months

compared to pre- operative levels was 269.6 ± 151 cells/mm amounting to 7.1% endothelial cell loss over 3 months which was statistically significant (P = 0.001). The mean CCT at 1 week, 1 month, and 3 months post-surgery were 525.3 ± 39.61 µm, 526.8 ± 39.43 µm, and 526.5 ± 39.17 µm. The modified technique of

endocapsular lens aspiration provides for a simple and effective way of removal of the lens-capsular bag complex through small incisions on the cornea

Pediatric cataract surgery complications

Childhood Lensectomy Is Associated with Static and Dynamic Reduction in Schlemm Canal Size: A Biomechanical Hypothesis of Glaucoma after Lensectomy

Moritz C. Daniel, Adam M. Dubis, Maria Theodorou, Ana Quartilho, et al. *Ophthalmology*. February 2019;126:233-241

Glaucoma after childhood cataract surgery occurs in almost 20% of children within five years after surgery. Since the etiology is unknown, the authors divide potential causes into two groups, chemical and mechanical, and explored the effects of accommodative effort on angle anatomy in normals and eyes after lensectomy using OCT. The study groups were matched in overall size and age, but the lensectomy group had a preponderance (~50%) of white subjects compared with only ~20% in the control group. The lensectomy group was almost evenly split between those with and without IOLs, but was enriched with glaucomatous eyes (~50%). Measurements of the size of Schlemm's canal and the trabecular meshwork were performed by a single unmasked observer. The horizontal dimension of Schlemm's canal was significantly reduced after lensectomy compared with normal in both the accommodative and nonaccommodative states, but the difference was small (80 microns) and similar between lensectomy eyes with and without glaucoma. The trabecular meshwork length and area were significantly larger after lensectomy, while the height of the trabecular meshwork was significantly smaller only in lensectomy subjects with glaucoma. The findings are confounded by a lack of control for surgical interventions, including angle surgeries like goniotomies and trabeculotomies, in subjects with glaucoma. In addition, while the authors provided evidence of accommodative effort by measuring the change in thickness of the ciliary body, attempted accommodation did not significantly affect the differences in angle anatomy between groups. So, lensectomy in children does appear to affect the relative size of angle structures compared with normals, but those differences are only slightly different for patients with and without glaucoma and do not provide strong evidence supporting a mechanical etiology for the glaucoma.

Primary versus secondary intraocular lens implantation in traumatic cataract after open-globe injury in pediatric patients.

Pradhnya Sen, Chintan Shah, Alok Sen, Elesh Jain, et al. *JCRS* Dec 2018;44(12):1446-1453.

This retrospective cases series reviewed the charts of 139 patients in India to compare the visual and refractive outcomes and complications of primary and

secondary intraocular lens (IOL) implantation after open globe injury in pediatric patients. Cataract extraction was either performed at the time of globe repair or secondarily following repair. The study included 139 patients. Mean follow up was around a year for both groups, and patients with less than 3 months of follow up were excluded from analysis. Thirty (49%) of 61 patients in Group A and 47 (60%) of 78 patients in Group B achieved a corrected distance visual acuity (CDVA) of 20/40 or better. In both groups, a central corneal scar and amblyopia were the main reasons for not achieving a CDVA better than 20/40. The mean spherical equivalent (SE) was 1.81 diopters (D) in Group A and 1.55 D in Group B. Forty patients (66%) in Group A and in 60 patients (77%) in Group B achieved a SE <2.00 D. A large wound was the greatest risk factor for not obtaining a desirable refractive outcome. Fibrinous uveitis was the most common postoperative complication in both groups. Pupillary optic capture and IOL decentration were significantly more common in Group A than in Group B (p=.02), while strabismus was significantly more common in Group B (p=.04). The authors conclude that both approaches had satisfactory and comparable visual and refractive outcomes but state that primary IOL implantation can be considered in cases with small peripheral corneal lacerations with the goal of providing early visual rehabilitation and avoiding repeat general anesthesia. This article provides some useful information derived from a large number of pediatric traumatic cataract cases but has the usual limitations of a retrospective study in that the patients were not randomly assigned to either primary or secondary IOL placement—the timing of their cataract surgery was based on the severity of the initial pathology. Also, some even longer term follow up in terms of IOL decentration, glaucoma, etc. would be informative.

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

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

J of Ped Ophth & Strabismus.2018;55(1):23-29

The purpose of this study is to compile international data on the risk factors, diagnosis, and treatment of endophthalmitis following pediatric cataract surgery.An e-mail containing a link to an online survey was sent to all members of the American Association for Pediatric Ophthalmology and Strabismus. The questionnaire examined the incidence, risk factors, treatment, outcomes, and prophylaxis of endophthalmitis following pediatric cataract surgery around the world.Two hundred thirty-seven ophthalmologists answered the questionnaire. Eight ophthalmologists (3.4%) encountered 22 cases of endophthalmitis following pediatric cataract surgery during their practice. Most patients with endophthalmitis following pediatric cataract surgery were 2 to 4 years of age (36.4%). An intraocular lens was implanted in 59.1% of cases, most of which were acrylic intraocular lenses (53.8%). The main presenting symptoms were photophobia (50%) and pain (40.9%). The most common signs were conjunctival injection (36.4%) and hypopyon (31.8%).

The final visual acuity was counting fingers or worse in 86% of cases. The most common cultured organism was *Staphylococcus aureus* (31.8%). The most common management of endophthalmitis following pediatric cataract surgery was a combination of intravitreal, systemic, and topical antibiotics (36.4%). Most ophthalmologists (68.2%) administered prophylactic intracameral antibiotic treatment during surgery and 50% used vancomycin. The authors conclude that endophthalmitis following pediatric cataract surgery is an uncommon, multifactorial complication with poor visual prognosis. Efforts directed at minimizing its risk, such as treating potential predisposing systemic conditions, improving sterilization techniques, optimizing operative conditions to reduce complications and surgery duration, and using subconjunctival and intracameral antibiotics, decrease its incidence. Early postoperative evaluation, subsequent follow-up visits, and keeping a high index of suspicion should facilitate the recognition of endophthalmitis following pediatric cataract surgery to avoid delaying treatment.

Pediatric cataract surgery – other topics

Evaluation of changes in axial length after congenital cataract surgery.

Seven E, Tekin S, Batur M, Artuc T, Yasar T. *JCRS* Apr 2019;45(4):470-474.

This retrospective study conducted in Turkey investigated the relationship between lens status and axial length in pediatric patients who had surgery for unilateral and bilateral congenital cataract. Records of pediatric patients who underwent surgery for unilateral or bilateral congenital cataract were analyzed. The patients were separated into three groups: bilateral aphakic (49 eyes of 25 patients), bilateral pseudophakic (103 eyes of 54 patients), and unilateral (40 eyes of 20 patients). The unilateral group was subdivided into operated cataract eyes (unilateral aphakic and unilateral pseudophakic) and unoperated fellow phakic eyes. The patients' age at surgery, follow-up time, preoperative and postoperative AL measurements, change in AL, and monthly growth rate were evaluated. The mean age at time of surgery in these groups was 8.17 months +/-10.65 (SD), 42.47 +/- 43.81 months, and 35.35 +/- 33.22 months, respectively. There were no significant differences in preoperative AL, postoperative AL, change in AL, or monthly growth rate between the aphakic and fellow phakic eyes in the unilateral group ($P > .05$). There were also no significant differences between unilateral pseudophakic eyes and fellow phakic eyes in the unilateral group withrespect to preoperative AL or change in AL, but there were significant differences in final AL and monthly growth rate ($P < .05$). The authors conclude that various factors can affect axial elongation. They found that the monthly growth rate was lower in pseudophakic eyes compared with phakic eyes and state that experimental studies are required to understand the mechanism underlying this effect. The main limitations of this paper are 1) that refractive parameters could not be assessed because of lack of patient data, 2) that while IOP is one of the major factors af-

fecting globe growth, digital palpation was used in most of the IOP measurements in this study, and 3) small sample size in the unilateral cataract group and its subgroups (operated eyes vs. unoperated fellow eyes).
Additionally, some of the data in the abstract and paper is not internally consistent: the number of bilateral aphakic patients is different in abstract and paper and age range of unilateral group was same as bilateral pseudophakic group in abstract but is noted to be something different in Table 1.

Comparison of Pediatric Cataract surgical techniques between pediatric Ophthalmology Consultants and fellows in training: a video based analysis.

Akshay Badakere, Preeti Patil Chhablani, Anjali Chandrashekaran, Mohamet Hasnat Ali et al. *J of Ped Ophth & Strabismus.*2019;56(2):83-87

The purpose of this retrospective study was to compare intraoperative technique and quality of surgical steps in pediatric cataract surgery between pediatric ophthalmology consultants and fellows in training.In a video-based analysis by two fellowship-trained pediatric ophthalmologists, 42 surgical videos of pediatric ophthalmology consultants and 34 videos of fellows in training were graded based on the International Council of Ophthalmology's Ophthalmology Surgical Competency Assessment Rubrics (ICO-OSCAR). Six steps in surgery were analyzed: wound construction, anterior continuous curvilinear capsulorrhexis, irrigation and aspiration, intraocular lens implantation, primary posterior capsulorrhexis with anterior vitrectomy, and wound suturing. Cohen's Kappa was used to rate inter-observer agreement. Cohen's Kappa scores ranged from 0.6 to 0.8. The median scores for surgical steps for both analyzed groups were similar. The mean duration of surgery was shorter for consultants (24 minutes, range: 10 to 45 minutes) than for fellows (40 minutes, range: 15 to 70 minutes). The median age of patients operated on by consultants was younger (24 months, range: 2 to 180 months) than fellows (58 months, range: 10 to 150 months). The study concluded that there was no statistically significant difference in the grading of the surgical steps performed by fellows and consultants. Although this was not entirely expected, the authors suspect that the age of the patients in each subgroup may cause this result. The median age of patients was 22 months in the consultant group and 58 months in the fellows group. The complexity and level of difficulty of pediatric cataract surgery is linked to the age of the patient, so surgery is easier with older patients. This may explain why the authors did not observe a difference in the scores in the two groups, despite a difference in the level of training. Additionally, the groups only included patients with uncomplicated cataracts; cases requiring a greater level of skill (eg, traumatic cataract or cataract after vitreoretinal or other intraocular surgery) were not included. A limitation of this study is that it was primarily a video-based analysis. Consequently, it was difficult to know the complexity of the surgical case, which could influence scores. Newer trainees start with older patients and relatively simpler cases, whereas more experienced trainees and faculty perform the complex procedures.

Goldmann applanation tonometer versus ocular response analyzer for measuring intraocular pressure after congenital cataract surgery

Feizi S, Faramarzi A, Kheiri B. *Eur J Ophthalmol.* Sep 2018;28(5):582-589.

This study sought to compare intraocular pressure measurement in pediatric patients undergoing lensectomy and vitrectomy with Goldmann applanation versus the ocular response analyzer. 113 eyes were included in the study. There was a statistically significant difference between the two diagnostic modalities with the ocular response analyzer measuring a higher IOP than the Goldmann tonometer:(16.75 ± 4.82 mmHg) versus (14.41 ± 2.27 mmHg, $p < 0.001$) respectively. This was influenced by central corneal thickness and corneal hysteresis. Subgroup analysis of pseudophakic versus aphakic patients revealed that there was better agreement between the two methods in pseudophakic patients. This study emphasizes that these two methods of IOP measurement cannot be used interchangeably in pediatric patients.

Influence of the vitreolenticular interface in pediatric cataract surgery.

Jan Van Looveren, Arnout Vael, Nick Ideler, Hedwig Sillen, et al. *JCRS* Oct 2018;44(10):1203–1210.

This case series was performed in order to report the status of Berger space in pediatric cataract cases and the influence of anterior vitreolenticular interface dysgenesis during primary posterior continuous curvilinear capsulorhexis (PCCC). Of 134 pediatric cataract surgeries performed using the bag-in-the-lens technique at Antwerp University Hospital November 2010-April 2016, 64 eyes of 64 children having surgical video recordings available for review were included. A video-based analysis of the surgical interventions included the type of crystalline lens opacification, presence of a posterior capsule plaque (PCP), presence of anterior vitreolenticular interface dysgenesis, complications during primary PCCC, integrity of the anterior hyaloid membrane, need for anterior vitrectomy, and feasibility of BIL IOL implantation. Abnormalities in Berger space were observed in 35 of the 64 pediatric cataract cases. Anterior vitreolenticular interface dysgenesis was most often found in cases with persistent fetal vasculature (PFV) and those with unilateral and posterior cataract. In pediatric cataract cases presenting with PCP and anterior vitreolenticular interface dysgenesis, the primary PCCC procedure was surgically more demanding, often resulting in detectable breaks in the anterior hyaloid membrane (58.6%) and sometimes necessitating an unplanned anterior vitrectomy (13.8%). Bag-in-the-lens IOL implantation was feasible in all except 1 eye with PFV, which was left aphakic. This article alerts us to

the fact that anterior vitreolenticular interface dysgenesis is common in pediatric cataract surgery and may complicate primary PCCC.

Follow-up patterns and associated risk factors after paediatric cataract surgery: observation over a 5-year period

Chougule P, Murat S, Mohamed A, Kekunnaya R. *Br J* Ophthalmol. November 2018;102:1150-1555.

In developing countries, follow-up of children undergoing cataracts surgery has known to be poor. The authors of this retrospective study aimed to evaluate the pattern of compliance and follow-up of children less than 5 years old undergoing cataract surgery in Hyderabad, India. 169 patients were included in the study, with median age at surgery of 10 months and median follow-up of 22 months. There was a significant correlation between age at surgery and follow-up duration, with higher age at surgery associated with poorer follow-up. Overall 15% of patients were lost to follow-up at 1 month, which increased to 61% at 3 months but slowed thereafter. Patients in higher socioeconomic status had longer follow up (media 35 months) compared to those of lower socioeconomic status (median 14 months). The drop out was steeper in the lower socioeconomic group. There was no difference between those in rural homes compared to urban, or to distance between residence and hospital. The authors conclude that there needs to be strategies to reduce the economic burden associated with frequent follow-ups in this vulnerable population.

Effects of cycloplegia on Optical Biometry in Pediatric Eyes.

Usha K.Raina, Shantanu Kumar Gupta, Anika Gupta, Apurva Goray
*J of Ped Ophth & Strabismus.*2018;55(4):260-265

The purpose of this observational study is to determine the effect of cycloplegia on optical biometry parameters in pediatric eyes using the Lenstar LS 900(Haag-Streit, Koeniz, Switzerland). 56 normal eyes and 20 cataractous eyes in children between 5 and 15 years of age were included. Measurements were taken before and after cycloplegia using 2% homatropine drops. Parameters studied were axial length, central corneal thickness, keratometry, anterior chamber depth, and lens thickness. The Wilcoxon test was used to compare the effects of cycloplegia on all parameters. The study showed that Cycloplegia resulted in a statistically significant decrease in axial length ($P < .05$), central corneal thickness ($P < .05$), and lens thickness ($P < .001$) and an increase in the anterior chamber depth ($P < .001$) in normal eyes. In the cataract group, cycloplegia resulted in an increase in anterior chamber depth ($P < .001$) and decrease in lens thickness ($P < .001$). The authors conclude that there were significant alterations in the various parameters in both groups. Although the study couldn't demonstrate any impact on the IOL power calculation, the results give scope for further research with other IOL power formulas that uses anterior chamber depth as one of their parameters.

14.GLAUCOMA

Pediatric glaucoma - surgical management

Correlation Between Trabeculodysgenesis Assessed by Ultrasound Biomicroscopy and Surgical Outcomes in Primary Congenital Glaucoma

Shi Y, Wang H, Han Y, et al. *Am J Ophthalmol.* 2018 December; 196: 57-64.

The purpose of this study is to evaluate the ultrasound biomicroscopy (UBM) characteristics in eyes with primary congenital glaucoma (PCG) and compare these UBM findings to surgical outcomes after trabeculotomy. To do this, the authors performed a prospective, interventional case series of 49 eyes of 33 patients with PCG. Microcatheter-Assisted -Trabeculotomy (MAT) was the planned first glaucoma surgery in these patients, though as expected some cases were completed with the Harms trabeculatome. All patients had a UBM prior to surgery and the authors classified the eye's trabeculodysgenesis into three types based on the severity of the anterior iris insertion and ciliary processes with type 1 being the most severe and type 3 being the least severe dysgenesis. The authors defined surgical success as a post op pressure less than or equal to 21mmHg and at least a 30% reduction compared to preoperative intraocular pressure without any additional treatment or optic nerve compromise for at least 6 months post op. At the 2-year follow up point, the type 1 trabeculodysgenesis (most severe type) had a success rate of 57.1%, those with type 2 had a 70.5% success rate, and those with type 3 achieved success in 95.5% of eyes (p=0.22). The authors concluded that the severity of the trabeculodysgeneisis was a good predictor of prognosis after MAT surgery. Some limitations of this study include the observer error when evaluating the type of trabeculodysgenesis and the small sample size. A discussion about the rate of conversion to the Harms trabeculotome and how this could have affected the results would have added to the breadth of the last section of the paper. This paper adds to the literature in that it helps with counseling patients about the risks of recurrent / uncontrolled glaucoma especially in cases of poorly formed angles.

Mitomycin C in Filtering Surgery for Primary Congenital Glaucoma: A Comparison of Exposure Durations

Nader H. Bayoumi *J of Ped Ophth & Strabismus.*2018; 55(3): 164-170

The purpose of this prospective study is to compare the effect of two exposure durations of mitomycin C in combined angle and filltering surgery for primary congenital glaucoma. Seventy-five eyes with primary congenital glaucoma that underwent combined trabeculotomy–trabeculectomy with intraoperative mitomycin

C application for 1 minute (MMC 1) or 2 minutes (MMC 2) and were followed up for 24 months. Success rates were studied and complications noted. Success was defined by a composite primary end point of an intraocular pressure (IOP) of less than 16 mm Hg under general anesthesia, without any IOP-lowering medications and with no hypotony-related complications and/or lack of IOP-related progression of the disease as evidenced by worsening of the ocular biometric characteristics. The mean age of the study participants was 6.7 ± 4.1 months (range: 2 to 16 months; median: 6 months) in the MMC 1 group (35 eyes) and 7.7 ± 5.7 months (range: 1 to 32 months; median: 6.5 months) in the MMC 2 group (40 eyes). The initial surgery was suc- cessful in 32 (91.5%) and 31 (77.5%) eyes in the MMC 1 and MMC 2 groups, respectively. The mean IOP was 18.4 ± 5.1 and 18.1 ± 6.1 mm Hg preoperatively and 5.5 ± 3.5 and 4.8 ± 2.8 mm Hg at the end of follow-up in the MMC 1 and MMC 2 groups, respectively. There was no statistically signi cant di erence in the clinical param- eters between the two groups. Complications included cataracts in each group and hypotony optic disc edema in 3 eyes (7.5%) in the MMC 2 group. The authors concluded that because both exposure durations of mitomycin C yielded comparable postoperative IOP values and the longer exposure durations were associated with a more unhealthy bleb appearance, higher reoperation rate, and higher chance of hypotony-related complications, there seems to be no advantage in using Mitomycin C with an exposure duration of 2 minutes. A mitomycin C exposure duration of 1 minute would be recommended for use in combined angle and filtering surgery for primary congenital glaucoma. This study has several limitations such as the addition of an angle procedure to the filtering procedure rather than testing the filtering procedure effect in isolation, the comparison of only two exposure durations of one concentration of mitomycin C rather than extending the study to include arms with different mitomycin C concentrations and/or different exposure durations, the lack of formal assessment of visual function for the study eyes, the inclusion of both eyes of some patients in the data analysis rather than one eye only, the relatively small sample size, and the relatively short follow-up duration of only 2 years.

Pediatric glaucoma – corneal biometry, OCT and visual field

Pediatric glaucoma – other topics

Functional Visual Ability and Quality of Life in Children With Glaucoma

Aldarrab A, Al Qurashi M, Al Thiabi S, et al. *Am J Ophthalmol.* 2019 April; 200:95-99.

This is a cross sectional study of 85 children (ages 8-18) aimed at evaluating the effect of glaucoma and its treatment on functional visual ability (FVA) and vision related quality of life (VR QoL). This study was conducted at a single

academic institution using the Cardiff Visual Ability Questionnaire for Children (CVAQC) to assess FVA and the Impact of Vision Impairment for Children for Children (IVI_C) tool to assess VR QoL. Scores for both FVA and VR QoL were reduced for pediatric patients with glaucoma. Patients with worse best corrected visual acuity, bilateral glaucoma, 3 or more glaucoma surgeries had significantly lower scores on both scales. The authors concluded that improving quality of life with low vision aids, psychosocial involvement, and visual rehabilitation services is important for these patients. The authors correctly highlight that these results might not be generalizable to those in the US since this study was done in the Kingdom of Saudi Arabia. Most patients in this study were not using low vision aids, which may not be representative of patients in the rest of the world. Nevertheless, this study is important in that it highlights how much childhood glaucoma affects the entire child.

Agreement profiles for rebound and applanation tonometry in normal and glaucomatous children

Esmael A, Ismail YM, Elhusseiny AM, Fayed AE, Elhilali HM *EJO* July 2019,29(4) 379–385

The study aimed to investigate agreement between intraocular pressure measurements by the rebound tonometer and handheld Perkins applanation tonometer in children with and without primary congenital glaucoma and test agreement with intraocular pressure and age variations. A prospective non-interventional comparative study done on 223 eyes of 115 children, 161 normal eyes, and 62 eyes with primary congenital glaucoma. Intraocular pressure measurements were obtained in the upright position by rebound tonometer first, followed by installation of topical anesthetic eye drops (benoxinate), then measured by Perkins applanation tonometer. For all eyes, mean difference between Perkins applanation tonometer and rebound tonometer was −0.59 • } 2.59 mmHg, p = 0.001. Regression analysis with (r) = 0.9, (r2) = 0.79, and p < 0.001. In primary congenital glaucoma: there was a mean difference of −.79 • } 2.82 (p = 0.032), a good correlation with (r) = 0.94, (r2) = 0.87%, and 95% level of agreement: –6.34 to +4.76. In normal eyes: mean difference was −.52 • } 2.5 (p = 0.01), correlation: (r) = 0.8,
(r2) = 0.64, and p = 0.001. The 95% level of agreement −5.41 and +4.36 mmHg. In intraocular pressure ⩽ 15 mmHg: mean difference −0.89 • } 2.15 mmHg, 95% level of agreement between −5.1 and +3.32 mmHg, p < 0.001. In intraocular pressure >15 mmHg: mean difference was 0.04 • } 3.28 mmHg, 95% level of agreement −6.38 and +6.46 mmHg, p = 0.914. There is a good correlation between rebound tonometer and Perkins applanation tonometer in children with and without primary congenital glaucoma; however, rebound tonometer overestimates the intraocular pressure, and in intraocular pressure >15 mmHg there is less agreement between the two devices. Hence, in higher intraocular pressure

measurement caution should be taken when interpreting rebound tonometer readings, and a confirmatory measurement using Perkins applanation tonometer is advised.

Systemic Associations of Childhood Glaucoma: A review

Neha Midha, MD; Talvir Sidhu, MD; Neha Chaturvedi, MD; Renu Sinha, MD; *J Ped Ophthal & Strabismus*.2018;55(6):397-402

The purpose of this article is to review the systemic associations of childhood glaucoma. The 371 patients diagnosed with glaucoma were divided into four groups: primary congenital glaucoma, glaucoma with other congenital ocular anomalies, congenital glaucoma with known systemic diseases, and secondary glaucoma. Prevalence and type of systemic associations in each group were studied. In the primary congenital glaucoma group, 13 of 218 (5.9%) patients had an associated systemic illness: congenital heart disease and global developmental delay were the most common systemic manifestations. In the congenital ocular anomalies group, 10 of 63 (15.8%) patients had an associated systemic illness. Axenfeld-Reiger syndrome, aniridia, and Peters' anomaly frequently had systemic comorbidities with congenital heart disease. In the known systemic diseases group, all 18 (100%) patients had systemic manifestations of an associated syndrome: Sturge-Weber and Down syndrome were the most frequent. In the secondary glaucoma group, 9 of 72 (12.5%) patients had systemic involvement, which was often seen as the most common cause after congenital cataract surgery. These children had congenital heart disease and global developmental delay as a consequence of congenital rubella and congenital cytomegalovirus infection.The study found that 12.9% of patients with childhood glaucoma had an associated systemic abnormality. Patients with congenital glaucoma and other ocular anomalies have a three times higher risk of an underlying systemic anomaly than patients with isolated primary congenital glaucoma. A team comprising an ophthalmologist, pediatrician, and anesthesiologist is recommended to treat these cases.

Icare-Pro Rebound Tonometer Versus Hand-held Applanation Tonometer for Pediatric Screening

Paula Arribas-Pardo, Carmen Mendez-Hernandez, Isabel Valls-Ferran, Diego Puertas-Bordallo. *J Ped Ophthal & Strabismus*.2018;55(6):382-386

The purpose of this prospective study to compare intraocular pressure (IOP) measurements obtained using the new rebound tonometer Icare-Pro (Icare, Tiolat Oy, Helsinki, Finland) and the hand-held version of the Goldmann applanation tonometer (Perkins; Clement Clarke, Haag-Streit, Harlow, United Kingdom) in healthy children during clinical practice. Three IOP measurements were made using each tonometer in a single session, starting with the Icare-Pro. Participants were 173 non-anesthetized patients aged 1 to 16 years. Measurements were

made in both eyes but only data for the right eye were entered in the analysis. Central corneal thickness, anterior chamber depth, and axial length were also measured in each patient. Data were compared by determining interclass correlation coefficients (ICCs) for each tonometer and representing the differences detected as Bland–Altman plots. The authors showed that there is good linear correlation between IOP readings obtained using the Perkins and Icare-Pro tonometers ($r = 0.87$, $P < .001$), although the Icare-Pro readings were slightly higher (mean IOP difference: 0.26 ± 1.58 mm Hg, $P = .037$). The 95% limits of agreement between the two methods were 2.8 to −3.4 mm Hg. The ICC was 0.857 (95% confidence interval: 0.810 to 0.893), indicating good agreement. For both tonometers, a low but significant correlation was detected between IOP and central corneal thickness or age. However, no correlation of IOP was found with axial length or anterior chamber depth. In conclusion, pediatric IOP measurements determined using the new Icare-Pro rebound tonometer showed good correlation with those obtained using the hand-held Perkins applanation tonometer in a routine clinical examination with no need for general anesthesia.

A Long-term Safety Study of Latanoprost in Pediatric Patients with Glaucoma and Ocular Hypertension: A Prospective Cohort Study.

Younus M, Schachar RA, Freedman SF, et *Am J Ophthalmol.* 2018 December; 196: 101-111.

This prospective cohort study aims to assess the safety of long-term latanoprost use in children. The authors prospectively studied 175 patients (102 in the latanoprost group) for 3 years. The primary endpoint of this study was a change in best-corrected visual acuity (BCVA) over the study period and secondary endpoints included corneal thickness and ocular hyperpigmentation. The authors found no significant difference in the change of BCVA in the two groups. Additionally, there were no differences found in corneal thickness or hyperpigmentation between the two groups. The authors looked at the longest eyelash and found no significant difference in lash growth in the two groups over the study time period. Of note, they did have one patient in the latanoprost group that developed iris hyperpigmentation. There was also not an appreciable difference between the two groups in terms of conjunctival hyperemia. The authors concluded that latanoprost has an acceptable safety profile in the pediatric patient. The important limitations were highlighted by the authors including the possibility that more adverse effects could be seen with a longer follow up period, specifically the possibility of developing enophthalmos and hyperpigmentation. This is an important study to the pediatric ophthalmologist who treats patients with glaucoma and is helpful when explaining the (low) risks of this therapy to parents and patients.

Effect of Chloral Hydrate Sedation on Intraocular Pressure in a Pediatric Population

Varadaraj V, Munoz B, Karaoui M, et al *Am J Ophthalmol.* 2018 October; 194:126-133.

The purpose of this study was to prospectively study the effect of oral chloral hydrate (CH) on intraocular pressure in children. This prospective, non-comparative case series was performed on 112 children (50.9% female) from 1-month to 5-years-old undergoing sedation with oral chloral hydrate. The intraocular pressure (IOP) was measured with an Icare tonometer prior to sedation, 25 minutes after sedation and then every 10 minutes after that until the patient was no longer sedated. The authors used linear regression to look at the change in IOP over time. The mean age of the patients was 2.1 years. Sixty-four (57%) of the patients had IOP measured prior to sedation, and of those about half were calm at the time of IOP measurement. Of those with pre sedation IOP, the mean was 19.5mmHg and after sedation their mean IOP was 18.7mmHg (p=0.12). There was no trend toward decline in IOP over time. The authors concluded that CH sedation in the outpatient setting did not impact IOP. The authors discuss that this CH is generally out of favor in the United States, and explain that it is the sedating agent with the least effect on IOP compared to other commonly used agents.

New classification system for pediatric glaucoma: implications for clinical care and a research registry

Avery Thau, Maureen Lloyd, Sharon Freedman et al. *Curr Opin Ophthalmol* 2018, 29:385-394 (Sept 2018)

A worldwide collaboration was established to create a standardization for the definition of glaucoma in the pediatric population. The Childhood Glaucoma Research Network (CGRN) has developed criteria for pediatric glaucoma. Childhood glaucoma is defined as two or more of the following: IOP >21mmHg, visual field defect, progressive increase in axial length, corneal findings such as Haab striae, corneal enlargement, increasing C:D ratio or asymmetry of > 0.2, and focal rim thinning. They also characterized childhood glaucoma suspect as having one of the following: IOP >21 on two separate occasions, suspicious visual fields, increasing axial length with normal IOP, increased corneal diameter with normal IOP, or suspicious optic nerves. A flowchart is provided to allow the user to arrive at the proper classification. Glaucoma after cataract surgery then has further classification based on open or closed angle appearance. All cataract etiologies are included in this subclassification if the glaucoma was acquired only after cataract surgery. If the patient has not had cataract surgery even if a cataract is present then the glaucoma is classified based on the presence of systemic or ocular congenital conditions. If the glaucoma is predominantly systemic or without significant ocular anomalies this is classified as glaucoma associated with nonacquired systemic disease of syndrome. This is regardless of the mechanism i.e. open or closed angle. The next category is glaucoma associated with nonacquired ocular anomalies i.e. congenital conditions with significant ocular

findings. Glaucoma associated with acquired conditions includes steroids, surgery, and the like and is subclassified into open and closed types. Primary congenital glaucoma (PCG) develops in the absence of all the conditions mentioned above and has buphthalmos. It is further subclassified into neonatal onset (0-1 month), infantile (>1-24 months), and late onset (>24 months). Lastly, juvenile onset glaucoma occurs between 4-40 years of age). The authors then describe the Robison D. Harley MD CGRN International Pediatric Glaucoma Registry as a repository for international reporting of glaucoma cases that uses the classification system for the purposes of studying rare disorders with any significant sample sizes. This registry is hosted by a private company and is available to any individual involved with pediatric eye care once their IRB approval is obtained. The registry is HIPAA compliant and allows for entry of both retrospective and prospective data. There is also the ability to submit DNA samples from patients with glaucoma as well.

This article elucidates a novel approach to the classification of glaucoma that standardizes it worldwide and has set up a database to allow for further research to impact the diagnosis and management of pediatric glaucoma patients.

Pretarsal skin height changes in children receiving topical prostaglandin analogue therapy for primary congenital glaucoma

Al-Zobidi M, Khandekar R, Cruz A, Craven RE, et al. *JAAPOS*. Aug 2018; 22(4):290-293.e1.

This goal of this paper is to compare pretarsal skin height (PTSH), as proxy indicator of deepening of the upper eyelid sulcus, in children with primary congenital glaucoma (PCG) treated with topical prostaglandin analogues (PGAs) to PTSH in healthy children (control group 1) and children with PCG but not using PGAs (control group 2). The authors recruited children with PCG who had been using PGAs for at least 6 months (PCG/PGA group). PTSH in all participants was measured using ImageJ software from photographs taken in a standardized manner. The PTSH was compared for the PCG group and both control groups. A total of 34 children with PCG and 41 controls (31 in group 1; 10 in group 2) were included in this study. The difference in PTSH between children in the PCG/PGA group and both control groups was statistically significant with the mean difference ≥1.7 mm [$P < 0.01$]. The PTSH was significantly greater in children with PCG using PGAs for at least 6 months compared to children with PCG not using PGAs and healthy children. The authors recommend that children and their parents should be counseled about lid abnormalities prior to commencing treatment with PGAs. Furthermore, it is unclear if reversal of the changes would occur once the PGA has been discontinued and how these changes vary in children of different ages.

Correlation of Corneal and Scleral Pneumatonometry in Pediatric Patients

Lee JH, Sanchez LR, Porco T, Han Y, et al. *Ophthalmology 2018* Aug;125(8):1209-1214.

Measuring IOP in pediatric patients can be a challenge, especially if there is a significant corneal disease. Scleral tonometry has been proposed as an alternative method. This study examined how the corneal ad scleral IOP correlate using pneumatonometry in pediatric patients. The goal of this study was to create a model from which corneal IOP can be derived from scleral IOP measurement. Consecutive patients age 0 to 15 years who were undergoing an exam under anesthesia or eye surgery at UCSF, Benioff Children's Hospital, from July 2015 to April 2016 were recruited for the study. Using pneumatonometry, IOP was obtained from the central corneal, and the inferonasal and inferotemporal sclera in a random order. All measurements were obtained under general anesthesia within 5 minutes of induction, without lid speculum. All patients underwent general anesthesia using 1 agent or a combination of 3 agents: sevoflurane, fentanyl, and propofol. IOP measurement was taken prior to intravenous agents being administered. Seventy-five eyes from 40 patients were included in the study. Spearman correlations between corneal versus inferonasal scleral IOP and corneal versus inferotemporal scleral IOP were calculated. A linear mixed-effect model was used to derive a predictive equation for corneal IOP from scleral IOP and to perform covariate analysis for age, axial length, central corneal thickness, and lens status. The standard deviation of the predicted corneal IOP was determined by bootstrap mixed-effect regression analysis. Spearman correlation coefficient for corneal versus inferotemporal scleral IOP was 0.79 ($P < 0.01$) and 0.48 for corneal versus inferonasal scleral IOP ($P < 0.01$). Corneal IOP may be predicted from scleral IOP via the following equations: corneal IOP = 0.73 × inferotemporal scleral IOP + 7.45 and corneal IOP = 0.21 × inferonasal scleral IOP + 17.83. Central corneal thickness ($P = 0.07$), lens status ($P = 0.4$), age ($P = 0.33$), and axial length ($P = 0.15$) did not affect significantly the relationship between corneal and scleral IOP in the multivariate regression analysis. The standard deviation of predicted corneal IOP was < 1.2 mmHg within an inferotemporal scleral IOP range of 10 to 35 mmHg. The authors concluded that there is a significant correlation in corneal and inferotemporal scleral IOP. Pneumatonometry on the inferotemporal sclera may be an alternative method to estimate IOP for pediatric patients from whom corneal OP measurement is difficult to obtain. The range of IOP tested in this study is in normal range and this could not be generalized to very low or high IOPs. This model should be tested in awake pediatric patients to see the impact of anesthesia on IOP.

15.REFRACTIVE SURGERY

Corneal indices following photorefractive keratectomy in children at least 5 years after surgery.

Ram R, Kang T, Weikert MP, Kong L, et al. *JAAPOS* 2019 June; 23 (3): 149.e1-149.e3

The literature regarding haze and keratectasia after refractive surgery in children is scarce. The aim of this prospective interventional case series was to evaluate long-term corneal outcomes in pediatric patients who underwent photorefractive keratotomy (PRK) for the treatment of refractive amblyopia. Children with refractive amblyopia underwent PRK between January 1, 2007, and December 31, 2011, at Texas Children's Hospital's Department of Ophthalmology, a single tertiary eye center, and were followed for at least 5 years after surgery. Main outcome measures were 5+ years postoperative indices of corneal thickness, keratometry, degree of corneal haze, and presence or absence of keratectasia. A total of 12 eyes of 8 subjects (aged 3-9 years) who underwent PRK and were followed for at least 5 years were included. The mean PRK treatment dose was 8.46 D for the myopic cohort and 4.49 D for the hyperopic cohort, which removed an average of 72 µm of corneal stromal tissue in addition to the 50 µm of corneal epithelium that was removed prior to laser ablation. The mean corneal thickness was 563 µm preoperatively, which decreased to 441 µm immediately following the PRK. The mean corneal thickness 5+ years after PRK was stable, at 498 µm, because of epithelial regrowth. None of the subjects developed visually significant corneal haze or topographic evidence of keratectasia. The authors conclude that in this study cohort, there were no topographic signs of keratectasia or corneal haze in children treated with PRK for high refractive error 5 years or more after surgery. The study main limitation is its small sample size.

Unilateral refractive surgery and Myopia progression.

Sara Sella; Nizan Duvdevan-Strier; Igor Kaiserman *J of Ped Ophth & Strabismus*.2019;56(2):78-82

The purpose of this study is to compare the progression of myopia in eyes that underwent unilateral refractive surgery with non-operated eyes. Three patients(n=3) who underwent refractive myopic correction in one eye are described. The collected preoperative and postoperative data included age, gender, subjective refraction, best corrected visual acuity, and uncorrected visual acuity. The first patient (19-year-old woman) had photorefractive keratectomy in her left eye and the myopic progression was 1.20 diopters (D) (3 years postoperatively) compared to −2.50 D in her non-operated eye. The second patient (30-year-old man) had laser-assisted in situ keratomileusis in his left eye with a myopic progression of 0.25 D compared to 0.75 D in his non-operated eye (10 years postoperatively). The third patient (22-year-old man) underwent photorefractive keratectomy in his right eye with no myopic progression compared to −1.50 D in his non-operated eye (3 years postoperatively). The authors suggest that, similar to orthokeratology, corneal reshaping with laser refractive surgery may slow the progression of myopia. However, this study is limited by its small number of cases and the fact that the changes in axial length of the eyes were not documented during the follow-up period. Large randomized studies with customized ablation protocols aiming to prevent the peripheral defocus are warranted to confirm this possibility.

Accommodative Esotropia Treatment Plan Utilizing Simultaneous Strabismus Surgery and Photorefractive Keratectomy

Eustis HS and Shah P *Am J Ophthalmol.* 2018; 187:125-129.

This was a retrospective interventional case series of 15 patients who the authors treated with simultaneous strabismus surgery and photorefractive keratectomy (PRK) for accommodative esotropia. The goal of this surgery was to determine if this approach was safe and effective, mainly looking to see if eyes were straight and spectacle free after 6 month follow up. The patients were 11 to 17 years old in this series and the PRK was done with a goal refractive error appropriate for their age, aiming to account for the fact that the eye is likely to still grow. The strabismus surgery was based on the alignment in the patient's physiologic refractive error (based on age), and patients with more than 8 prism diopters were treated with strabismus surgery (11 of 15 patients). The strabismus surgery was performed first, then the PRK. All 15 of the patients were spectacle free at the 6 month visit, though 3 eyes had a one line reduction in vision and 3 eyes had 2 or more lines of reduction in their visual acuity. Thirteen patients had post op alignment of 10 diopters or less, two patients had 10-15 prism diopters of esodeviation, and no patients complained of diplopia. This paper is important in that it is a novel treatment of accommodative esotropia, but there are some glaring limitations, only some of which are discussed in the limitations section. The sample size is small, there were some patients with large overcorrection of their hyperopic PRK (1.5D), the tables are redundant and confusing, the doses for the strabismus surgery don't seem standard, there is a lack of explanation of the of strabismus evaluation in the methods section, it is unclear what kind of binocularity these patients had pre op since that may change diplopia outcomes.

16. GENETICS

Primary congenital glaucoma in Vietnam: analysis and identification of novel CYP1B1 variants

Ha Thu Tran, Huy Thinh Tran, Long Hoang Luong, Tung Son Nguyen, et al (2019) *Ophthalmic Genetics*, 40:3, 286-287, DOI 10.1080/13816810.2019.1616304

Primary congenital glaucoma (PCG) is an autosomal recessive disorder caused by mutations in the CYP1B1 gene. Classic characteristics of the disease include onset before 3 years of age, buphthalmos (enlarged globe) and breaks in Descemet's membrane (Haab's striae). More than 400 variants have been identified. The authors conducted genetic analysis in 85 Vietnamese patients diag-

nosed with congenital glaucoma. The study was performed on a non-consanguineous population. The authors report 7 novel mutations in CYP1B1 in this population who were clinically diagnosed with PCG. The authors state that the discovery of these additional genetic variants will allow for continued improvements in genetic counseling of patients and families.
This study shows that we will continue to see variants of known genetic abnormalities.

A high prevalence of biallelic RPE65 mutations in Costa Rican children with Leber congenital amaurosis and early-onset retinal dystrophy.

Glen, W. Bailey, Peterseim, M. Millicent W., Badilla, Ramses, Znoyko, Iya, et al
Ophthalmic Genetics. Apr2019, Vol. 40 Issue 2, p110-117. 8p.

The authors review a technique where sequencing studies from genetically isolated populations with increased prevalence of a disorder are useful for identifying genetic abnormalities. They wished to demonstrate genetic causes of Leber congenital amaurosis (LCA) and early-onset retinal dystrophy (EORD) and used an affected population in Costa Rica. Twenty-eight affected children (25 LCA, three EORD) and their immediate family members, totaling 52 individuals (30 affected) from 22 families, were sequenced with whole exome sequencing. Four recurrent RPE65 mutations were observed in 97% of individuals and 95% of families. All patients with LCA and two of the three individuals with EORD had biallelic mutations in RPE65. This data is important in light of approved genetic treatment for patients with biallelic RPE65.

Stem Cell Therapies, Gene-based Therapies, Optogenetics, and Retinal Prosthetics: Current State and Implications for the Future

EDWARD H. WOOD, MD,* PETER H. TANG, MD, PHD,† IRINA DE LA HUERTA, MD, PHD,* EDWARD KOROT, MD, et al
RETINA 39:867–878, 2019

The authors discuss four scientific discoveries that are either currently impacting the clinical care of patients with vitreoretinal disease or are in trials to make a significant near-term impact. The technologies described herein include stem cell therapies, gene-based therapies, optogenetic therapies, and retinal prosthetic devices. The authors review the basic science of each technique. Gene based therapies target compensating for a genetic defect to allow for normal function of the retina. The strategies most commonly used are gene therapy and gene editing. In addition to reviewing the basic science, the authors give pros and cons of each therapy as well as regulatory and financial challenges.

This paper is valuable in its review of current and emerging therapies but is a review with opinion-not new research.

Novel gene targets for miRNA146a and miRNA155 in anterior uveitis

Micheal O'Rourke, Michelle Trenkmann, Mary Connolly, Ursula Fearon, et al
Br J Ophthalmol 2019;103:279–285. doi:10.1136/bjophthalmol-2018-312885

Micro RNA's are modulators of the immune system that can have an effect on anterior uveitis. The authors tested peripheral blood samples of patient's with anterior uveitis and controls. PCR was used to identify five miRNA's. miRNAs control immune responses involved in pathologic conditions by affecting the multiple genes in immune cells and modulating toll-like receptor (TLR) responses. The authors state that these specific genes are biological markers that can be modulated for therapeutic use.
This article demonstrates there are continued opportunity to find new modulators that can be developed to treat anterior uveitis.

Iris anomalies and the incidence of ACTA2 mutation

Kenneth J Taubenslag, Hannah L Scanga, Jennifer Huey, Jennifer Lee, et al
Br J Ophthalmol 2019;103:499–503. doi:10.1136/bjophthalmol-2018-312306

Iris flocculi, are central iris pigment epithelial cysts, that are reported in the literature to be associated with thoracic aortic aneurysm and dissection due to smooth muscle alpha-actin 2 (ACTA2) mutations. Children with the ACTA2 mutation may also present with congenital mydriasis. The authors retrospectively reviewed all children who presented over a 4 year period at their institution with iris floccule or congenital mydriasis. None of the 10 children presenting with iris flocculi had ACTA2 mutation. All children with congenital mydriasis had multisystem smooth muscle dysfunction while 2 had R179 ACTA2 mutations. The child who was negative had no cardiac disease and may have had a different unknown genetic mutation. This is a limitation of this study as well as small sample size. The authors suggest that all patients with congenital mydriasis should have genetic testing for ACTA2 mutation and cardiac workup while patients with iris flocculi should have workup guided by history and physical in order to identify those patients who should have genetic and cardiac workup. This paper is important as it challenges the theory that iris flocculi are associated with with thoracic aortic aneurysm and dissection challenging previous literature.

Association of human antigen class I genes with cold medicine-related Stevens-Johnson syndrome with severe ocular complications in a Korean population

Ikhyun Jun, John Hoon Rim, Mee Kum Kim, Kyung-Chul Yoon, et al
Br J Ophthalmol April 2019 Vol 103 No 4

Stevens-Johnson Syndrome (SJS) is an inflammatory disorder with vesiculobullous reaction involving skin and mucous membranes that occurs after exposure to a virus or medication. Toxic Epidermal Necrolysis (TEN) is a more severe form of the pathologic process with a worse prognosis. Approximately 35% of patients with SJS/TEN experience long term ocular consequences that may be vision threatening. Various human leukocyte antigens (HLA) modulate immune response and have been shown to be associated with the development of SJS. Various studies have shown cold medicines (CM) to be one of the most common medication antecedent to the development of SJS in several populations (80% of Japanese, 69% of Thai and 53% of Brazilian). The authors set out to study the association between human leucocyte antigen (HLA) class I genes and CM-related SJS/TEN (CM-SJS/TEN) with severe ocular complications (SOC) in the Korean population. The authors conducted a multicenter case controlled study with 40 Korean patients diagnosed with CM SJS/TEN and 120 age matched and sex matched controls. Of the patients in this study, 5 took acetaminophen (12.5 %), 11 took NSAIDs (27.5 %) and 24 took unspecified cold medication (60 %). Patients with SOC were defined as those with pseudomembrane formation including an epithelial defect on the ocular surface in the acute stage, dry eye, trichiasis, symblepharon and conjunctival invasion into the cornea. HLA genotyping was performed for both groups in a standard fashion. Analysis of data revealed HLA-A*02:06 and HLA-C*03:04 variants may be positively associated with SJS/TEN with SOC while HLA-C*03:04 may have a protective effect against this disease in this Korean population. Limitations of this study include small study size, subjective reporting of medication use before the occurrence of SJS and the possible use of multiple medications. The study is useful in that it may identify a genetic predisposition to SOC as well as a protective HLA in the Korean population although the answer to a treatment to prevent SOC remains elusive.

Progressive cone and cone-rod dystrophies: clinical features, molecular genetics and prospects for therapy

Jasdeep S Gill, Michalis Georgiou, Angelos Kalitzeos, Anthony T Moore, et al
*Br J Ophthalmol 2*019;103:711–720. doi:10.1136/bjophthalmol-2018-313278

The authors conducted a literature search of inherited retinal disease, specifically progressive cone dystrophies (CODs) and cone-rod dystrophies (CORDs). They review retinal physiology in great detail. The authors discuss the genetics, and clinical, psychophysical, electrophysiological and retinal imaging characteristics of CORs and CORDs, focusing particularly on four of the most common disease-associated genes: GUCA1A, PRPH2, ABCA4 and RPGR. Genetic testing, including whole gene sequencing has identified at least 30 genetic mutations associated with CORs/CORDs although many still remain without genetic diagnosis. Although research, including human trials, are ongoing there is no definitive treatment at this time for CORs/CORDs Advances in retinal imaging allow for a greater correlation of structure and function associated with a particular genotype

and phenotype .At this time, certain genetic mutation identification can allow for recommendations that may slow the disease progression. In the future, the authors hope that all of this knowledge will lead to clinical trials for cures.
This article is very in depth in the details of the chemical reactions that are controlled by the genetic mutations causing CORs/CORDs. It may more in depth than most clinical ophthalmologists will find useful.

Gene Augmentation and Readthrough Rescue Channelopathy in an iPSC-RPE Model of Congenital Blindness

Pawan K. Shahi, Dalton Hermans, Divya Sinha, Simran Brar et al
The American Journal of Human Genetics 104, 310–318, February 7, 2019

There are variants of at least 21 genes known to cause Leber congenital amaurosis (LCA16) including *KCNJ13.* This gene encodes a potassium channel Kir7.1 which maintains K+ hemostasis providing for normal photoreceptor function. An abnormality in Kir7.1, or channelopathy leads to cell death.The authors attempted to delineate genetic modifications that could treat vision loss caused by abnormality in *KCNJ13*. Pluripotent stem cells from an individual with homozygous pathogenic variant were determined to be structurally normal but physiologically abnormal because they did not express a working Kir7.1 channel. Two precision-medicine methodologies, readthrough drug treatment and lentiviral gene delivery, were tested for efficacy as therapies. Both modalities restored Kir7.1 channel function in cells derived from an affected person. Authors conclude that their research using a “disease in a dish” approach supports precision-medicine approach for treatment of Leber congenital amaurosis (LCA16).
This is an interesting article describing how the technical work is done to come up with treatments of genetic dieases using precision-medicine techniques. It may be too highly technical for some clinicians.

GRIK5 Genetically Regulated Expression Associated with Eye and Vascular Phenomes: Discovery through Iteration among Biobanks, Electronic Health Records, and Zebrafish

Gokhan Unlu, Eric R. Gamazon, Xinzi Qi, Daniel S. Levic, et al
The American Journal of Human Genetics 104, 503–519, March 7, 2019

Eye disease pathologies are a diverse group of problems. The authors set out to identify a disease-mechanism hypothesis using a “big data” (using EHR data linked to DNA biobanks) approach as opposed to studying a single individual’s DNA. Gene based tests create a SNP based prediction model that can then be tested for in a large population data base for phenotypic associations. The association can then be validated in animal models using gene editing techniques such as CRISPER. The authors begin with discovery of the association between reduced genetically determined expression of GRIK5, which encodes the glutamate ionotropic receptor kainate-type subunit 5, and various eye diseases and

vascular systemic conditions in a large EHR-linked DNA biobank. They test the association in zebrafish by a genetic modification causing a GRIK5 deficiency which is associated with decreased blood vessel architecture and increased vascular permeability. The authors state that their data supports the hypothesis that abnormal vascularization of the developing human eye may be linked to an increase in the risk of a number of different eye diseases and pathologies in adulthood. They also agree that there is probably a polygenic effect that causes predisposition rather than just one genetic abnormality.
This paper is important to pediatric ophthalmologist in exposing a new technique using a “big data” approach to identify genetic risk and an association of vascular defects caused by a genetic defect that could be pertinent in diseases involving vasculature and blood supply.

IMI - Myopia Genetics Report.

Tedja MS, Haarman AEG, Meester-Smoor MA, Kaprio J, et al. *Invest Ophthalmol Vis Sci.* 2019 Feb 28;60(3):M89-M105.

The knowledge on the genetic background of refractive error and myopia has expanded dramatically in the past few years. This white paper aims to provide a concise summary of current genetic findings and defines the direction where development is needed. An extensive literature search was performed and the authors conducted informal discussions with key stakeholders. Specific topics reviewed included common refractive error, any and high myopia, and myopia related to syndromes. To date, almost 200 genetic loci have been identified for refractive error and myopia, and risk variants mostly carry low risk but are highly prevalent in the general population. Several genes for secondary syndromic myopia overlap with those for common myopia. Polygenic risk scores show overrepresentation of high myopia in the higher deciles of risk. Annotated genes have a wide variety of functions, and all retinal layers appear to be sites of expression. The current genetic findings offer a world of new molecules involved in myopiagenesis. As the missing heritability is still large, further genetic advances are needed. The paper recommends expanding large-scale, in-depth genetic studies using complementary big data analytics, consideration of gene-environment effects by thorough measurement of environmental exposures, and focus on subgroups with extreme phenotypes and high familial occurrence. Functional characterization of associated variants is simultaneously needed to bridge the knowledge gap between sequence variance and consequence for eye growth.

A Genome-Wide Association Study for Susceptibility to Visual Experience-Induced Myopia.

Huang Y, Kee CS, Hocking PM, Williams C, et al. *Invest Ophthalmol Vis Sci.* 2019 Feb 1;60(2):559-569.

The rapid rise in prevalence over recent decades and high heritability of myopia suggest a role for gene-environment (G × E) interactions in myopia susceptibility. Few such G × E interactions have been discovered to date. This study aimed to test the hypothesis that genetic analysis of susceptibility to visual experience-induced myopia in an animal model would identify novel G × E interaction loci. Chicks aged 7 days (n = 987) were monocularly deprived of form vision for 4 days. A genome-wide association study (GWAS) was carried out in the 20% of chicks most susceptible and least susceptible to form deprivation (n = 380). There were 304,963 genetic markers tested for association with the degree of induced axial elongation in treated versus control eyes (A-scan ultrasonography). A GWAS candidate region was examined in the following three human cohorts: CREAM consortium (n = 44,192), UK Biobank (n = 95,505), and Avon Longitudinal Study of Parents and Children (ALSPAC; n = 4989). A locus encompassing the genes PIK3CG and PRKAR2B was genome-wide significantly associated with myopia susceptibility in chicks (lead variant rs317386235, P = 9.54e-08). In CREAM and UK Biobank GWAS datasets, PIK3CG and PRKAR2B were enriched for strongly-associated markers (meta-analysis lead variant rs117909394, P = 1.7e-07). In ALSPAC participants, rs117909394 had an age-dependent association with refractive error (-0.22 diopters [D] change over 8 years, P = 5.2e-04) and nearby variant rs17153745 showed evidence of a G × E interaction with time spent reading (effect size -0.23 D, P = 0.022).
This study identified the PIK3CG-PRKAR2B locus as a mediator of susceptibility to visually induced myopia in chicks and suggests a role for this locus in conferring susceptibility to myopia in human cohorts.

Retinal findings in pediatric patients with Usher syndrome Type 1 due to mutations in *MYO7A* gene.

Subirà O, Català-Mora J, Díaz-Cascajosa J, Padrón-Pérez N, et al. *Eye* (Lond). 2019 Jul 18.

This study describes retinal alterations detected by swept-source optical coherence tomography (SS-OCT) in pediatric patients with Usher syndrome type 1 (USH1) and compares these findings to previously published reports.
Thirty-two eyes from 16 patients (11 males and 5 females) with a genetic diagnosis of USH1 because of *MYO7A* mutations underwent SS-OCT. Patients ranged in age from 4 to 17 years (mean, 11,13 ± 4,29). The subfoveal and macular area were analyzed with SS-OCT at 1050 nm using 12 radial scans of 12.0 mm. Structural abnormalities were evaluated and correlated with best-corrected visual acuity (BCVA). The most common qualitative retinal abnormality was external layer damage in macular area. Specific alterations included external limiting membrane loss/disruption (27 eyes; 84.4%), disruption of the Myoid zone (27 eyes; 84.4%); Ellipsoid zone disruption (28 eyes; 87.5%), and loss of the outer segments (29 eyes; 90.6%). The damage of the retinal pigment epithelium was divided according to the loss of the different layers: phagosome zone (30 eyes; 93.8%), melanosome zone (29 eyes; 90.6%) and mitochondria zone (0 eyes;

0%). The presence of cystoid macular edema (CME) was significantly correlated with alterations in photoreceptors. Disruption or absence of the myoid and ellipsoid zones of the photoreceptors were the only variables independently associated with decreased BCVA. The findings of this study suggest that the physiopathologic basis of early-stage Usher syndrome (USH) may be changes in the outer retinal layer, particularly the photoreceptors, which in turn may cause alterations-such as CME in the inner retinal layers. Accordingly, monitoring the condition of photoreceptors during follow-up may be advisable for the early detection of pathologic changes.

Evaluation of TGFBI corneal dystrophy and molecular diagnostic testing.

Chao-Shern C, DeDionisio LA, Jang JH, Chan CC, et al. *Eye* (Lond). 2019 Jun;33(6):874-881.

To date, 70 different TGFBI mutations that cause epithelial-stromal corneal dystrophies have been described. At present one commercially available test examines for the five most common of these mutations: R124H, R124C, R124L, R555W, and R555Q. To expand the capability of identifying the causative mutation in the remaining cases, 57 mutations would need to be added. The aim of this study was to obtain a better understanding of the worldwide distribution and population differences of TGFBI mutations and to assess which mutations could be included or excluded from any potential assay. A total of 184 published papers in Human Gene Mutation Database (HGMD) and PubMed from 34 countries worldwide reporting over 1600 corneal dystrophy cases were reviewed. Global data from 600,000 samples using the commercially available test were analyzed. Case studies by University College of London (UCL), Moorfield's Corneal Dystrophy Study data and 19 samples from patients with clinical abnormality or uncertainty for which the current test detected no mutation were used to predict an achievable detection rate. Data from the literature search showed no difference in the spectrum and frequency of each mutation in different populations or geographical locations. According to this analysis, an increase to the worldwide detection rate in all populations from 75 to 90% could be achieved by the addition of six mutations-H626R, A546D, H572R, G623D, R124S, and M502V-to the currently available test. This may be beneficial for LASIK pre-screening worldwide.

Considerations in multi-gene panel testing in pediatric ophthalmology.

Turriff AE, Cukras CA, Brooks BP, Huryn LA. *J AAPOS*. 2019 Feb 12. pii: S1091-8531(19)30048-5.

Multi-gene panel testing is used increasingly in ophthalmology practice as an efficient and cost-effective method for diagnosing inherited eye conditions. Panel testing is a powerful diagnostic tool, and it has the potential to reveal syndromic

information in patients with seemingly isolated eye findings. This case series highlights the experience with 4 children in 3 families who were referred for evaluation of an isolated retinal degeneration and diagnosed with neuronal ceroid lipofuscinosis based on panel testing. These cases are important reminders that several neurodegenerative conditions can present initially with isolated eye findings in childhood and pretest genetic counseling is critical.

Potential lifetime quality of life benefits of choroideremia gene therapy: projections from a clinically informed decision model.

Halioua-Haubold CL, Jolly JK, Smith JA, Pinedo-Villanueva R, et al. *Eye* (Lond). 2019 Aug;33(8):1215-1223.

The first gene therapy for an inherited retinal dystrophy recently received market approval in the United States; multiple other gene therapies are in the clinical pipeline. Thus far, gene therapy has commanded prices in the range of $500,000 to over $1,000,000 for the one-time doses and have been indicated for highly orphan diseases where there is no other viable treatment option. To be adopted by healthcare systems, gene therapy will need to show clinical benefit in line with its increased costs. Before longitudinal patient studies are available, model-based estimations will be necessary to project the full clinical benefit of gene therapy. This study aims to investigate the lifetime benefit of gene therapy for the retinal dystrophy choroideremia, based on a Markov model of disease progression informed by clinical data of AAV.REP1 and voretigene neparvovec (Luxturna, Spark Therapeutics). Gene therapy patient benefit was estimated by quality-adjusted life years (QALYs) in three hypothetical disease severity patient groups. The severity of disease was defined by the combined effect of remaining retinal area and visual acuity and assigned corresponding health utility values. Early-stage patients treated with gene therapy were estimated to gain, in average, 14.30 QALYs over standard-of-care, mid-stage patients 6.22 QALYs, and late-stage patients 1.48 QALYs over untreated patients during their lifetime owing to treatment. Cost-effectiveness was not assessed as AAV.REP1 is still in clinical trials. In young adults in the earlier stages of choroideremia, successful gene therapy is expected to provide a significant increase in health-related quality of life.

Clinical and molecular characterization of familial exudative vitreoretinopathy associated with microcephaly.

Hull S, Arno G, Ostergaard P, Pontikos N, et al. *Am J Ophthalmol.* 2019 May 8.

Familial exudative vitreoretinopathy (FEVR) is a rare finding in patients with genetic forms of microcephaly. This study documents the detailed phenotype and expands the range of genetic heterogeneity. The design is a retrospective case-

series including twelve patients (ten families) with a diagnosis of FEVR and microcephaly who were ascertained from pediatric genetic eye clinics and underwent full clinical assessment including retinal imaging. Molecular investigations included candidate gene Sanger sequencing, whole-exome sequencing (WES) and whole-genome sequencing (WGS).
All patients had reduced vision and nystagmus. Six were legally blind. Two probands carried bi-allelic *LRP5* variants, both presenting with bilateral retinal folds. A novel homozygous splice variant, and two missense variants were identified. Subsequent bone density measurement identified osteoporosis in one proband. Four families had heterozygous *KIF11* variants. Two probands had a retinal fold in one eye and chorioretinal atrophy in the other; the other two had bilateral retinal folds. Four heterozygous variants were found, including two large deletions not identified on Sanger sequencing or WES. A family of two children with learning difficulties, abnormal peripheral retinal vasculogenesis and rod-cone dystrophy were investigated. They were found to have bi-allelic splicing variants in *TUBGCP6*.Three families remained unsolved following WES and WGS. WGS enabled molecular diagnosis in three families after prior negative Sanger sequencing of the causative gene. This has enabled patient-specific care with targeted investigations and accurate family counseling.

The Natural History of Inherited Retinal Dystrophy Due to Biallelic Mutations in the *RPE65* Gene.

Chung DC, Bertelsen M, Lorenz B, Pennesi ME, et al. *Am J Ophthalmol*. 2019 Mar;199:58-70.

This study delineates the natural history of visual parameters over time in individuals with biallelic *RPE65* mutation-associated inherited retinal dystrophy (IRD); describes the range of causative mutations; determines potential genotype/phenotype relationships; and describes the variety of clinical diagnoses. The design is a global, multicenter, retrospective chart review. Seventy individuals with biallelic *RPE65* mutation-associated IRD were identified and relevant data was extracted from patient charts. This included measurements of visual acuity (VA), Goldmann visual field (GVF), optical coherence tomography, color vision testing, light sensitivity testing, and electroretinograms (retinal imaging and fundus photography were collected and analyzed when available).
VA decreased with age in a nonlinear, positive-acceleration relationship ($P < .001$). GVF decreased with age ($P < .0001$ for both V4e and III4e), with faster GVF decrease for III4e stimulus vs V4e ($P = .0114$, left eye; $P = .0076$, right eye). On average, a 1-year increase in age decreased III4e GVF by ~25 sum total degrees in each eye while V4e GVF decreased by ~37 sum total degrees in each eye, although individual variability was observed. A total of 78 clinical diagnoses and 56 unique *RPE65* mutations were recorded, without discernible *RPE65* mutation genotype/phenotype relationships.
The number of clinical diagnoses and lack of a consistent *RPE65* mutation-to-phenotype correlation underscore the need for genetic testing. The data may

have implications for optimal timing of treatment for IRD attributable to biallelic *RPE65*
mutations.

The Oculome Panel Test: Next-Generation Sequencing to Diagnose a Diverse Range of Genetic Developmental Eye Disorders.

Patel A, Hayward JD, Tailor V, Nyanhete R, et al. *Ophthalmology*. 2019 June;126(6):888-907.

The authors develop a comprehensive next-generation sequencing panel assay that screens genes known to cause developmental eye disorders and inherited eye
disease and to evaluate its diagnostic yield in a pediatric cohort with malformations of the globe, anterior segment anomalies, childhood glaucoma, or a combination thereof. The study population consisted of two hundred seventy-seven children, 0 to 16 years of age, diagnosed with nonsyndromic or syndromic developmental eye defects without a genetic diagnosis.
The custom-designed panel captures and performs parallel high-throughput sequencing analysis of 429 genes associated with eye disorders. Bidirectional Sanger sequencing confirmed suspected pathogenic variants. Panel genes are subdivided into 5 overlapping virtual subpanels for anterior segment developmental anomalies including glaucoma (ASDA; 59 genes), microphthalmia-anophthalmia-coloboma (MAC; 86 genes), congenital cataracts and lens-associated conditions (70 genes), retinal dystrophies (RET; 235 genes), and albinism (15 genes), as well as additional genes implicated in optic atrophy and complex strabismus (10 genes). Panel development and testing included analyzing 277 clinical samples and 3 positive control samples using Illumina sequencing platforms; more than 30× read depth was achieved for 99.5% of the targeted 1.77-Mb region. Bioinformatics analysis performed using a pipeline based on Freebayes and ExomeDepth to identify coding sequence and copy number variants, respectively, resulted in a definitive diagnosis in 68 of 277 samples, with variability in diagnostic yield between phenotypic subgroups: MAC, 8.2% (8 of 98 cases solved); ASDA, 24.8% (28 of 113 cases solved); other or syndromic, 37.5% (3 of 8 cases solved); RET, 42.8% (21 of 49 cases solved); and congenital cataracts and lens-associated conditions, 88.9% (8 of 9 cases solved).
The oculome enabled molecular diagnosis of a significant number of cases in this sample cohort of varied ocular birth defects.

Gene Therapy

High KA, Roncarolo MG. *N Engl J Med***.** Aug 2019;381:455-464

Since 2016, six gene therapy products have been approved by the European Medicines Agency and/or the U.S. Food and Drug Administration. Pediatric ophthalmologists are familiar with gene therapy for RPE65 mutation related Lebers Congenital Amaurosis. Other approved gene therapies are two chimeric antigen

receptor T-cell products for B-cell cancers and gene therapies for the monogenic diseases: β-thalassemia, spinal muscular atrophy, and adenosine deaminase deficient severe combined immunodeficiency.

There are two basic gene therapy strategies: (1) an integrating vector is introduced into a precursor or stem cell so that the gene is passed to every daughter cell, or (2) the gene is delivered in a nonintegrating vector to a long-lived postmitotic or slowly dividing cell, ensuring the expression of that gene for the life of the cell. (1) Transduction of stem cells is generally an ex vivo process and requires an integrating vector, whereas (2) delivery to long-lived postmitotic cells is usually achieved through in vivo gene delivery, and the transferred DNA is stabilized extrachromosomally. An example of (2) in vivo gene therapy is the treatment of loss-of-function in the *RPE65 gene*, which encodes an enzyme that converts all-trans-retinyl ester to 11-cis-retinol, part of the visual cycle that takes place in the retinal pigment epithelium. The gene is delivered within an adeno-associated viral vector by injection into the subretinal space after vitrectomy. The vector transduces retinal pigment epithelial (RPE) cells. The transgene remains episomal; it does not integrate into the DNA of the RPE cell.
The first proofs of gene therapy are now market-approved pharmaceuticals, including the AAV vector product voretigene neparvovec-rzyl for RPE65 mutation related Lebers Congenital Amaurosis. With more than 800 cell- and gene-therapy programs now in clinical development, including for previously untreatable diseases such as Duchenne's muscular dystrophy and Huntington's disease, more therapies will likely follow.

Mutation screening of the USH2A gene in retinitis pigmentosa and USHER patients in a Han Chinese population.

Huang L, Mao Y, Yang J, Li Y et al. *Eye* (Lond). 2018 Oct;32(10):1608-1614.

This study aims to detect USH2A mutations in a Chinese cohort of 75 small RP families and 10 Usher syndrome families using a direct Sanger sequencing analysis of the USH2A gene. Reported are a total of eight mutations in four of the 75 small RP families (5.3%) and two mutations in one of the 10 Usher families (10%); all families were detected to have compound heterozygous mutations. In families with nonsyndromic RP, the authors identified the compound heterozygous mutations p.Pro4818Leuand p.Leu2395Hisfs*19 in family No. 19114, p.Arg4493His and p.His1677Glnfs*15 in family No.19162, c.8559-2A > G and p.Arg1549* in family No.19123 and p.Ser5060Pro and p.Arg34Leufs*41 in family No.19178. In addition, reported is the heterozygous mutations p.Arg3719His and p.Cys934Trp in family No.19124, which was the Usher syndrome family. These mutations were predicted to be harmful by SIFT, PROVEAN, Mutation Taster or PolyPhen-2. The paper revealed six novel mutations in the USH2A gene in a Chinese population, which is beneficial for the clinical use of genetic testing of USH2A in patients with autosomal-recessive or sporadic RP and Usher syndrome.

Mutations in known disease genes account for the majority of autosomal recessive retinal dystrophies.

Patel N, Alkuraya H, Alzahrani SS, Nowailaty SR et al. *Clin Genet.* 2018 Dec;94(6):554-563.

Retinal dystrophies (RDs) are hereditary blinding eye conditions that are highly variable in their clinical presentation. The remarkable genetic heterogeneity that characterizes RD was a major challenge in establishing the molecular diagnosis in these patients until the recent advent of next-generation sequencing. It remains unclear, however, what percentage of autosomal recessive RD remain undiagnosed when all established RD genes are sequenced. This study enrolled 75 families in which RD segregates in an apparently autosomal recessive manner. The authors show that the yield of a multigene panel that contains known RD genes is 67.5%. The higher yield (82.3%) when whole exome sequencing was implemented instead was often due to hits in genes that were not included in the original design of the panel. They also show the value of homozygosity mapping even during the era of exome sequencing in uncovering cryptic mutations. In total, they describe 45 unique likely deleterious variants (of which 18 are novel including one deep intronic and one genomic deletion mutation). This study suggests that the genetic heterogeneity of autosomal recessive RD is approaching saturation and that any new RD genes will probably account for only a minor role in the mutation burden.

Genome-Wide Association Study Identifies a Susceptibility Locus for Comitant Esotropia and Suggests a Parent-of-Origin Effect.

Shaaban S, MacKinnon S, Andrews C, Staffieri SE et al. *Invest Ophthalmol Vis Sci.* 2018 Aug 1;59(10):4054-4064.

This study aims to identify genetic variants conferring susceptibility to esotropia, the most common form of comitant strabismus (with highest incidence in European ancestry populations). Esotropia is believed to be inherited as a complex trait.
White European American discovery cohorts with nonaccommodative (826 cases and 2991 controls) or accommodative (224 cases and 749 controls) esotropia were investigated. White European Australian and United Kingdom cohorts with nonaccommodative (689 cases and 1448 controls) or accommodative (66 cases and 264 controls) esotropia were tested for replication. A genome-wide case-control association study was performed using a mixed linear additive model. Meta-analyses of discovery and replication cohorts were then conducted. A significant association with nonaccommodative esotropia was discovered (odds ratio [OR] = 1.41, P = 2.84 × 10-09) and replicated (OR = 1.23, P = 0.01) at rs2244352 [T] located within intron 1 of the WRB (tryptophan rich basic protein) gene on chromosome 21 (meta-analysis OR = 1.33, P = 9.58 × 10-11). This single nucleotide polymorphism (SNP) is differentially methylated, and there is a

statistically significant skew toward paternal inheritance in the discovery cohort. Meta-analysis of the accommodative discovery and replication cohorts identified an association with rs912759 [T] (OR = 0.59, P = 1.89 × 10-08), an intergenic SNP on chromosome 1p31.1.
This is the first genome-wide association study (GWAS) to identify significant associations in esotropia and suggests a parent-of-origin effect. Additional cohorts will permit replication and extension of these findings. Future studies of rs2244352 and WRB should provide insight into pathophysiological mechanisms underlying comitant strabismus.

RDH12 Mutations Cause a Severe Retinal Degeneration With Relatively Spared Rod Function.

Aleman TS, Uyhazi KE, Serrano LW, Vasireddy V et al. *Invest Ophthalmol Vis Sci.* 2018 Oct 1;59(12):5225-5236.

This article describes the retinal phenotype of pediatric patients with mutations in the retinol dehydrogenase 12 (RDH12) gene. Twenty-one patients from 14 families (ages 2-17 years) with RDH12-associated inherited retinal degeneration (RDH12-IRD) underwent a complete ophthalmic exam and imaging with spectral domain optical coherence tomography (SD-OCT) and near infrared and short-wavelength fundus autofluorescence. Visual field extent was measured with Goldmann kinetic perimetry, visual thresholds with dark-adapted static perimetry or with dark-adapted chromatic full-field stimulus testing (FST) and transient pupillometry. Visual acuity ranged from 20/40 to light perception. There was parafoveal depigmentation or atrophic maculopathies accompanied by midperipheral intraretinal pigment migration. SD-OCT revealed foveal thinning in all patients and detectable but thinned outer nuclear layer (ONL) at greater eccentricities from the fovea. Photoreceptor outer segment (POS) signals were only detectable in small pockets within the central retina. Measurable kinetic visual fields were limited to small (<5-10°) central islands of vision. Electroretinograms were reported as undetectable or severely reduced in amplitude. FST sensitivities to a 467 nm stimulus were rod-mediated and reduced on average by ~2.5 log units. A thinned central ONL colocalized with severely reduced to nondetectable cone-mediated sensitivities. Pupillometry confirmed the psychophysically measured abnormalities. The authors conclude that RDH12-IRD causes an early-onset, retina-wide disease with particularly severe central retinal abnormalities associated with relatively less severe rod photoreceptor dysfunction, a pattern consistent with an early-onset cone-rod dystrophy. Severely abnormal POS but detectable ONL in the pericentral and peripapillary retina suggest these regions may become targets for gene therapy.

Prevalence of *FOXC1* Variants in Individuals With a Suspected Diagnosis of Primary Congenital Glaucoma.

Siggs OM, Souzeau E, Pasutto F, Dubowsky A, et al. *JAMA Ophthalmol*. 2019 Jan 17.

This article investigates the prevalence of *FOXC1* variants in participants with a suspected diagnosis of primary congenital glaucoma. Australian and Italian cohorts were recruited from January 1, 2007, through March 1, 2016. Australian individuals were recruited through the Australian and New Zealand Registry of Advanced glaucoma and Italian individuals through the Genetic and Ophthalmology Unit of l'Azienda Socio-Sanitaria Territoriale Grande Ospedale Metropolitano Niguarda in Milan, Italy. The authors performed exome sequencing, in combination with Sanger sequencing and multiplex ligation-dependent probe amplification, to detect variants of *FOXC1* in individuals with a suspected diagnosis of primary congenital glaucoma established by their treating specialist. Data analysis was completed from June 2015 to November 2017. The main outcome is identification of single-nucleotide and copy number variants in *FOXC1*, along with phenotypic characterization of the individuals who carried them.
A total of 131 individuals with a suspected diagnosis of primary congenital glaucoma were included. The mean (SD) age at recruitment in the Australian cohort was 24.3 (18.1) years; 37 of 84 Australian participants (44.0%) were female, and 71 of 84 (84.5%) were of European ancestry. The mean (SD) age at recruitment was 22.5 (18.4) years in the Italian cohort; 21 of 47 Italian participants (44.7%) were female, and 45 of 47 (95.7%) were of European ancestry. Rare, predicted deleterious *FOXC1* variants were observed in 8 of 131 participants (6.1%), or 8 of 166 participants (4.8%) when including those explained by variants in *CYP1B1*. On reexamination or reinvestigation, all of these individuals had at least 1 detectable ocular and/or systemic feature associated with Axenfeld-Rieger syndrome. The authors conclude that the data highlight the genetic and phenotypic heterogeneity of childhood glaucoma and support the use of gene panels incorporating *FOXC1* as a diagnostic aid, especially because clinical features of Axenfeld-Rieger syndrome can be subtle. Further replication of these results will be needed to support the future use of such panels.

GNAQ Mutations in Diffuse and Solitary Choroidal Hemangiomas.

Francis JH, Milman T, Grossniklaus H, Albert D, et al. *Ophthalmology.* 2018 Dec 8.

GNAQ mutations have been identified in port wine stains (both syndromic and nonsyndromic) and melanocytic ocular neoplasms. This study investigates the presence of GNAQ mutations in diffuse (those associated with Sturge-Weber syndrome [SWS]) and solitary choroidal hemangiomas.
Tissue samples from 11 patients with the following diagnoses were studied: port wine stain (n = 3), diffuse choroidal hemangioma (n = 1), solitary choroidal hemangioma (n = 6), and choroidal nevus (n = 1). Ten specimens were interrogated with Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets, a hybridization capture-based next-generation sequencing assay for targeted deep sequencing of all exons and selected introns of 468 key cancer

genes in formalin-fixed, paraffin-embedded tumors. Digital polymerase chain reaction was used to detect *GNAQ* Q209 mutation in 1 specimen.
Activating somatic *GNAQ* mutations (c.547C > T; p.Arg183Cys) were found in 100% (3 of 3) of the port wine stain and in the diffuse choroidal hemangioma. Somatic *GNAQ* mutations (c.626A > T; p.Gln209Leu) were found in 100% (6 of 6) of the solitary choroidal hemangiomas and (c.626A > C; p.Gln209Pro) in the choroidal nevus. The authors conclude that *GNAQ* mutations occur in both diffuse and solitary hemangiomas, although at distinct codons. An R183 codon is mutant in diffuse choroidal hemangiomas, consistent with other Sturge-Weber vascular malformations. By contrast, solitary choroidal hemangiomas have mutations in the Q209 codon, similar to other intraocular melanocytic neoplasms.

Choroideremia Gene Therapy Phase 2 Clinical Trial: 24-Month Results.

Lam BL, Davis JL, Gregori NZ, et al. *Am J Ophthalmol.* 2019 Jan;197:65-73.

Choroideremia is a rare X-linked recessive disorder in which gradual vision loss results from a mutation or deletion of the *CHM* gene and absence of the *CHM* gene product, Rab escort protein 1 (REP1), essential for intracellular trafficking. Vision loss progresses from nyctalopia in children to visual field constriction in early adulthood and ultimately to near complete blindness by age 40-50 years. There are no current treatments for choroideremia. The authors report the final results of a phase 2 high dose gene therapy clinical trial in choroideremia. Six men (aged 32-72 years) with genetically-confirmed advanced choroideremia were included in the study. Patients received subfoveal injection of AAV2-REP1 (10^{11} genome particles in 0.1 mL) in the worse-sighted eye. Primary measure was best-corrected visual acuity (BCVA) change from baseline in the treated eye compared to the untreated eye. Secondary endpoints included change from baseline in microperimetry, fundus autofluorescence, and spectral-domain optical coherence tomography (OCT). Safety evaluations included adverse events, viral shedding in body fluids, and vector antibody responses. Baseline mean ETDRS BCVA was 65.3 ± 8.8 (SD, range 56-77, 20/32-20/80) letters in the treated eyes and 77.0 ± 4.2 (69-81, 20/25-20/40) letters in the untreated eyes. At 2 years, 1 treated eye improved by 10 letters and another by 5 letters, while 1 untreated eye improved by 4 letters. All other eyes were within 2 letters of baseline. Baseline microperimetry sensitivities in the treated eyes were poor (1.2± 2.1 (0, 5.1) dB) and showed no significant change. No serious adverse event occurred. Two patients developed an atrophic retinal hole in a nonfunctioning macular area where baseline OCT showed preexisting thinning. Intraoperative microscope-integrated OCT allowed proper subretinal injection with avoidance of excessive foveal stretching and macular hole formation. In conclusion, the study provides evidence that treatment of choroideremia with high-dose subfoveal gene therapy has the potential to maintain BCVA, as well as improve BCVA in some cases, indicating that improvement in BCVA could be used as a viable primary outcome for future choroideremia gene

therapy trials for patients with advanced choroideremia. Choroideremia gene therapy safety is enhanced with automated injection guided by real-time MIOCT. Larger-scale studies are required to ascertain the significance of these initially encouraging result

Quantitative Analysis of Hyperautofluorescent Rings to Characterize the Natural History and Progression in *RPGR*-Associated Retinopathy.

Tee JJL, Kalitzeos A, Webster AR, et al. *Retina.* 2018 Dec;38(12):2401-2414.

Retinitis pigmentosa (RP) as a collection of genetically diverse disorders is a common form of retinal degeneration with a prevalence of 1:3,000; with 30% to 40% of cases inherited through an autosomal dominant (AD) route, 45%to 60% through an autosomal recessive (AR) route, and 5% to 15% as an X-linked trait. Three quarters of X-linked RP (XLRP) can be attributed to mutations arising within the retinitis pigmentosa GTPase regulator (*RPGR*) gene. *RPGR*-associated retinopathy is especially severe, as characterized by early disease onset in childhood and fast progression. The authors did quantitative analysis of hyperautofluorescent rings and progression in subjects with retinitis pigmentosa associated with *RPGR* gene mutations. It was a prospective observational study of 46 subjects. Ring area, horizontal and vertical diameter measurements taken from outer and inner ring borders were documented. Intraobserver repeatability, baseline measurements, progression rates, interocular symmetry, and association with age and genotype were investigated. Baseline ring area was 11.8 ± 13.4 mm and 11.4 ± 13.2 mm for right and left eyes, respectively, with very strong interocular correlation ($r = 0.9398$; $P < 0.0001$). Ring area constriction was 1.5 ± 2.0 mm/year and 1.3 ± 1.9 mm/year for right and left eyes, respectively, with very strong interocular correlation ($r = 0.878$, $P < 0.0001$). Baseline ring area and constriction rate correlated negatively with age ($r = -0.767$; $P < 0.0001$ and $r = -0.644$, $P < 0.0001$, respectively). Constriction rate correlated strongly with baseline area ($r = 0.850$, $P < 0.0001$). Age, but not genotype, exerted a significant effect on constriction rates ($P < 0.0001$), with greatest rates of progression seen in younger subjects. An exponential decline overall was found. This study provides disease-specific baseline values and progression rates together with a repeatability assessment of fundus autofluorescence metrics. Our findings can guide future treatment trials and contribute to the clinical care of patients with R*PGR*-associated retinitis pigmentosa.

Clinical and imaging characteristics of posterior column ataxia with retinitis pigmentosa with a specific FLVCR1 mutation.

Lee J, Scanga HL, Dansingani KK, et al. *Ophthalmic Genet*. 2018 Dec;39(6):735-740.

Posterior column ataxia with retinitis pigmentosa (PCARP) is an autosomal recessive, slowly progressive, neurodegenerative syndrome due to malfunction of heme-iron transport, that typically presents in early childhood. PCARP primarily leads to sensory ataxia due to degeneration of proprioceptive neurons in the posterior column and retinitis pigmentosa (RP), a progressive retinal degenerative disease. This disorder is caused by a known pathogenic mutation in the feline leukemia virus subgroup C cellular receptor 1 (*FLVCR1*) gene, which encodes for a plasma membrane receptor protein responsible for heme transport. PCARP has been predominately reported from a neurological viewpoint in the current literature. Ophthalmic descriptions are limited to fundus exam, visual acuity, and visual fields. The authors conducted a retrospective case series study of patients diagnosed with PCARP and genetic testing positive for *FLVCR1* mutation between 1 January 2015 and 1 October 2017 at the Children's Hospital of Pittsburgh. Clinical charts, visual fields, fundus autofluorescence, and spectral-domain optical coherence tomography (SD-OCT) were reviewed. Seven patients from three families were identified to have PCARP and *FLVCR1* mutation. The median age at presentation was 13 years (range, 7-28 years). Common clinical exam findings were astigmatism, cataracts, and vitreous syneresis. Funduscopy on all patients revealed bull's eye maculopathy, retinal vessels attenuation, and bone spicule changes in the peripheral retina. Fundus autofluorescence showed bilateral hyperautofluorescent rings. SD-OCT demonstrated morphological changes, which differed based on age. The youngest sibling family exhibited peripheral loss, but subfoveal preservation of the outer retinal layers. These layers were lost in the oldest sibling family. Visual fields loss paralleled SD-OCT findings. There is limited published ophthalmic data on *FLVCR1*-related PCARP. The authors describe clinical and retinal imaging features in the one of the largest cohorts of affected patients in the literature. Given the availability of genetic testing for this phenotype, testing for *FLVCR1* mutations should be considered in pediatric and adult patients with sensory ataxia and retinitis pigmentosa.

Analysis of multiple genetic loci reveals *MPDZ-NF1B* rs1324183 as a putative genetic marker for keratoconus.

Wang YM, Ma L, Lu SY, et al. *Br J Ophthalmol.* 2018 Dec;102(12):1736-1741.

Keratoconus is a complex disease involving both genetic and environmental factors. Eye rubbing, asthma, allergies and eczema are some of the major risk factors. In addition, the role of inheritance had been demonstrated in twin studies, familial aggregation studies, and linkage analyses. So far, however, no specific gene variant had been found to directly cause keratoconus. The authors investigate the associations between 16 single-nucleotide polymorphisms (SNPs) in 14 genetic loci and keratoconus in an independent Chinese cohort. This cross-sectional, case-control association study included a Chinese cohort of 133 patients with keratoconus and 371 control subjects. In a recent meta-analysis study, the

authors identified association of 16 SNPs in 14 gene loci with keratoconus. In this study, these 16 SNPs were genotyped in all the patients and controls and their association with keratoconus was analyzed (clinical severities and progression profiles). The authors also analyzed the genotype-phenotype correlation between individual SNPs and steep keratometry, flat keratometry (Kf), average keratometry (Avg K) and best-fit sphere diameter (BFS) of the anterior and posterior corneal surface. Among the 16 selected SNPs, rs1324183 in the *MPDZ-NF1B* locus showed a significant association with keratoconus (OR=2.22; 95% CI 1.42 to 3.45, $p=4.30\times10^{-4}$), especially severe keratoconus (OR=5.10, 95% CI 1.63 to 15.93, p=0.005). The rs1324183 A allele was positively associated with anterior Kf (p=0.008), anterior Avg K (p=0.017), posterior Kf (p=0.01) and negatively associated with apex pachymetry (p=0.007) and anterior BFS (p=0.023) in keratoconus. The other 15 SNPs had no significant association with keratoconus or genotype-phenotype correlations. In summary, the authors have confirmed the association of SNP rs1324183 in *MPDZ-NF1B* with keratoconus in the Chinese population, providing new evidence to support *MPDZ-NF1B* as a susceptibility gene of keratoconus. In particular, this SNP conferred a higher, more than 5-fold of risk to severe keratoconus. Moreover, more copies of the risk allele A of rs1324183 were correlated with higher anterior Kf and Avg K and lower posterior Kf and apex pachymetry, suggesting its association with corneal thickness and curvature and keratoconus severity. Therefore, the SNP rs1324183 in *MPDZ-NF1B* may potentially play a role in differentiating different severities of keratoconus, thus facilitating earlier intervention.

CFH Y402H polymorphism in Italian patients with age-related macular degeneration, retinitis pigmentosa, and Stargardt disease.

Sodi A, Passerini I, Bacherini D, et al. *Ophthalmic Genet.* 2018 Dec;39(6):699-705.

The complement system has been implicated in the pathogenesis of age-related macular degeneration (AMD) and the CFHY402H polymorphism has been suggested as a major risk factor for AMD. Recent evidences supported the role of inflammation in the pathogenesis of some retinal dystrophies. The aim of this study was to evaluate the prevalence of CFHY402H polymorphism in a group of Italian patients affected by atrophic AMD, Stargardt disease (STGD), or retinitis pigmentosa (RP). It included 116 patients with atrophic AMD, 77 with RP, 86 with STGD, and 100 healthy controls. All the patients were evaluated by a standard ophthalmologic examination and OCT. ERG was performed on STGD and RP patients. All the subjects underwent a blood drawing for genetic testing and the CFHY402H polymorphism was genotyped with the TaqMan real-time polymerase chain reaction single nucleotide polymorphism assay. The prevalence of the risk genotype

C/C was higher in the AMD group than in controls ($p < 0.001$). The risk allele C was more frequent in the AMD group than in controls ($p < 0.001$). The prevalence of the risk genotype was higher in the RP patients than in controls ($p < 0.001$) and similarly the risk allele C was more frequent in the RP group ($p = 0.008$). The CFHY402H genotype distribution was not different between patients with STGD and the controls, for the biallelic ($p = 0.531$) and for the monoallelic ($p = 0.318$) evaluation. In this series of Italian patients, the CFHY402H genotype is associated with atrophic AMD and RP, but not with STGD. This result may support the hypothesis of a complement system dysregulation in the pathogenesis of AMD and RP. This may have potential impact on future treatments for these diseases.

Efficacy Outcome Measures for Clinical Trials of USH2A Caused by the Common c.2299delG Mutation.

Calzetti G, Levy RA, Cideciyan AV, et al. *Am J Ophthalmol.* 2018 Sep;193:114-129.

Usher syndrome (USH), an autosomal recessive disorder with 3 clinical types and multiple molecular subtypes, leads to retinal degeneration with accompanying hearing and vestibular impairment. There are no therapies at this time for the progressive retinal degeneration of any form of USH. One of the common forms of USH is owing to mutations in the *USH2A* gene, and the most common *USH2A* mutation is the c.2299delG variant in exon 13, which causes a frameshift at codon 767 resulting in a premature termination or a splicing defect. The goal of this paper was to determine the change in vision and retinal structure in patients with the common c.2299delG mutation in the *USH2A* gene in anticipation of clinical trials of therapy. Eighteen patients, homozygotes or compound heterozygotes with the c.2299delG mutation in *USH2A*, were studied with regard to visual acuity, kinetic perimetry, dark- and light-adapted static perimetry, optical coherence tomography (OCT), and autofluorescence (AF) imaging. Serial data were available for at least half of the patients, depending on the parameter analyzed. The kinetics of disease progression in this specific molecular form of USH2A differed between the measured parameters. Visual acuity could remain normal for decades. Kinetic and light-adapted static perimetry across the entire visual field had similar rates of decline that were slower than those of rod-based perimetry. Horizontal OCT scans through the macula showed that inner segment/outer segment line width had a similar rate of constriction as co-localized AF imaging and cone-based light-adapted sensitivity extent. The rate of constriction of rod-based sensitivity extent across this same region was twice as rapid as that of cones. In conclusion, in patients with the c.299delG mutation in *USH2A*, rod photoreceptors are the cells that express disease early and more aggressively than cones. Rod-based vision measurements in central or extracentral-peripheral retinal regions warrant monitoring in order to complete a clinical trial in a timely manner.

Longitudinal Changes of Fixation Location and Stability Within 12 Months in Stargardt Disease: ProgStar Report No. 12.

Schonbach EM, Strauss RW, Kong X, et al. *Am J Ophthalmol.* 2018 Sep;193:54-61.

The most common type of juvenile macular degeneration is Stargardt disease (STGD1; OMIM: 248200). Affected individuals start to develop progressive decline in best-corrected visual acuity (BCVA), often within the first or second decades of life. Currently, no treatment to preserve or restore vision is available for STGD1 patients. New therapeutic approaches, such as pharmacotherapy, gene therapy, stem cell therapy, retinal prostheses, and optogenetics are being developed; some of them are already being investigated in clinical trials. Outcome parameters for STGD1 require special considerations with respect to the centrifugal progression of atrophy in STGD1 (initially affecting the macula before the periphery). The authors sought to investigate the natural history of Stargardt disease (STGD1) using fixation location and fixation stability in a multicenter, international, prospective cohort study. This is the first prospective longitudinal analysis of continuous fixation parameters in a large cohort of genetically confirmed cases of *ABCA4*-related STGD1. Fixation testing was performed using the Nidek MP-1 microperimeter as part of the prospective, multicenter, natural history study on the Progression of Stargardt disease (ProgStar). A total of 238 patients with *ABCA4*-related STGD1 were enrolled at baseline (bilateral enrollment in 86.6%) and underwent repeat testing at months 6 and 12. Outcome measures included the distance of the preferred retinal locus from the fovea (PRL) and the bivariate contour ellipse area (BCEA). After 12 months of follow-up, the change in the eccentricity of the PRL from the anatomic fovea was -0.0014 degrees (95% confidence interval [CI], -0.27 degrees, 0.27 degrees; P = .99). The deterioration in the stability of fixation as expressed by a larger BCEA encompassing 1 standard deviation of all fixation points was 1.21 degrees squared (deg^2) (95% CI, -1.23 deg^2, 3.65 deg^2; P = .33). Eyes with increases and decreases in PRL eccentricity and/or BCEA values were observed. Based on the presented results, a follow-up period of 12 months does not provide statistically significant changes for a large cohort of patients that could be used to compare effects of treatments in clinical trials. Underlying reasons may be the
complex heterogeneity of the changes of fixation parameters that include both deteriorations and improvements. Neuronal adaptation processes may be involved in cases where fixation becomes more central or more stable over time. It is also possible that a follow-up period of 12 months is too short a period to demonstrate significant centrifugal displacement and destabilization of fixation despite the large number of study participants. However, fixation parameters may serve as useful secondary outcome parameters in selected cases and for counseling patients to explain changes to their visual functionality. In addition, the observed changes may explain cases of improvement in BCVA.

Ocular findings in Loeys-Dietz syndrome.

Busch C, Voitl R, Goergen B, et al**.** *Br J Ophthalmol.* 2018 Aug;102(8):1036-1040.

Loeys-Dietz syndrome (LDS), an autosomal-dominant connective tissue disorder, is characterized by systemic manifestations including arterial aneurysm and craniofacial dysmorphologies. Although ocular involvement in LDS has been reported, detailed information on those manifestations is lacking. Based on case reports or small case series, ophthalmological findings include myopia, blue or dusk sclera, cataract, retinal detachment, retinal tortuosity, strabismus and amblyopia, but their frequencies, severities and diagnostic value have not been reported. The authors performed a retrospective chart review of patients with diagnosed LDS and comparison with age-matched control patients. Mean age was 37.8±14.6 years (patients with LDS) and 38.4±13.5 years (controls). Patients with LDS less frequently had iris transillumination, cataract and glaucoma compared with controls. Scleral and retinal vascular abnormalities were not found in any of the LDS eyes. Ectopia lentis was found in one patient with LDS. The eyes of patients with LDS tended to be more myopic (spherical equivalent, -2.47±2.70 dioptres (dpt) vs -1.30±2.96dpt (controls); P=0.08) and longer (24.6±1.7mm vs 24.1±1.5mm (controls); P=0.10). Central corneal thickness was significantly reduced in LDS eyes (521±48µm vs 542±37µm (controls); P=0.02). Corneal curvature (43.06±1.90dpt (LDS) versus 43.00±1.37dpt (controls); P=0.72) and interpupillary distance (65.0±6.0mm (LDS) vs 64.3±4.8mm (controls); P=0.66) did not differ significantly between both groups. Visual acuity was similar between both groups for LDS eyes and for control eyes. Ocular features of LDS include decreased central corneal thickness and mild myopia. Ectopia lentis may be slightly more common than in controls but appears less common than in Marfan syndrome. Hypertelorism, scleral and retinal vascular abnormalities were not features of LDS.

Genome-Wide Association Study Identifies a Susceptibility Locus for Comitant Esotropia and Suggests a Parent-of-Origin Effect.

Shaaban S, MacKinnon S, Andrews C, Staffieri SE et al. *Invest Ophthalmol Vis Sci.* 2018 Aug 1;59(10):4054-4064.

This study aims to identify genetic variants conferring susceptibility to esotropia, the most common form of comitant strabismus (with highest incidence in European ancestry populations). Esotropia is believed to be inherited as a complex trait. White European American discovery cohorts with nonaccommodative (826 cases and 2991 controls) or accommodative (224 cases and 749 controls) esotropia were investigated. White European Australian and United Kingdom cohorts

with nonaccommodative (689 cases and 1448 controls) or accommodative (66 cases and 264 controls) esotropia were tested for replication. A genome-wide case-control association study was performed using a mixed linear additive model. Meta-analyses of discovery and replication cohorts were then conducted. A significant association with nonaccommodative esotropia was discovered (odds ratio [OR] = 1.41, P = 2.84 × 10-09) and replicated (OR = 1.23, P = 0.01) at rs2244352 [T] located within intron 1 of the WRB (tryptophan rich basic protein) gene on chromosome 21 (meta-analysis OR = 1.33, P = 9.58 × 10-11). This single nucleotide polymorphism (SNP) is differentially methylated, and there is a statistically significant skew toward paternal inheritance in the discovery cohort. Meta-analysis of the accommodative discovery and replication cohorts identified an association with rs912759 [T] (OR = 0.59, P = 1.89 × 10-08), an intergenic SNP on chromosome 1p31.1. This is the first genome-wide association study (GWAS) to identify significant associations in esotropia and suggests a parent-of-origin effect. Additional cohorts will permit replication and extension of these findings. Future studies of rs2244352 and WRB should provide insight into pathophysiological mechanisms underlying comitant strabismus.

Genome-Wide Association Study Identifies a Susceptibility Locus for Comitant Esotropia and Suggests a Parent-of-Origin Effect

Shaaban S, MacKinnon S, Andrews C, Staffieri SE, et al. *Invest Ophthalmol Vis Sci*. Aug 2018;59:4054-64.

The purpose of this study was to identify genetic variants conferring susceptibility to esotropia. Esotropia is the most common form of comitant strabismus, has its highest incidence in European ancestry populations, and is believed to be inherited as a complex trait. White European American discovery cohorts with nonaccommodative (826 cases and 2991 controls) or accommodative (224 cases and 749 controls) esotropia were investigated. White European Australian and United Kingdom cohorts with nonaccommodative (689 cases and 1448 controls) or accommodative (66 cases and 264 controls) esotropia were tested for replication. The authors performed a genome-wide case–control association study using a mixed linear additive model. Meta-analyses of discovery and replication cohorts were then conducted. A significant association with nonaccommodative esotropia was discovered (odds ratio [OR] = 1.41, P = 2.84 x 10^{-09}) and replicated (OR = 1.23, P = 0.01) at rs2244352 [T] located within intron 1 of the WRB (tryptophan rich basic protein) gene on chromosome 21 (meta-analysis OR = 1.33, P = 9.58 x 10^{-11}). This single nucleotide polymorphism (SNP) is differentially methylated, and there is a statistically significant skew toward paternal inheritance in the discovery cohort. Methylation status is known to be influenced by the environment; and a meta-analysis has specifically identified reduced methylation of WRB in offspring of mothers who smoked during pregnancy, raising the possibility that genetic and epigenetic influences are working through a common pathway to increase the risk of developmental strabismus. Meta-analysis of the accommodative discovery and replication cohorts identified an association with

rs912759 [T] (OR =0.59, P = 1.89 x 10^{-08}), an intergenic SNP on chromosome 1p31.1. This is the first genome-wide association study (GWAS) to identify significant associations in esotropia and suggests a parent-of-origin effect. Additional cohorts will permit replication and extension of these findings. Future studies of rs2244352 and WRB should provide insight into pathophysiological mechanisms underlying comitant strabismus.

Pediatric Primary Calcific Band Keratopathy With or Without Glaucoma from Biallelic *SLC4A4* Mutations.

Khan AO, Basamh OS. *Ophthalmic Genet.* 2018 Aug;39(4):425-427.

Biallelic mutations in the gene *SLC4A4* (Solute Carrier Family 4 Member 4) cause protean manifestations in children that include proximal retinal tubular acidosis, developmental delay, band keratopathy, and glaucoma. A unique *SLC4A4* mutation causes an ocular-only phenotype. In this retrospective case series, the authors highlight six children (four families) referred to a pediatric ophthalmologist who were found to harbor underlying biallelic *SLC4A4* mutations. All were from consanguineous or endogamous families.

A Novel Deletion Downstream of the *PAX6* Gene Identified in a Chinese Family with Congenital Aniridia.

Liu X, Wu Y, Miao Z, et al. *Ophthalmic Genet.* 2018 Aug;39(4):428-436.

Congenital aniridia, a severe bilateral panocular visual disorder, is an autosomal dominantly inherited eye anomaly. Mutations in the paired box 6 gene (*PAX6*) have been shown to be responsible for congenital aniridia in most patients. The congenital aniridia is characterized by partial-to-complete absence of the iris and is normally accompanied by developmental defects of the cornea, lens, retina, optic nerve, and/or the anterior chamber angle. The purpose of the present study was to report clinical features of a Chinese family with congenital aniridia and to screen novel genetic mutations for congenital aniridia. All members of a three-generation family underwent comprehensive ophthalmic examination, and 8 of its 25 members were diagnosed with congenital aniridia. The proband was analyzed by exome sequencing and whole genome sequencing, and linkage analysis was performed for the family. The mutation was confirmed by direct DNA sequencing. Using Illumina's Human Linkage-12 beadchip microarray (including 6090 SNPs) whole genome scan, the LOD score value showed that the interval on chromosome 11 between rs1389423 to rs910090 exhibited a strong linkage. A novel heterozygous 469 kb deletion mutation within the downstream region of *PAX6* (chr11:31189937–31659379) was identified in all affected family members, but not in unaffected family members or 2000 ethnically matched controls. This study identified a novel deletion mutation in the *PAX6* gene located downstream of its 3' UTR in a Han Chinese family with congenital aniridia by using exome sequencing, whole genome sequencing, and linkage analysis.

Preimplantation Genetic Diagnosis as a Strategy to Prevent having a Child Born with an Heritable Eye Disease.

Yahalom C, Macarov M, Lazer-Derbeko G, et al. *Ophthalmic Genet.* 2018 Aug;39(4):450-456.

Hereditary forms of eye disease account for 14% of all childhood blindness cases in African countries and up to 53% of cases in developed countries such as Europe and the United States. Childhood-onset visual impairment can have major socioeconomic, educational, and psychological consequences. According to a report published by the Vision Cost- Effectiveness Study Group, in 2012 the economic burden associated with vision loss among children age 0–17 years was $5.9 billion in the United States alone. Preimplantation genetic diagnosis (PGD) is a screening technique first introduced in 1990. PGD involves the genetic analysis of one cell, or a few cells, extracted from an in vitro fertilization (IVF)-derived embryo; following analysis, only the embryos that are free of the specific genetic mutation are implanted. Isolated case reports of the successful use of PGD have been reported for several inherited eye diseases, including retinoblastoma, X-linked retinoschisis, and Stargardt disease. The authors report their experience using PGD in order to avoid transmitting a genetic form of eye disease associated with childhood visual impairment and ocular cancer. This is a retrospective case series of women who underwent in vitro fertilization (IVF) and PGD due to a familial history of inherited eye disease and/or ocular cancer, in order to avoid having a child affected with the known familial disease. Each family underwent genetic testing in order to identify the underlying disease-causing mutation. IVF and PGD treatment were performed; unaffected embryos were implanted in their respective mothers. Thirty-five unrelated mothers underwent PGD, and the following hereditary conditions were identified in their families: albinism (10 families); retinitis pigmentosa (7 families); retinoblastoma (4 families); blue cone monochromatism, achromatopsia, and aniridia (2 families each); and Hermansky-Pudlak syndrome, Leber congenital amaurosis, Norrie disease, papillorenal syndrome, primary congenital cataract, congenital glaucoma, Usher syndrome type 1F, and microphthalmia with coloboma (1 family each). Following a total of 88 PGD cycles, 18 healthy (i.e., unaffected) children were born. These findings underscore the importance an ophthalmologist plays in informing patients regarding the options now available for using prenatal and preimplantation genetic diagnosis to avoid having a child with a potentially devastating genetic form of eye disease or ocular cancer. This strategy is highly relevant, particularly given the limited options currently available for treating these conditions.

17. TRAUMA

Ocular Exposures Reported to Poison Control Centers from 2011 to 2015

Heise CW and Agarwal S *Am J Ophthalmol.* 2019 August; 204: 46-50.

This was a pooled cross-sectional study of ocular exposures reported to poison control centers over a 5-year period. The goal was to identify and characterize these injuries by medical outcome, reason and location of exposure, and causative agent. The authors analyzed 477,274 calls regarding ocular exposure and found that most exposures were accidents, occurred at home, and involved a child under the age of 5 years. Adult injuries were more often alkali injuries and were more likely to occur at work. About a third of cases either presented to or were referred to a healthcare facility and the rest were treated onsite with irrigation. Seven hundred nine (0.15%) reported a major outcome, which suggests significant visual disability, and most of those were due to alkali injury. For children under the age of 10, 0.2% (25) had major outcomes – 20 of these were from detergent pods and 5 from bleach – all occurring in the home. Overall pesticides were the most common reason for exposure (4.9%) and the next most common was wrong medication taken or incorrect dosing route. This paper adds to the growing literature about the dangers of detergent pods.

Pediatric ocular injuries: a 3-year review of patients presenting to an emergency department in Canada

Archambault C, Gabias C, Fallaha N, Belanger C, et al. *Can J Ophthalmol.* February 2019;54(1):83-86.

This study's purpose was to examine causes of pediatric ocular trauma in the Quebec pediatric population. The authors performed a retrospective review of all children younger than 18 years who presented to a single emergency department due to ocular trauma between 2007 and 2010. 289 patients were identified with a mean age of 7.22 years. Males accounted for 65%. 54% of the injuries were in children between ages 2 and 9 years. January and October had the higher frequency of injuries, and November the least. Most of the injuries occurred during "free play". 43 injuries were sports-related, with the most common sport hockey (19 patients). 45.7% of injuries occurred at home. Surgery was required in 23 patients, but more extensive surgery was required in 6 patients (corneoscleral lacerations). The authors note the differences in mechanism in this population, discussing how in other countries different sports were involved (eg most injuries in the UK were soccer, in the US basketball and baseball). Organized hockey in schools and leagues require mandatory helmet and face shields, while unorganized hockey does not (all 19 injuries from hockey in the study were from non-organized activities). The authors note that greater emphasis could be placed on ocular protection discussions during emergency room visits, and ocular protection should be mandated for all sports in this population.

Trends in US Emergency Department Visits for Pediatric Acute Ocular Injury.

Eleftheria Matsa, Junxin Shi, Krista K. Wheeler, Tara McCarthy, et al.

JAMA Ophthalmology. August 2018;136(8):895-903.

This was a retrospective cohort study from 2006 to 2014 to characterize pediatric acute ocular injury in the United States from children and teenagers up to age 17 years old who presented to the Emergency Departments (EDs) with acute traumatic ocular injuries. This data was obtained from the Nationwide Emergency Department Sample (NEDS) from a cross-section of U.S. hospitals. Of note, approximately 387,000 patients per year present to the U.S. EDs with ocular injuries and one-third of those injured are children. The authors highlight the importance of pediatric ocular trauma because ocular injuries are among the leading causes of deprivational amblyopia and long-term acquired visual disability. In the data analysis, the authors noted that male children were more often injured (63% with 95% CI) and especially males in the youngest age category of birth to 4 years old (35.3% with 95% CI). Of the ocular injuries noted from trauma, the majority of injuries had a low risk for vision loss (84.2% with 95% CI) with only 1.3% of the injuries being high risk for vision loss. Of data from 376,040 children and teenagers, the authors found a decline in overall ocular injury between 2006 and 2014 with a decline by 26.1% with 95% CI. This decline over the eight-year-period existed across all patient demographics and with the greatest decline in high-risk injuries noted in two areas: motor vehicle crashes (-79.8% with 95% CI) and guns (-68.5% with 95% CI). However, although the authors report a trend of ocular injury decline in children and teenagers over an eight-year-period, ocular injuries remain a source of preventable monocular blindness. Limitations of this study include the data collections from NEDS, which is from EDs billing data, which may not accurately capture diagnosis codes. In particular, certain sports and home activity related ocular injuries E-codes were introduced in 2009 and there could be a bias regarding missing data from 2006 to 2009 regarding sports-related ocular injuries and house-hold related ocular injuries. Further studies should include analysis about which prevention efforts have contributed to the decrease in pediatric ocular injuries. The authors suggest that identification of the further interventions to protect children from vision loss is important.

Prospective analysis of pediatric ocular chemical burns: laundry detergent pods

Breazzano MP, Day HR, Tanaka S, Tran U. *JAAPOS.* Dec 2018;22(6):426-428.

The purpose of this paper is to present data on chemical ocular burns in children seen at a single tertiary care facility resulting from accidental eye exposure to the contents of laundry detergent pods. All emergent pediatric ophthalmology consultations specific for chemical ocular burns at a level I trauma center were included as part of a prospective quality improvement investigation over a 13-month period. Age, causative agent, and examination findings at presentation and final follow-up were recorded and analyzed. A total of 12 children with chemical ocular burns were seen during the study period. All patients were ≤5 years of age. Most chemical ocular burn consultations (n = 8) were specific to

ocular exposure of laundry detergent pod contents; the remainder were associated with conventional cleaning agents or pesticides (n = 4). There was a significant association between laundry detergent pod as causative agent and a patient age of 2-5 years, compared to <2 years and any other agent (P = 0.018 [Fisher exact test]). The average extent of corneal epithelial defect in the patients was 43.45% and all of the defects resolved at last follow up in this group, with no patients suffering visual deficits. In this study, laundry detergent pods were the most frequent cause of chemical ocular burns in children. Additionally, preschoolers may be at a higher risk of sustaining these injuries. Increased public awareness, product safety improvements, and/or regulation may be advisable to decrease the ocular hazards associated with laundry detergent pods.

Pediatric traumatic brain injury and ocular injury

Gise R, Truong T, Pouson D, Soliman Y, et al. *JAAPOS.* Dec 2018;22(6):42-425.e3

Traumatic brain injury (TBI) is a leading cause of pediatric disability and mortality. Together with sight-threatening ocular injuries, TBIs may lead to devastating consequences in developing children and complicate rehabilitation. The authors sought to investigate the relationship between ocular injuries and TBI in pediatric patients admitted with major trauma. The records of pediatric patients admitted with ocular injury and concomitant TBI were reviewed retrospectively using the National Trauma Data Bank (2008-2014). Of 58,765 pediatric patients admitted for trauma and also had ocular injuries, 32,173 were diagnosed with TBI. Mean patient age was 12.3 ± 7 years. Most were male (69.8%) and white (61.2%). The most frequent injuries were contusion of the eye/adnexa (39.1%) and orbital fractures (35.8%); globe ruptures occurred less frequently (5.1%). The youngest age groups had greatest odds of falls in home locations, whereas older groups were more likely to suffer motor vehicle trauma as occupants (MVTO), struck by or against injuries, and firearms injuries in street locations (P < 0.001). Blacks and Hispanics were most likely to suffer assault (P < 0.001) and Whites were more likely to suffer unintentional (P < 0.001) and self-inflicted (P < 0.012) injury. Blacks were at a higher risk of firearms injury, Whites of MVTO, and Hispanics of motor vehicles as pedestrians (P < 0.001). In this study, the abducens nerve was the most commonly injured nerve, followed by oculomotor and trochlear nerves; this differs from other studies in which the trochlear nerve is the most commonly injured. TBI frequently is experienced by trauma patients with concomitant ocular injury and should be considered in children admitted with major trauma. Resultant demographic patterns may help identify patients that have a higher risk of TBI leading to earlier diagnosis and treatment.

NON-ACCIDENTAL HEAD TRAUMA

MISCELLANEOUS

18. RETINA

Rapid Progression of Foveomacular Retinoschisis in Young Myopics

Zhongcui Sun, Jua Gao, Min Wang, Qing Chang, et al. *Retina.* July 2019 ;39(7):1278-1288

Progressive foveomacular retinoschisis is seen in patients with pathologic myopia and hypothesized to be related to continuous vitreomacular traction and posterior staphyloma. This is a study that reports a group of patients with this condition with a younger age of onset and more significant vision loss. This is a prospective case series of 10 young myopic patients with foveamacular retinoschisis. Familial retinoschisis was excluded by doing an extensive family exam and testing for the RS1 gene. Most of these patients were young age of onset, female, not highly myopic, bilateral involvement and rapid progression. Vitrectomy was performed in 13 eyes an effect in restoring anatomical structure. This is a small series of patients with interest onset.

Utility of Ultra-Widefield Retinal Imaging for the Staging and Management of Sickle Cell Retinopathy

Ian C. Han, Alice Y. Zhang, Tin Y. A. Liu, Marguerite O. Linz, et al. *Retina.* May 2019 ;39(5):836-843

Sickle cell retinopathy affects both macular and peripheral retina vasculature by stages. This study, the authors evaluate the role of ultra-widefield (UWF) imaging on detecting and staging of sickle cell retinopathy and compare this to clinical examination. This is a single institution prospective study on 35 patients. These patients had a clinical examination, UWF fundus photo, and UWF fluorescein angiography with Goldberg and Penman classification by 2 retina surgeons and by 2 masked ophthalmologists. Based on clinical examination, most eyes were classified as having no retinopathy. By UWF-fundus photo, about half of the eys were found to be stage 2 or above. On UWF-FA, most eyes overall were stage 2 or above. 7 eyes were recommended by the clinician for treatment based on clinical examination. No treatment decisions were altered by the use of UWF imaging. The use of UWF imaging helped to detect a higher stage of sickle cell retinopathy but did not change the treatment decisions of these patients.

Outcomes of Vitrectomy with Silicone Oil Tamponade for Management of Retinal Detachment in Eyes with Chorioretinal Coloboma

Mumin Hocaoglu, Murat Karacorlu, Mehmet G. Ersoz, Isil Sayman Muslubas *Retina.* April 2019 ;39(4):736-742

Patients with a chorioretinal coloboma are at an increased risk of retina tear and detachment. The authors report the experience of a single surgeon in managing these patients using pars plana vitrectomy and silicone oil tamponade. The study is a retrospective chart review of 10 eyes of 10 patients ages (1-59 years) with retina detachment undergoing PPV with SO (with or without lensectomy), retinectomy when needed, and laser retinopexy. Anatomic success was classified by attached retina for 6 months after silicone oil was removed. Silicone oil tamponade duration was 9.8 (SD 3.5) weeks. The mean final visual acuity was 20/200. The retina was attached in 90% of the eyes. Postoperative complications included cataract, ocular hypertension, band keratopathy, and proliferative vitreoretinopathy. The authors concluded that this procedure is effective for retina detachment management in patients with chorioretinal colobomas even with the removal of silicone oil as early as possible, and reduced the incidence of silicone oil related complications. However, this study had a rather small sample.

Prevalence and Onset of Pediatric Sickle Cell Retinopathy

Jonathan Li, Lloyd Bender, James Shaffer, Daniel Cohen, et al
Ophthalmology. July 2019;126(7): 1000-1006.

This retrospective cohort study sought to determine the prevalence, age of onset, and risk factors associated with sickle cell retinopathy (SCR) to inform development screening guidelines for asymptomatic children. Risk factors evaluated included markers of sickle cell hemoglobinopathy (SCH) severity (number of emergency room or hospital admissions for crises, number of transfusions, hydroxyurea therapy, and transcranial Doppler-confirm cerebral vasculopathy), genotype, gender, and race. Of 398 children (mean age, 9.6+ +/- 4.6 years; age 0–18 years), 208 (52%) showed sickle cell homozygote (SS) genotype, 113 (28%) showed sickle cell hemoglobin C (SC) genotype, and 77 (19%) showed trait genotype. Forty-eight children (12.1%) demonstrated SCR, 44 of 398 children (11.1%; 95% confidence interval, 8.3%-14.5%) demonstrated NPR, and 9 of 398 children (2.3%; 95% confidence interval, 1.2%-4.2%) demonstrated PR. Prevalence was higher for SC than SS genotype for NPR (21% vs 9%) and PR (5% vs 1%); onset for SC genotype was earlier than that for SS genotype for NPR (youngest diagnosis 4.8 vs 6.1 years) and PR (12.2 vs 15.4 years). No other risk factors were associated significantly with SCR. This is the largest study of children with SCH to date in North America even if children with sickle cell trait are excluded from the cohort. The study period is also the most recent permitting and analysis of new potential risk factors that have emerged as standard of care for children with SCH and have not been analyzed previously. The authors identify potential referral bias relating to referral of sicker children which makes their recommendations more conservative in terms of not missing any treatable SCR. They suggest screening to identify PR in children without ophthalmologic symptoms begin by nine years of age for children with SC disease and by 13 years of age for children with SS disease. Clinical markers SCH severity evaluated in the study do not seem to have value in determining screening guidelines

Head and Gaze Behavior in Retinitis Pigmentosa

Samuel A. Titchener, Lauren N. Ayton, Carla J. Abbott, James B. Fallon, et al

Invest Ophthalmol Vis Sci. May 2019;60:2263–2273.

This study evaluates “eye-head coordination” in patients with early-moderate Retinitis Pigmentosa (RP), late stage RP, and control patients. They measured saccades, smooth pursuit, head movements, and oculomotor range. The authors noted that patients with early-moderate RP had increased head movements, though decreased oculomotor range when compared to the control group. The severe RP group was noted to have significantly decreased eye movements when compared to both groups. While each group had small number of subjects, and did not control for the Hawthorne Effect, the study may indicate that the early-moderate RP patients learned to compensate for their visual field loss. Lastly, the different groups were not clinically defined, but based on ability to do tasks though that was broadly interpreted.

Diabetic retinopathy screening in a Canadian community pediatric diabetes clinic

Abdella K, McReelis K, and Strungaru M. *Can J Ophthalmol.* February 2019;54(1):27-32.

Screening for diabetic retinopathy in children is dependent on the age of onset of disease, the type of diabetes, and the length of time the patient has had the disease. The Canadian Diabetes Association recommends initial screening at five years after the diagnosis of type I DM in children 15 years or older, or at age 15 if the patient has had type 1 for greater than 5 years. Screening is recommended at time of diagnosis for all patients with type 2 DM. This study was to analyze the screening rates of patients with DM and to determine primary care physician’s adherence to the guidelines. A retrospective study of 82 patients seen at a pediatric diabetes clinic in Canada was performed. The mean age was 12 years with a mean duration of diabetes of 4 years. 96.3% had type 1 diabetes with mean HbAlc of 9.1. Only 16 patients (19.5%) were screened based on the published Canadian guidelines. 66 patients received more exams than recommended under the guidelines, and one patient had too few exams. All dilated exams were normal without diabetic retinopathy identified. While previous studies shoe low compliance and low rates of referrals for screening, this study actually showed excessive eye examinations in relation to the guidelines. Despite the low numbers in this cohort, no retinopathy was detected and the authors conclude that the patients in this population were overscreened. Additional community education may help prevent unnecessary screenings and compliance with published guidelines.

The use of bevacizumab in pediatric retinal and choroidal disease: A review

Belin PJ, Lee AC, Greaves G, Kosoy J and Lieberman RM *EJO* May 2019, 29(3) 338–347

The use of intravitreal bevacizumab in pediatric retinal and uveitic disease has become more widespread over the past decade. This article serves to outline the rationale underlying the use of intravitreal bevacizumab, and which disease entities it should be appropriately thought of as a primary or solo therapy, as opposed to an adjuvant one. Also presented is the relevant literature regarding each of these retinopathies

Laser Pointer-Induced Maculopathy: more than Meets the Eye

Kamal Mtanes, Michael Mimouni, Shiri Zayit-Soudry.*J Ped Ophth & Strabismus.*2018;55(5):312-318

The purpose of this study is to describe the clinical findings in patients with laser-induced retinal injury.Eight eyes of seven young patients(mediasn age 16 years;range 12 to 36 years) had sustained inadvertent ocular exposure to a 5mW green laser. Evaluation included a full ophthalmic exmaination and spectrl-domain optical coherence tomography(SD-OCT). At presentation, all patients complained of a central/paracentral scotoma. Snellen best corrected visual acuity (BCVA) at presentation ranged from counting fingers to 6/6. In 5 eyes, a round, well-defined deep yellowish-orange discoloration at the level of the retinal pigment epithelium in the foveola, ranging from 150 to 350 µm in diameter, was noted on ophthalmoscopic examination. Additional findings were macular subhyaloid hemorrhage in 2 eyes and a full-thickness macular hole with cystoid macular edema in 1 eye. In all cases, baseline SD-OCT revealed disruption involving the photoreceptor inner segment/outer segment junction/ellipsoid zone band, and extended toward the inner aspect of the retinal pigment epithelium band, ranging from focal interruption to extensive full-thickness macular hole. All patients received oral corticosteroid treatment with prednisone (0.5 to 1 mg/kg). Follow-up ranged between 2 and 12 months. Over time, improvement in visual acuity to 6/8 and 6/6 was noted in all eyes but one, which remained poor at counting fingers from 2 meters. The visual improvement was associated with complete or near-complete restoration of the integrity of macular structure noted on SDOCT. The authors consulded that Commercial handheld laser pointers may inflict notable macular injury and damage vision permanently. Although good visual recovery was often noted, access to commercially available laser devices is potentially hazardous, especially to minors, and public awareness should be raised.

Phenotypic Characteristics of a French Cohort of Patients with X-Linked Retinoschisis

Orès R, Mohand-Said S, Dhaenens CM, Antonio A, et al. *Ophthalmology* 125; 10 Oct 2018: 1587-1596.

X-linked retinoschisis (XLRS) is associated with a mutation in RS1 located in Xp22. Previous clinical studies assessed correlations between best-corrected visual acuity and OCT characteristics, such as full foveal thickness, photoreceptor thickness, or choroidal features with various results. The purpose of this study was to analyze and report clinical characteristics of XLRS in a large cohort of French patients with molecularly confirmed RS1 mutations using spectral-domain OCT and to correlate the morphologic findings with visual acuity, electroretinographic results, and patient age. Data from 52 consecutive male patients with molecularly confirmed XLRS were collected retrospectively. These patients underwent complete clinical evaluation including best-corrected visual acuity, full-field electroretinography, fundus photography, spectral-domain OCT, and fundus autofluorescence. Spectral-domain OCT images were analyzed to determine full thickness of the retina and tomographic structural changes. One hundred four eyes of 52 patients were included. The mean age at inclusion was 24±15 years (range, 3–57 years). The best-corrected visual acuity ranged from no light perception to 0.1 logarithm of the minimum angle of resolution (mean, 0.6±0.38 logarithm of the minimum angle of resolution). Macular schisis was found in 88% of eyes and macular atrophy was found in 11% of eyes, whereas peripheral schisis was present in 30% of eyes. A spoke-wheel pattern of high and low intensity was the most frequently observed fundus autofluorescence abnormality (51/94 eyes [54%]). The b-to-a amplitude ratio on bright-flash dark-adapted electroretinography was reduced significantly in 45 of 64 eyes (70%). Spectral-domain OCT was available for 97 eyes and showed foveoschisis in 76 of 97 eyes (78%), parafoveal schisis in 10 of 97 eyes (10%), and foveal atrophy in 11 of 97 eyes (11%). Mean central macular thickness (CMT) was of 373.6±140 μm. Cystoid changes were localized mainly in the inner nuclear layer (85/97 eyes [88%]). Qualitative defects in photoreceptor structures were found in most eyes (79/97 eyes [81%]), and the most frequent abnormality was an interruption of the photoreceptor cell outer segment tips (79/79 eyes [100%]). Older age correlated well with lower CMT (correlation coefficient [CC], –0.44; $P < 0.001$) and with lower photoreceptor outer segment (PROS) length (CC, –0.42; $P < 0.001$). Lower visual acuity correlated strongly with lower PROS length (CC, –0.53; $P < 0.001$). This study underlined the wide variety of clinical features of XLRS. It highlighted the correlation between visual acuity, patient age, and OCT features, particularly the IZ and the PROS length, emphasizing the relevance of the OCT as potential outcome measure in clinical trials.

Longitudinal Changes in the Optic Nerve Head and Retina Over Time in Very Young Children with Familial Exudative Vitreoretinopathy.

Lee J, El-Dairi MA, Tran-Viet D, et al. *Retina*. 2019 Jan;39(1):98-110.

Familial exudative vitreoretinopathy (FEVR) is a rare hereditary disorder principally affecting retinal angiogenesis. Incomplete peripheral retinal vascularization results in ischemia and subsequent complications such as retinal neovascularization, exudation, vascular dragging, retinal fold, and retinal detachment. Although it may progress at any age with sight-threatening manifestations, visually significant FEVR most often presents in childhood, but many patients with Stage 1 to 3 remain undiagnosed. Subtle abnormalities, which are often hardly noticeable in the posterior pole, include an increased distance from the fovea to the disk, more radiating and straightened retinal vessels extending from the optic nerve head (ONH), and smaller than normal ONH size. This paper sought to explore vitreoretinal pathologies and their longitudinal changes visible on handheld optical coherence tomography (OCT) of young children with FEVR. The authors hypothesize that OCT could help detect abnormal findings at the posterior pole in earlier stages of FEVR in infants and young children. The authors retrospectively analyzed handheld OCT images for vitreoretinal interface and retinal abnormalities and optic nerve head (ONH) elevation. From 26 eyes of 16 children (mean age 32 months) with FEVR, 10 had ONH dragging on photographs, and in these, handheld OCT revealed temporal and anterior retinal displacement, prominent vitreopapillary adhesion or traction, and retinal nerve fiber layer thickening at ONH margins with adjacent retinal elevation. Despite a nearly normal photographic appearance, handheld OCT revealed ONH elevation with vitreopapillary traction (6/16 eyes), ONH edema (1/16 eye), and retinal vascular protrusion (5/16 eyes). Handheld OCT-visualized vitreous abnormalities (18/26 eyes) were more prevalent at higher stages of disease. Handheld OCT-visualized elevation of ONH and the retina worsened over time in nine eyes and improved in 5/6 eyes after vitrectomy. Handheld OCT can detect early ONH, retinal, and vitreous changes in eyes with FEVR. Contraction of strongly adherent vitreous in young patients with FEVR appears to cause characteristic ONH dragging and tractional complications without partial posterior vitreous. Vitreopapillary dragging may be visible only on OCT and may progress in the absence of obvious retinal change on conventional examination.

Optical Coherence Tomography Angiography in Patients with Retinitis Pigmentosa.

Alnawaiseh M, Schubert F, Heiduschka P, et al. *Retina*. 2019 Jan;39(1):210-217.

Retinitis pigmentosa (RP) is a hereditary disease characterized by progressive retinal degeneration and loss of photoreceptors and retinal pigment epithelium with corresponding loss of function. The prevalence of RP is estimated at one case in 3,000 to 5,000 individuals. Patients with RP complain typically of night blindness and symmetric, bilateral, and progressive concentric constriction of the visual field (VF). Severity of RP can be evaluated using different examination and imaging modalities, including visual acuity (VA), VF testing, electroretinography (ERG), OCT, and fundus autofluorescence. Optical coherence tomography angi-

ography (OCTA) is a new, noninvasive imaging technique that enables visualization and quantification of blood flow in normal and pathologic vascularization in different retinal layers and in the ONH. The authors evaluate the correlation between the flow density measured by optical coherence tomography angiography and functional parameters in patients with retinitis pigmentosa. Twenty eyes of 20 patients with retinitis pigmentosa and 21 eyes of 21 healthy subjects were prospectively included in this study. Optical coherence tomography angiography was performed using RTVue XR Avanti with AngioVue (Optovue Inc). The macula was imaged with a 6 × 6-mm scan, whereas for the optic nerve head a 4.5 × 4.5-mm scan was taken. Visual acuity, visual field parameters (mean deviation and visual field index), full-field electroretinography, and multifocal electroretinography were tested for correlation with flow density data. The flow density (whole en face) in the superficial/deep retinal OCT angiograms and in the optical coherence tomography angiography of the optic nerve head was significantly lower in the retinitis pigmentosa group when compared with the control group ($P < 0.001$). The flow density in the superficial retinal OCT angiogram (fovea) correlated significantly with the visual acuity ($rSpearman = -0.77$, $P < 0.001$) and the visual field parameters (visual field index: $rSpearman = 0.56$, $P = 0.01$; mean deviation: $rSpearman = 0.54$, $P = 0.01$). Patients with retinitis pigmentosa show a decreased macular and optic nerve head perfusion compared with healthy subjects. The flow density measured using optical coherence tomography angiography correlated with subjective and objective functional parameters. Optical coherence tomography angiography is a novel technology that can help in the diagnosis and follow-up of patients with RP.

Choroidal Structural Changes and Vascularity Index in Stargardt Disease on Swept Source Optical Coherence Tomography.

Ratra D, Tan R, Jaishankar D, et al. *Retina*. 2018 Dec;38(12):2395-2400.

It has become easier to study the choroidal structure with the advent of newer optical coherence tomography (OCT) techniques such as the enhanced depth imaging and the swept source OCT. Swept source OCT uses longer wavelength and faster scanning speed which allows for deep range imaging. Various studies have compared the subfoveal choroidal thickness (SFCT) in patients with Stargardt disease compared with matched normal controls. However, the studies could not reach a consensus. The authors sought to evaluate structural changes in the choroid of patients with Stargardt disease using swept source OCT scans. A retrospective comparison cohort study was conducted on 39 patients with Stargardt disease, and on 25 age and gender matched-healthy controls. SFCT was computed from the swept source OCT machine, and the scans were binarized into luminal area and stromal areas, which were then used to derive choroidal vascularity index (CVI). Choroidal vascularity index and SFCT were analyzed independently using linear mixed effects model. There was no significant difference in SFCT between the 2 groups (347.20 ± 13.61 μm in Stargardt disease vs. 333.09 ± 18.96 μm in the control group, $P = 0.548$). There was a significant decrease in the CVI among eyes

with Stargardt disease as compared with the normal eyes (62.51 ± 0.25% vs. 65.45 ± 0.29%, P < 0.001). There was a negative association between visual acuity and CVI (correlation coefficient = -0.75, P < 0.001) and a positive association between visual acuity and SFCT (correlation coefficient = 0.21, P = 0.035). In summary, choroidal vascularity index is a novel and noninvasive imaging tool, which is a sensitive surrogate marker to monitor the choroidal angiopathy in patients with Stargardt disease. Choroidal vascularity index appears to be a more robust tool compared with SFCT for choroidal changes in Stargardt disease. A decrease in CVI was associated with a decrease in visual function in eyes with Stargardt disease. Further studies can be conducted to verify the findings in patients with genetically proven Stargardt disease.

Visual Acuity in Patients with Stargardt Disease after Age 40.

Collison Ft, Fishman GA. *Retina* 2018 Dec;38(12):2387-2394.

Stargardt disease is an inherited retinal disease with a prevalence of approximately 1 in 8,000 to 1 in 10,000, making it the most common juvenile onset form of macular dystrophy. Onset of symptoms in Stargardt disease occurs most often between the ages of 8 and 16 years, but onset can also occur in adulthood and even late into adulthood. In the conventional characterization of Stargardt disease, visual acuity loss often stabilizes around Snellen acuity of 20/200 to 20/400, but this observation has been expanded in studies that have demonstrated that some proportion of patients progress to worse than 20/400 vision. Some subsets of patients with Stargardt disease have been found to maintain good acuity later in life as well. The authors sought to better define visual acuity loss in patients with Stargardt disease later in life. The most recent best-corrected visual acuities in the better-seeing eye of 221 patients with Stargardt disease over 40 years of age were recorded. Also included were the age at subjective onset for symptoms and duration of symptoms. Juvenile onset was defined as onset before age 21; adult onset was defined as onset between 21 and 40 years; and late onset was defined as onset at age 41 or later. The median age of the patients with Stargardt disease was 53.1 years. Twenty-four patients (10.9%) had worse than 20/400 best-corrected visual acuity, and none had either light perception or no light perception vision. Whereas 17 of the 52 juvenile onset patients had best-corrected visual acuity worse than 20/400, only 4 of 80 adult-onset patients and 1 of 70 late-onset patients reached this level of acuity loss. Although many patients with Stargardt disease lose visual acuity to the 20/200 to 20/400 range, and some lose visual acuity beyond 20/400, none of these patients reached either light perception or no light perception. The numbers found in this study will be valuable in counseling patients with Stargardt disease and could have value in planning treatment trials.

Deep Scleral Exposure: A Degenerative Outcome of End-Stage Stargardt Disease.

Lee W, Zernant J, Nagasaki T, et al. *Am J Ophthalmol.* 2018 Nov;195:16-25.

Autosomal recessive Stargardt disease (STGD1; MIM #248200) is the most common inherited retinal dystrophy, responsible for mostly adolescent-onset progressive central vision loss. The causal gene, the photoreceptor-specific ATP-binding cassette transporter, *ABCA4*, was identified in 1997; since then >1000 disease-associated variants have been reported. The authors describe a distinct phenotypic outcome of outer retinal degeneration in a cohort of genetically confirmed patients with STGD1 and advanced degeneration. It was a retrospective case series of twelve patients, who were clinically diagnosed with STGD1 and exhibited a unique degenerative phenotype. Two disease-causing mutations were found in all patients by direct sequencing of the *ABCA4* gene. Clinical characterization of patients were defined on fundus photographs, autofluorescence images (488-nm and 532-nm excitation), spectral-domain optical coherence tomography (SD-OCT), and full-field electroretinogram (ffERG) testing. Mean age at initial presentation was 67.8 years and reported age of symptomatic onset was 14.1 years (mean disease duration = 53.8 years). Best-corrected visual acuity ranged from 20/400 to hand motion. All patients exhibited advanced degeneration across the posterior pole resulting in a reflectively pale, blonde fundus owing to unobstructed exposure of the underlying sclera. SD-OCT revealed complete loss of the outer retinal bands (external limiting membrane, ellipsoid zone, interdigitation zone, and retinal pigment epithelium) and choroidal layers. Scotopic and photopic waveforms on ffERG were nonrecordable or severely attenuated in 8 patients who were tested. In summary, an end-stage sub-phenotype of genetically confirmed STGD1 characterized by complete loss of the outer retina and choroid, resulting in widespread scleral exposure, is associated with long disease duration (> 50 years) in older patients. This clinical stage exhibits significant phenotypic overlap with aggressive chorioretinal dystrophies such as choroideremia, but can be distinguished, in addition to genetic screening, by an ocular history of central vision loss and a cone-rod pattern of functional attenuation on ffERG.

Quantitative Comparison of Near-infrared Versus Short-wave Autofluorescence Imaging in Monitoring Progression of Retinitis Pigmentosa.

Jauregui R, Park KS, Duong JK, et al. *Am J Ophthalmol.* 2018 Oct;194:120-125.

Two noninvasive imaging techniques are traditionally used to monitor disease progression in patients with retinitis pigmentosa (RP): spectral-domain optical coherence tomography (SD-OCT) and short-wave autofluorescence (SW-AF). SW-AF is another classical technique that derives its signals (488 nm excitation) from retinal pigment epithelium (RPE) lipofuscin, originally formed in photoreceptors as a product of reactions involving all-trans-retinal. Patients with RP often exhibit

a ring of hyperautofluorescence that encircles an area of the fundus with relatively normal autofluorescence. Studies have shown that the inner border of this hyperautofluorescent ring corresponds spatially to the lateral ends of the ellipsoid zone (EZ) line on SD-OCT. Though less widespread, the use of near-infrared autofluorescence (NIR-AF) has been expanding over the last several years, as multiple studies have applied this modality to RP and other diseases such as recessive Stargardt disease (STGD1) and Best vitelliform macular dystrophy. The authors sought to quantitatively compare NIR-AF and SW-AF as imaging modalities used to monitor RP disease progression, measured as a function of hyperautofluorescent ring constriction over time. NIR-AF and SW-AF images were acquired from 22 participants (44 eyes) at 2 clinic visits separated by an average of 2 years. On the images from each modality, the horizontal and vertical diameters and area of the hyperautofluorescent rings were measured twice, 2 weeks apart. A progression rate for each parameter was obtained. Descriptive and comparative statistics were calculated to analyze these parameters and their respective progression rates. At both visits, the hyperautofluorescent ring exhibited a larger horizontal diameter (both visits: $P < .001$), vertical diameter (visit 1: $P < .001$, visit 2: $P = .040$), and ring area (visit 1: $P = .001$, visit 2: $P = .011$) in SW-AF vs NIR-AF images. In SW-AF, the horizontal diameter, vertical diameter, and ring area decreased yearly by 168 ± 204 μm, 131 ± 159 μm, and 0.7 ± 1.1 mm^2, respectively, while in NIR-AF, they decreased by 151 ± 156 μm, 135 ± 190 μm, and 0.7 ± 1.0 mm^2. No difference was observed in these rates between SW-AF and NIR-AF. Similar results were observed in the left eye. In SW-AF and NIR-AF images, similar rates of RP disease progression are observed. Although there is no current treatment available for RP, the recent emergence of multiple clinical trials for potential treatment methods, including but not limited to gene therapy, has augmented the need for detailed characterization of RP disease progression. Traditionally, EZ line width measurements and SW-AF have commonly been used as noninvasive tools for tracking disease progression in patients with RP. However, NIR-AF, though less commonly used, may confer greater advantages over SW-AF. In contrast to NIR-AF, patient comfort and cooperation are diminished when patients are imaged with SW-AF; while patients observe a dim, reddish light when undergoing NIR-AF scans, they experience a more intense light with SW-AF scans. Owing to diminished patient comfort, the acquisition times for SW-AF scans are longer as compared to NIR-AF. These issues are of particular importance for pediatric and photophobic patients - two populations for which obtaining SW-AF scans is challenging. Furthermore, concerns have been raised about the long-term consequences of exposure to SW-AF during clinical imaging. Thus, given that there appears to be no significant difference between NIR-AF and SW-AF as tools for measuring RP disease progression, NIR-AF may serve as a more efficient substitute for SW-AF in the clinic and in routine practice.

Rates of Bone Spicule Pigment Appearance in Patients With Retinitis Pigmentosa Sine Pigmento.

Takahashi VKL, Takiuti JT, Jauregui R, et al. *Am J Ophthalmol.* 2018 Nov;195:176-180.

Retinitis pigmentosa (RP) is an inherited retinal disorder that causes progressive photoreceptor death and subsequent irreversible vision loss. There are more than 1 million affected individuals worldwide with a prevalence of 1 in 4000. The characteristic funduscopic features of RP are a pale, waxy optic nerve head; attenuated retinal blood vessels; and intraretinal pigment (bone spicule) migration in regions of photoreceptor degeneration. This bone spicule pigment corresponds to melanin-containing cells clustered around branching blood vessels in the inner retina. The origin of these cells remains controversial, but they have been interpreted as pigment-laden macrophages, Muller cells that have phagocytosed melanin granules, or translocated cells from the retinal pigment epithelium (RPE). Previous studies have suggested that after photoreceptor death in RP, reactive RPE cells migrate to the inner retina and form remarkably polarized epithelial layers around retinal blood vessels and against the inner limiting membrane. The authors sought to determine rate of bone spicule pigmentation appearance in patients with retinitis pigmentosa (RP). A total of 240 patients were analyzed for this retrospective, observational case series. An analysis was conducted at the Electrodiagnostic Clinic at Columbia University Medical Center of all patients' medical records with a diagnosis of RP between July 2017 and January 2018. The medical records of these patients were analyzed to determine whether the patients presented with pigment migration on their first and last visit to our clinic. Among those who did not have bone spicule at first visit, we examined the time to appearance of newly formed bone spicule. The survival distribution was then estimated using the Kaplan-Meier estimator, where the event is bone spicule and time starts at first visit. From the 240 patients analyzed, 213 patients presented with intraretinal pigmentation on the first visit to our clinic, and 27 patients presented without intraretinal pigmentation. Of these 27 patients, 10 patients developed pigmentation by their follow-up, with a median time to appearance of bone spicule of 5.4 years from first visit, according to the Kaplan-Meier estimates. The timeline of bone spicule pigment appearance in RP has important implications in the natural history characterization of disease progression and application as a biomarker for interventional trials.

Choroidal neovascular membrane in paediatric patients: clinical characteristics and outcomes

Padhi T, Anderson B, Abbey A, Yonekawa Y, et al. *Br J* Ophthalmol. September 2018;102:1232-1237.

The incidence of choroidal neovascular membrane (CNVM) is relatively small compared to adults, but when present can have a profound impact on children. The authors of this study performed a retrospective review of patients 18 years old or less with CNVM. They analyzed demographics, vision, pathology, and other parameters. 35 subjects (43 eyes) were identified with mean age of 11.2

years. The CNVMs were mostly type 2, classical, and subfoveal. The most common association was with Best vitelliform macular dystrophy (32.5%). The CNVM was active in 36 of 43 eyes. 30 of these underwent treatment, of which anti-VEGF injection was the initial therapy choice in all. Responsive eyes required a mean of 2.11 injection. 50% of recurrent CNVM stabilized with repeat injection, with the remaining requiring photodynamic therapy, laser or surgery. Mean visual acuity gain for peripapillary and subfoveal groups was 0.7752 and 0.4361 log-MAR. However, mean gain in visual acuity on comparison for all CNVM subgroups was not statistically significant. The authos note that overall recurrent rate and number of recurrences were lower in children compared to adult patients, with a lower average number of injections needed for resolution.

Intraretinal Hyperreflective Foci in Best Vitelliform Macular Dystrophy

Maurizio Parodi, Francesco Romano, Riccardo Sacconi, Stefano Casati, et al. *Retina* December 2018; 38:2379-2386.

This prospective cross-sectional study reports on the presence of hyperreflective foci (HF) on spectral domain OCT in patients with Best vitelliform macular dystrophy (BVMD), and describes the relationship between HF and stages of the disease. Consecutive patients with BVMD were enrolled and, along with control subjects, underwent a complete ophthalmologic examination including best corrected visual acuity and SD-OCT. The main outcome measure was identification of HF in BVMD; the secondary outcome was assessment of the HF in each stage and correlation with best corrected visual acuity. 75 eyes of 39 patients were included in the study, Stage 1: 13%, Stage 2: 43%, Stage 3: 15%, Stage 4: 1%, Stage 5: 8%. On SD-OCT, intraretinal HF were present in 83% of all eyes, in 91% of eyes affected by clinical BVMD (Stages 2-5), and in 100% of patients in Stages 4 and 5. In 46% of clinically diseased eyes, HF were localized in the fovea and in correspondence with the BVMD lesions at the level of the outer nuclear layer and outer plexiform layer. HF were present in 16% of control eyes. The mean number of HF in eyes affected by clinical BVMD was 7.67. These were predominately small HF localized in the outer nuclear layer and presented mostly in the extrafoveal area. Analysis of HF distribution revealed that the control group and Stage 1 eyes had the fewest HF; Stage 4 displayed a significant increase in the number of HF compared to Stages 2 and 3; Stage 5 also showed an increased number of HF, a significant difference compared to Stage 3 eyes. The best-corrected visual acuity deteriorated as the number of HF increased in Stages 2 to 5.

The number of patients in this study is relatively small, though all stages of the disease were represented. Data regarding the modification of HF over a longitudinal follow-up period are not presented and could be useful. In addition, the au-

thors acknowledge that the identification of HF can be challenging and it is possible that not all of the HF were picked up in the 19 horizontal linear B-scans that were performed. Finally, the statistical analysis included both eyes of the same patients, 20% of whom revealed a different stage in their own eyes. Nevertheless, these data suggest that HF identification is correlated with the progression of BVMD and could represent a useful biomarker or be a target in BVMD therapy. Further studies with long-term follow-up and histological examinations are necessary to evaluate the origin and nature of these HF.

Traumatic macular retinoschisis in infants and children

Shouldice M, Al-Khattabi F, Thau V, McIntyre S, et al. *JAAPOS*. Dec 2018;22(6):433-437.e2.

The purpose of this paper is to provide detailed description of pediatric traumatic retinoschisis. The medical records of children with either abusive head trauma and traumatic macular retinoschisis seen at a single center from 1993 to 2006 were reviewed retrospectively. Clinical details were extracted from the record and photographic documentation. Evaluation regarding abuse excluded ophthalmology findings to avoid circular reasoning. Of 134 patients with suspected abusive head trauma, 31 (23/1%) had retinoschisis; no other patients were identified who had retinoschisis during this time period. Mean age of these patients was 9 months. Of the 31 patients, 22 (71%) offered a history of injury, and 9 (29%) were found unresponsive without history of injury; 6 were reportedly shaken. All patients had seizures, vomiting, and/or altered responsiveness. All had subdural hemorrhage, with cerebral edema in 17 (55%). In 10 (32%), there were findings of blunt force head injuries; in 4 of these there was no impact history. Retinal hemorrhages were present in all cases. Agreement between sidedness of retinoschisis and subdural hemorrhage was poor. Two thirds of the patients had associated physical injury. One third of the patients had associated vitreous hemorrhage. Eleven patients had retinal folds, 3 of which had a hemorrhagic edge to the schisis; nine of these patients suffered from future neurological conditions or cortical visual impairment, reinforcing the fact that retinal folds are associated with worse visual and neurological outcomes. Nine patients had extracranial manifestations of abuse. Multidisciplinary team adjudications were as follows: of the 31 cases, 18 were suspicious for abuse, 11 were indeterminate, and 2 were possibly accounted for by accidental severe crush injury. Three children died, and 11 suffered neurological sequelae. The authors conclude that traumatic retinoschisis in children is highly associated with subdural hemorrhage, neurologic symptoms, and poor outcomes. Even with a conservative approach to opinion formulation, traumatic retinoschisis was associated with likely abuse.

Unilateral retinitis pigmentosa in children

Mercado CL, Pham BH, Beres, S, Marmor MF, et al. *JAAPOS*. Dec 2018;22(6):457-461.e4.

Retinitis pigmentosa (RP) is a group of rare inherited retinal disorders characterized by diffuse progressive degeneration of the retina that typically presents bilaterally. Unilateral RP has not often been reported in children. The authors present a series of cases that illustrate discrimination between unilateral and asymmetric disease and between dystrophy and acquired degeneration. Four patients (9-15 years of age; 3 females) were referred to the authors' institution for possible unilateral RP based on fundus appearance and unilateral symptoms. All underwent full-field electroretinography (ERG), spectral domain optical coherence tomography (SD-OCT), widefield and color fundus photography, and fundus autofluorescence (FAF) imaging. Genetic testing and a vitamin and essential fatty acids panel were also conducted in 1 patient. Unilateral retinal degeneration was confirmed in 2 patients, whose fellow eyes showed no abnormalities on ERG or imaging. The other 2 patients were found to have highly asymmetric retinal degeneration based on ERG, wide-angle images, and repeated examinations (range, 0.3-9.8 years). Genetic testing and blood testing in 1 unilateral case were negative. Childhood-onset "unilateral RP" remains a difficult and uncertain diagnosis. ERG testing and longitudinal and widefield fundus examination are necessary to exclude asymmetrical disease. Although unilateral degeneration may exist in some children, its inherited or acquired etiology remains poorly understood.

Comparison Study of Fundoscopic Examination Using a Smartphone-Based Digital Ophthalmoscope and the Direct Ophthalmoscope

Amy Ruomei Wu, Samiksha Fouzdar-Jain, Donny W.Suh *J of Ped Ophth & Strabismus*.2018; 55(3): 201-206

The purpose of this study is to assess the ease of use of the D-EYE digital ophthalmoscope (D-EYE Srl, Padova, Italy) in retinal screening against the conventional direct ophthalmoscope. The digital ophthalmoscope used comprised a smartphone equipped with a D-EYE lens that produces digital retinal images. Twenty-five medical students were given 30 minutes of instruction regarding how to use a direct ophthalmoscope and D-EYE digital ophthalmoscope by a pediatric ophthalmologist. Afterwards, they used two methods to view the fundus under dim light on two undilated volunteer participants under supervision of the pediatric ophthalmologist.Each student had to describe their findings and show the video taken from the smartphone to the pediatric ophthalmologist. Students also completed a survey rating their experience using each method. The study showed that Ninety-two percent of the medical students preferred the D-EYE digital ophthalmoscope to the direct ophthalmoscope. Students were also able to identify the optic nerve and macula in a shorter amount of time and review the images to confirm their findings. Overall, the medical students showed a strong preference for the D-EYE digital ophthalmoscope that was statistically significant ($P < .001$). The D-EYE digital ophthalmoscope is a practical device that could be incorporated into medical education and clinical practice. Survey results revealed that most students preferred the D-EYE digital ophthalmoscope due to the recording features and larger image of the fundus.

Diagnosis and treatment option for Achromatopsia: a review of the literature.

Isable Pascual-Camps, Honorio Barranco-Gonzalez, Juan Avino-Martinez, Eduardo Silva et al *J of Ped Ophthalmol & Strabismus*.2018; 55(2): 85-92

Achromatopsia is a complex inherited retinal disease that affects the cone cell function. It is usually an autosomal recessive disease and is characterized by pendular nystagmus, poor visual acuity, lack of color vision, and marked photophobia. CNGA3, CNGB3, GNAT2, PDE6H, and ATF6 gene mutations have been identified as associated with this disease. New diagnostic and therapeutic tools are being investigated. Optical coherence tomography and fundus autofluorescence are important imaging techniques that provide significant information about the progression of the disease. The genetic approach for these patients is a current important issue and gene therapy in an ongoing therapeutic option already being studied in clinical trials.

Progressive Expansion of the Hyperautofluorescent Ring in Cone-Rod Dystrophy Patients.

Lima LH, Zett C, Kniggendorf V, et al. *Ophthalmic Genet.* 2018 Aug;39(4):492-499.

Perifoveal hyperautofluorescent rings have been reported in diseases such as retinitis pigmentosa, cone-rod dystrophy (CRD), X-linked retinoschisis, autoimmune retinopathy, and Leber congenital amaurosis and may represent an abnormal perifoveal accumulation of lipofuscin in the RPE as a result of an increased outer segment degeneration as a precursor to apoptosis. Although the presence of a hyperautofluorescent ring has already been reported in CRD patients, the optical coherence tomography (OCT) ring structure and the fundus autofluorescence (FAF) area change over time had not been described yet. The authors evaluated the expansion of the hyperautofluorescent ring and the retinal structure changes over time in CRD patients, using FAF and spectral-domain optical coherence tomography (SD-OCT). Retrospective case series study. Six eyes of three CRD patients with a parafoveal hyperautofluorescent ring were studied. The diagnosis of CRD was established by the presence of the implicit time shift at 30-Hz flicker and prevalent decrease of photopic over scotopic responses on electroretinography. External and internal ring expansion was evaluated by measurements of its area at baseline and at 24-month follow-up using FAF. SD-OCT analyzed the retinal structure of the ring and the length of devoid ellipsoid zone (EZ) was measured over time. The mean age of study patients was 21 years old and the mean baseline visual acuity was 20/200. The external and internal FAF rings involving the fovea were identified in all study eyes. SD-OCT showed a normal retinal structure outside the ring. At the transitional zone of the

ring, disorganization of both EZ and external limiting membrane (ELM) was observed. Inside the hyperautofluorescent ring, EZ and ELM were not identified. At 24-month follow-up examination, the mean % area increase of external and internal rings were 18.32% and 20.42%, respectively, and was concordant with the EZ band defect length enlargement. Progressive expansion of hyperautofluorescent macular ring with a correspondent EZ band defect enlargement was observed over time in CRD patients.

Investigation of the Effect of Dietary Docosahexaenoic Acid (DHA) Supplementation on Macular Function in Subjects with Autosomal Recessive Stargardt Macular Dystrophy.

MacDonald IM, Sieving PA. *Ophthalmic Genet.* 2018 Aug;39(4):477-486.

Currently, there is no treatment available to individuals affected by Stargardt macular dystrophy. Docosahexaenoic acid (DHA) is the major very long chain polyunsaturated fatty acid of the retina and is found in high concentration in the photoreceptor cells. The major source of DHA for humans is directly through the diet. The North American diet is rich in fats, but it appears that our diets are relatively poor in omega-3 fatty acids, including DHA. Deficiency of DHA has been implicated as a factor in macular degeneration. The purpose of this study was to test the effect of DHA dietary supplementation on macular function in patients with Stargardt disease. It was a single center, double-masked, randomized placebo-controlled trial of 11 subjects (2 males, 9 females) with Stargardt disease in a crossover design. Six participants were randomized to two sequences of three month periods of DHA supplementation (2000 mg/day) followed by three months of placebo. Five participants were randomized to the opposite sequence. All participants were evaluated with a food frequency and NEI-VF25 questionnaires, complete ophthalmic examination, multifocal electroretinography (ERG, primary outcome), 30-Hz flicker ERG, Humphrey 10-2 visual field, D15 color tests and serum lipid analysis. During periods of DHA supplementation, serum rose and then fell with transition to periods of placebo. None of the participants experienced greater than 20% change from baseline values of the mfERG during periods of DHA supplementation or placebo, while the average change in peak amplitude and phase angle of the flicker ERG remained similar at all visits. No significant change was observed for any of the secondary outcome measures. Eight adverse events occurred but these were not considered to be due to the treatment. The author found no perceived effect of DHA supplementation on macular function. This study will help design future studies of the effect of DHA supplementation on retinal function in cohorts with retinal dystrophies.

OCT IMAGING IN DISEASE

Optical Coherence Tomography and Optical Coherence Tomography Angiography Evaluation of Combined Hamartoma of the Retina and Retinal Pigment Epithelium

Alessandro Arrigo, Eleonora Corbelli, Amanuela Aragona, Maria Pia Manitto, Et al. *Retina.* May 2019 ;39(5):1009-1015.

Combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) is a rare, unilateral pigmented elevated mass of the retina. This study evaluated the OCT and OCTA features of 6 children. OCT in all patients showed loss of normal retinal architecture with poor definition of the intraretinal layers. 5/6 patients had an ERM. No patients had PVD, IRH, exudation or RPE abnormalities. All patients had multiple little hyperreflective triangular alterations located at the edges of the hamartoma in the outer retina, which they refer to the “shark-teeth” sign. OCTA revealed rarefaction in the superficial capillary plexus, deep capillary, and the choriocapillary plexa. These patients also had poor FAZ detection. This study confirms previously documented findings on the OCTA and the new “shark-teeth” sign on OCT, but in a small cohort.

Spectral Domain Optical Coherence Tomography Imaging of the Macula and Vitreomacular Interface in Persistent Fetal Vasculature Syndrome with Posterior Involvement

Irina de La Huerta, Oltion Mesi, Breanne Murphy, Kimberly A. Drenser, et al. *Retina.* March 2019 ;39(3):581-586.

Persistent fetal vasculature syndrome (PFVS) can have various features including anterior and poster segment. Even those with mild posterior PFVS without surgical intervention can have variation in vision suggesting the presence of mild structural anomalies. This study’s purpose was to evaluate for these abnormalities in posterior PFVS using SD-OCT in a retrospective case series. Interpretable images from a total of 10 eyes were used. Anomalous features of the vitreomacular interface were detected including posterior hyaloidal organization, vitreomacular and vitreopapillary adhesion, and vitreoretinal traction. 50% of the patients had a hyperreflective posterior hyaloid. Intraretinal microstruction anomalies were detected in 8/10 eyes. This included disruption of the outer retinal structure including the ellipsoid zone, external limiting membrane, and the indterdigitation zone. Diminshed foveal contour was observed in 5/10 eyes. Patients with posterior hyaloidal organization, disruption of outer retinal structure and diminished foveal architecture were associated with worth visual acuity. This identification of structural changes may help in developing a management plan and discussion with patient/family on visual prognosis.

Optical coherence tomography analysis of the inner retinal layers in children

Gama R, Santos J, Costa R, Costa D, et al. *Can J Ophthalmol.* December 2018;53(6):614-620

This cross-sectional study aimed to determine if there was a correlation between the optic nerve head area (ONH), the peripapillary retinal nerve fiber layer (pRNFL) thickness, and the ganglion cell inner plexiform layer (GCIPL) thickness, as measured by OCT in children. 358 eyes were included, and were measured with the Cirrus HD-OCT. The mean age of participants was 6.4 years, and they had a mean spherical equivalent of 0.22D. The average pRNFL thickness was 100.19 microns. The average GCIPL thickness was 85.29 microns. Interestingly, 38 eyes (10.6%) were deemed to have megalopapilla. A positive correlation was found between pRNFL thickness and the ONH are, the GCIPL thickness and ONH area, and the pRNFL and GCIPL thickness. The correlation of ONH area with pRNFL and GCIPL thicknesses supports other observations that larger discs have a higher number of ganglion cells. Therefore, because the OCT scan has a fixed diameter, the scan does not influence these measurements and any future normative database of OCT measurements in children should adjust the pRNFL and GCIPL thicknesses with the ONH area.

Longitudinal Changes in the Optic Nerve Head and Retina Over Time in Very Young Children with Familial Exudative Vitreoretinopathy

Jonghyun Lee, Mays El-Dairi, Du Tran-Viet, Shwetha Mangalesh, et al. *Retina* January 2019; 39:98-110.

This single-center, retrospective case series included patients with a clinical diagnosis of FEVR who were enrolled in an observational hand-held OCT imaging study at Duke. The authors sought to explore the vitreoretinal pathologies and their longitudinal changes visible on HHOCT. Images from 26 eyes of 16 children (mean age 32 months) with FEVR were analyzed for vitreoretinal interface and retinal abnormalities and optic nerve head (ONH) elevation. 10 eyes had ONH dragging on photographs, and in these HHOCT revealed temporal and anterior retinal displacement, prominent vitreopapillary adhesion or traction, and retinal nerve fiber layer thickening at ONH margins with adjacent retinal elevation. Despite a nearly normal photographic appearance, HHOCT revealed ONH elevation with vitreopapillary traction (6/16 eyes), ONH edema (1/16 eye), and retinal vascular protrusion (5/16 eyes). HHOCT-visualized vitreous abnormalities (18/26 eyes) were more prevalent at higher stages of disease. HHOCT-visualized elevation of ONH and retina worsened over time in 9 eyes and improved in 5/6 eyes after vitrectomy.

Study limitations include a lack of standardized follow-up time for examinations, suboptimal image quality for some patients, image graders unmasked to the OCT findings, and limited data regarding visual function precluding the correlation of OCT findings with functional outcome. Nevertheless, this study demonstrates that HHOCT can detect early ONH, retinal, and vitreous changes in eyes with

FEVR. Contraction of strongly adherent vitreous in young patients with FEVR appears to cause ONH dragging and tractional complications without partial posterior vitreous detachment. Vitreopapillary dragging may be visible only on OCT and may progress in the absence of obvious retinal change on conventional examination. The authors argue that the potential impact of vitreous traction on the ONH and the peripheral retinal status in FEVR is important to recognize, and this information could be valuable in preoperative assessment and clinical monitoring in young children.

Choroidal Structural Changes and Vascularity Index in Stargardt Disease on Swept Source Optical Coherence Tomography

Dhanashree Ratra, Roy Tan, Durgasri Jaishankar, Neha Khandelwal, et al. *Retina* December 2018; 38:2395-2400.

This retrospective comparison cohort study evaluated structural changes in the choroid of patients with Stargardt disease using swept source OCT scans. The study included 39 patients with Stargardt disease recruited from two tertiary eye centers in Southern India and 25 age and gender matched healthy controls. Subfoveal choroidal thickness (SFCT) was computed from the swept source OCT machine, and the scans were binarized into luminal area and stromal areas, which were then used to derive choroidal vascularity index (CVI). CVI ad SFCT were analyzed independently using linear mixed effects model. There was no significant difference in SFCT between the 2 groups (347.20 um in Stargardt disease vs 333.09 um in the control group, $p=0.548$). There was a significant decrease in the CVI among eyes with Stargardt disease compared to the normal eyes (62.51 vs 65.45, $p<0.001$). There was a negative association between visual acuity and CVI and a positive association between visual acuity and SFCT.

This study was limited by a small sample size and the absence of genetic testing for the confirmation of Stargardt disease (genetic testing was not performed due to financial constraints). CVI was measured using one horizontal scan across the fovea, and more information may have been obtained if the technique was applied to a volume scan over a broader area of the macula. Despite these limitations, CVI is a novel and noninvasive imaging tool and may be a robust and sensitive marker to monitor the choroidal angiopathy in patients with Stargardt disease. CVI showed a negative trend with decreasing visual acuity in patients with Stargardt disease and may be considered in future studies as an end point for clinical trials.

Diurnal Variations of Foveoschisis by Optical Coherence Tomography in Patients with *RS1* X-Linked Juvenile Retinoschisis.

Abalem MF, Musch DC, Birch DG, et al. *Ophthalmic Genet.* 2018 Aug;39(4):437-442.

Several small and nonrandomized studies have reported the use of oral and topical carbonic anhydrase inhibitors (CAIs) in the management of schisis cavities in patients with th X-linked juvenile retinoschisis (XLRS). Documentation of an efficacious response to these agents is lacking in consistency. While in some patients there was a reduction of macular cavities; in others, there was no improvement and even an increase in the macular thickness. The authors evaluate diurnal variations in macular schisis cavities in patients with XLRS with pathogenic variants in the *RS1* gene using spectral-domain optical coherence tomography (SD-OCT). Three consecutive patients with a clinical diagnosis of XLRS and pathogenic variants in the *RS1* were treated with carbonic anhydrase inhibitors (CAIs). SD-OCT scans of the macula were acquired at 9 a.m., 1 p.m., and 4 p.m. within 24 h. All patients demonstrated increased measures of central foveal thickness in the morning with gradual decrease through the day (9–43%). Major changes were observed between 9 a.m. and 1 p.m. in the central foveal thickness. The authors determined the central foveal thickness varies during daytime hours in patients with XLRS. This finding may explain the inconsistent and heterogeneous responses to treatment with CAIs and necessitate standardization of measurement times in treatment trials for XLRS as well as in the routine ophthalmic evaluation of these patients.

OCT IMAGING – DATA ON NORMAL EYES

COAT'S DISEASE

Spectral Domain Optical Coherence Tomography Findings in Coats Disease

Mrinali P. Gupta, Eliot Dow, Karen W. Jeng-Miller, Shizuo Mukai, et al.
Retina. June 2019 ;39(6):1177-1185

Coats disease is an idiopathic congenital retinal vasculopathy traditionally diagnosed with FA. The authors systemically evaluated the microstructural abnormalties of eyes with Coats disease with SD-OCT in a multicenter, retrospective, observational cohort. Of the 27 eyes without treatment included in this study, findings include intraretinal edema, intraretinal exudates, subretinal fluid, subretinal exudate, ellipsoid zone disruption, external limiting membrane disruption, and subfoveal nodues. All of these correlated with worse visual acuity. No microstructural abnormalities were seen in the fellow eyes. This authors suggest that OCT can help in diagnosis and management of patients with Coat's disease. This may help find signs that can predict visual prognosis, but a larger cohort of patients would be needed to make these firm conclusions.

Swept-source Optical Coherence Tomography Angiography Assessment of Fellow Eyes in Coats Disease

Paulo E. Stanga, Francesco Romano, Katarzyna Chwiejczak, Emmanouil Tsamis, et al. *Retina.* March 2019 ;39(3):608-613.

Coats disease is a progressive retinal vascular disorder with peripheral retinal telangiectasia, exudation and retinal detachment. It is typically thought of as a unilateral disease, but recent studies showed their may be vascular defects in the fellow eye. This study is evaluating the retinal vascular network using OCTA in the fellow eyes of patients with Coats disease. This was a observational, prospective study in which the investigators performed an ocular exam, swept-source OCT and OCTA on 13 patients. The study found that the study eyes had an enlarged FAZ zone at the superficial capillary plexus and the superficial capillary plexus of the fovea. This was more dense in the temporal and superior sectors of the foveal region. There was no statistically significant correlation when associated with the stage of the affected eye. This study shows that there is a bilaterally component to this disease, which could aid in the diagnosis.

Younger Age at Presentation in Children with Coats Disease is Associated with More Advanced Stage and Worse Visual Prognosis: A Retrospective Study

Alejandra Daruich, Alexandre Matet, Francis Munier. *Retina* November 2018; 38:2239-2246.

This retrospective study assessed the age distribution of children with Coats disease and the impact of age at diagnosis on visual prognosis. 98 consecutive Coats disease cases aged 18 years or younger at diagnosis were included. Clinical and imaging parameters were analyzed. Mean age was 5.4 years at the time of diagnosis. Younger age at diagnosis was correlated with more severe disease stage, which was confirmed with survival analysis. Comparative analysis was performed between patients younger and older than 4 years at diagnosis. Leukocoria or strabismus was more frequent at presentation in patients younger than 4 years, and areas of peripheral nonperfusion and peripheral telangiectasia were more extensive. Foveal sparing at diagnosis was less frequent in younger than older patients (2% vs 23%). The incidence of structural complications or enucleation during mean 5.9 year follow-up was higher, and last-recorded visual acuity as lower in younger than older patients. Final logmar visual acuity was negatively correlated with age at diagnosis; multivariate analysis indicated that disease stage, but not age at diagnosis, independently influenced the last-recorded visual acuity.

This study was limited by its retrospective inclusion of patients over a long period of time and the loss of patients during follow-up, as well as by possible referral bias with a tertiary referral center possibly concentrating more severe, younger cases. However, this study showed that onset of Coats disease in children of younger age is associated with more severe manifestations, more advanced

stage, and worse visual outcome. Age, correlated with disease stage, may be considered a prognostic marker in Coats disease.

MISCELLANEOUS

Macular Microvascular Networks in Healthy Pediatric Subjects

Enrico Borrelli, Marcela Lonngi, Siva Balasubramanian, Tudor Tepelus, et al. *Retina.* June 2019 ;39(6):1216-1224.

OCTA is a noninvasive evaluation of the retinal and choroidal vascular circulations without the need for dye like the traditional FA. This study is to report the macular microvascular measurements of OCTA in a healthy pediatric population. Of the 77 eyes evaluated (23 males and 29 females), the mean age was 11 years. The mean FAZ area was 0.261 (SD 0.149). Larger FAZ was associated with older age. The superficial capillary plexus perfusion and vessel densities were 0.33 (SD 0.24) and 0.12 (SD 0.01) and associated with male age. The mean deep capillary plexus perfusion and vessel density were 0.35 (SD 0.13) and 0.13 (SD 0.01). The mean choriocapillaris plexus perfusion density as 0.65 (SD 0.04), which was associated with younger age only. This study is helpful to report normative data in OCTA for normal healthy pediatric patients. A larger cohort by age and gender would be helpful.

19.RETINOBLASTOMA / INTRAOCULAR TUMORS

RETINOBLASTOMA

Retinoblastoma awareness among first contact physicians in Jordan

Yacoub A. Yousef, Tamara Al Nawaiseh, Reem AlJabari, Sana' Muhsen, et al (2019) Retinoblastoma awareness among first contact physicians in Jordan, *OphthalmicGenetics*, 40:3, 191-195, DOI: 10.1080/13816810.2019.1605387

Early diagnosis of retinoblastoma is essential to saving the globe involved, maintaining sight and improving survival. The authors sought to identify the level of knowledge concerning physicians who may have primary contact with a patient who needed to be referred for early diagnosis and treatment of retinoblastoma. A questionnaire was sent to medical students, pediatricians and ophthalmologists. Ophthalmologists fared best on knowledge about retinoblastoma compared to medical students and pediatricians although 42% of the ophthalmologists lacked sufficient knowledge. Although most respondents recognized leukocoria as an abnormal finding, the group lacked sufficient knowledge to refer patients for a timely diagnosis and treatment. The authors identified a gap in medical education

for first contact physicians in Jordan. This is an important study showing that assumptions about medical knowledge in primary care providers should be assessed and supplemented through on going medical education.

Retinoblastoma incidence trends in Canada: A national comprehensive population-based study.

Rami Darwich, PhD; Feras M. Ghazawi, MD, PhD; Elham Rahme, PhD; Nebras Alghazawi, BSc; et al.*J of Ped Ophth & Strabismus*.2019;56(2):124-130.

The purpose of this study is to determine the incidence rates and geographic distribution of retinoblastoma in Canada to aid cancer control programs. Patients with retinoblastoma whose data were available from the Canadian Cancer Registry (CCR) and Le Registre Québécois du Cancer (LRQC) were studied. Using third edition International Classification of Diseases for Oncology (ICD-O) codes, the authors examined the incidence rates and geographic distribution of patients with retinoblastoma between 1992 and 2010. Patient data including sex, age, and laterality of the retinoblastoma were analyzed. Between 1992 and 2010 in Canada, the average annual incidence rate of retinoblastoma was 11.58 cases per 1 million children younger than 5 years (95% CI [confidence interval]: 10.48 to 12.76). The incidence rate was stable over time, with an average age at diagnosis of 2.30 ± 6.85 years and no gender predilection. The laterality of the reported cases was 81.48% for unilateral cases and 18.52% for bilateral cases. Provincially, Nova Scotia had twice the national average and the highest incidence rates of retinoblastoma across the Canadian provinces. This is the first study to define the disease burden of retinoblastoma and to highlight important longitudinal, geographic, and spatial differences in the distribution of retinoblastoma in Canada between 1992 and 2010. The results of this study indicate continuity of clinical trends between Canada, the United States, and other developed countries. This study had limitations. There are no available data on the ethnicity and clinical stage at the time of diagnosis for patients with retinoblastoma. To further emphasize the laterality, reporting only 32% of cases and the lack of genetic testing results in the CCR/LRQC databases is an important limitation. Another important limitation is the inability to present all of the data due to federal confidentiality regulations. Although mandatory case rounding does not affect trends in the presented results, suppressed data (due to low numbers) in some cities, provinces, or territories limits our ability to present the detailed picture of retinoblastoma burden in Canada. Analyzing the epidemiology for retinoblastoma in Canada and around the world will help identify its triggers and improve our understanding of the disease. Furthermore, this study provides a foundation on which to monitor Canadian retinoblastoma incidence patterns and can serve to further stimulate etiologic research.

Routine Fundus Screening of Families of Children with Retinoblastoma, A Prospective Study of 131 Consecutive Families

Swathi Kaliki, Shweta Gupta Rathi, Anamika Patel *Retina.* July 2019 ;39(7):1326-1332

Retinoblastoma is the most common intraocular malignancy in children. It can be hereditary or nonhereditary. Hereditary retinoblastoma is autosomal dominant with high penetrance. This form is seen in 40% of children with RB. Given the inheritance pattern, it is routine to examine parents and siblings for RB patients as standard of care. This study, the authors examined families of patients with RB to estimate the risk of RB in patients without a family history in the absence of genetic testing. A patient with newly diagnosed RB without a family history were included in the study. The parents and siblings were examined. A total of 184 patients were diagnosed with RB during the study period. Out of this cohort, 10 patients had a least one parent with spontaneously regressed RB or an affected sibling. Of the 262 parents, 10 parents were detected to have spontaneously regressed RB. Of the 23 siblings who had an eye exam, active RB was detected in 3 siblings. These siblings were asymptomatic. Although the numbers of this study were limited since the authors excluded patients where a parent or sibling was not available to be examined, this is important in areas where genetic testing is not readily available and may be a marker if detected for a germline RB mutation and subsequent counselling.

Optical Coherence Tomography Angiography Findings of Deep Capillary Plexus Microischemia after Intravenous Chemotherapy for Retinoblastoma

Kareen Sioufi, Emil Say, Sandor Ferenczy, Ann Leahey, et al. *Retina.* Feb 2019 ;39(2):371-378

Optical Coherence tomography angiography (OCTA) has been used to provide qualitative and quantitative evaluation of the retina and choroidal vasculature, especially in the foveal region. This study aims to assess the use of OCTA in retinoblastoma treated with intravenous chemotherapy in the pediatric population. The study evaluated 10 patients in each group: 10 age-matched controls (control group), 10 patients with unilateral RB with a normal fellow eye (RB fellow group), and 10 with bilateral retinoblastoma with extramacular tumors (RB tumor group). Patients with any other form of treatment or retina pathology such as edema were excluded. Assessment was done with OCT and OCTA and central macular thickness, subfoveal choroidal thickness, foveal avascular zone area (superficial and deep plexus), and capillary density (superficial and deep plexus). The study showed there was no difference in any of these factors, except in the deep plexus capillary density was decreased in eyes exposed to chemotherapy. This may demonstrate subclinical retinal microvascular ischemia at the level of the deep capillary plexus without visual compromise after intravenous chemotherapy.

Retinoblastoma in India, Clinical Presentation and Outcome in 1457 Patients (2074 Eyes)

Swathi Kliki, Anamika Patel, Sadiya Iram, George Ramappa, et al. *Retina.* Feb 2019 ;39(2):379-391.

Several studies report the clinical presentation and survival patterns of retinoblastoma from various countries but have smaller cohorts. The authors have presented the presentation, treatment patterns, and outcomes in a large cohort of patients in India with Retinoblastoma. This is a retrospective study conducted at the Operation Eyesight University Institute for Eye Cancer at L V Prasad Eye Institute in Hyderabad, India from Jan 2000-Mar 2015. The most common presenting symptoms were leukocoria, proptosis, and strabismus. The age of presentation is much higher than with developed nations. The presence of extraocular extension was also more common in this cohort. The primary treatment was systemic chemotherapy and enucleation. The survival outcomes were favorable, but this may be due to referral bias.

Vision and visual potential for perifoveal retinoblastoma after optical coherence tomographic-guided sequential laser photocoagulation

Soliman S, VandenHoven C, Mackeen L, Gallie B. *Br J* Ophthalmol. June 2019;103:753-760.

The authors of this study hypothesized that avoiding direct laser treatment to the foveal edge of perifoval RB tumors might enhance visual potential while still adequately achieving tumor control. Therefore they performed this retrospective interventional case series of children with perifoveal RB treated with laser after chemotherapy monitored at each session by optical coherence tomography (OCT). 22 eyes (20 patients) were analyzed, including 14 juxtafoveal (fovea <3000 µm from tumor edge) and 8 foveolar (tumor underlying fovea) tumors. After tumor chemoreduction, laser was performed under general anesthesia with OCT guidance. The OCT was used to identify and document the fovea to design the foveal sparing laser crescent. In later sessions OCT was also used to dermine residual tumor areas and height. Post-laser OCT ensured accuracy of laser treatments. With juxtafoveal tumors, foveal pit preservation was observed in 13/14 eyes (with >= 500 µm of perifoveal retina tumor free). In 1 eye the fovea was flattened by an epiretinal membrane. 12 eyes had normal central fovealor thickness. Foveolar tumors had worse anatomical outcomes: 5/8 had tumor recurrences and none had restored foveal pit or perifoveal retina. Acceptable (>= 1.0 logMAR or good (>= 0.5 logMAR) visual acuity was found in 12/14 and 8/14 eyes with juxtafoveal tumors, and 5/6 and 0/6 eyes with foveolar tumors respectively. This study did not include data on children who underwent amblyopia therapy. The authors summarize that visual potential and anatomical results were better in juxtafoveal RB compared to foveolar RB in children treated with foveal-sparing laser photocoagulation guided by OCT.

The predictive value of magnetic resonance imaging of retinoblastoma for the likelihood of high-risk pathologic features

Hiasat J, Saleh A, Al-Hussaini M, Al Nawaiseh I, et al. *EJO,* March 2019, 29(2) 262–268

The goal was to evaluate the predictive value of magnetic resonance imaging in retinoblastoma for the likelihood of high risk pathologic features. A retrospective study of 64 eyes enucleated from 60 retinoblastoma patients. Contrast-enhanced magnetic resonance imaging was performed before enucleation. Main outcome measures included demographics, laterality, accuracy, sensitivity, and specificity of magnetic resonance imaging in detecting high-risk pathologic features. Optic nerve invasion and choroidal invasion were seen microscopically in 34 (53%) and 28 (44%) eyes, respectively, while they were detected in magnetic resonance imaging in 22 (34%) and 15 (23%) eyes, respectively. The accuracy of magnetic resonance imaging in detecting prelaminar invasion was 77% (sensitivity 89%, specificity 98%), 56% for laminar invasion (sensitivity 27%, specificity 94%), 84% for postlaminar invasion (sensitivity 42%, specificity 98%), and 100% for optic cut edge invasion (sensitivity100%, specificity 100%). The accuracy of magnetic resonance imaging in detecting focal choroidal invasion was 48% (sensitivity 33%, specificity 97%), and 84% for massive choroidal invasion (sensitivity 53%, specificity 98%), and the accuracy in detecting extrascleral extension was 96% (sensitivity 67%, specificity 98%). Magnetic resonance imaging should not be the only method to stratify patients at high risk from those who are not, even though it can predict with high accuracy extensive postlaminar optic nerve invasion, massive choroidal invasion, and extrascleral tumor extension.

Ophthalmic Vascular Events after Primary Unilateral Intra-arterial Chemotherapy for Retinoblastoma in Early and Recent Eras

Dalvin LA, Ancona-Lezama DA, Lucio-Alvarez JA, Masoomian B, et al. *Ophthalmology* 125;11 Nov 2018: 1803-1811.

The purpose of this study was to assess risk factors for ophthalmic vascular events after intra-arterial chemotherapy (IAC) for retinoblastoma. Although IAC is efficacious in achieving tumor control, it can lead to thromboembolic or hemorrhagic events due to the technique itself or secondary to chemotherapy-induced toxicity. Ophthalmic vascular events include choroidal ischemia, branch or central retinal artery occlusion, ophthalmic artery spasm or occlusion, vitreous hemorrhage and others. Although early series reported ophthalmic vascular event rates as high as 35%, more recent series have described a lower rate of 1%. In this study, the authors conduct a retrospective, consecutive, comparative analysis to describe ophthalmic vascular events at a single center during two time periods: early IAC era (2009–2011) compared with the recent era (2012–2017). The study population included patients who received unilateral IAC as primary treatment for retinoblastoma from January 1, 2009, to November 30, 2017, at Wills Eye Hospital. All patients underwent complete eye exam under anesthesia prior to administration of IAC and then monthly exams were performed, which included

anterior and posterior indirect ophthalmoscopy, B-scan ultrasonography, RetCam fundus photography, Fluorescein angiography, and OCTS as needed. After tumor control was achieved, the interval between examinations under anesthesia was extended. Records were reviewed for patient demographics, tumor features, IAC parameters, and treatment-related vascular events. Change in event rates over time were assessed using Poisson regression analysis, with Spearman's rho used to test correlation. There were 243 chemotherapy infusions in 76 eyes of 76 patients, divided into early (22 eyes, 57 infusions) and recent (54 eyes, 186 infusions) eras. Intra-arterial chemotherapy consisted of melphalan (243 infusions), topotecan (124 infusions), and carboplatin (9 infusions). A comparison (early vs. recent era) revealed fewer mean number of infusions (2.6 vs. 3.4, $P = 0.02$) with similar mean patient age and presenting tumor features. Event rates decreased over time ($P < 0.01$), with fewer ophthalmic vascular events (early era vs. recent era) in the recent era (59% vs. 9% per eye, 23% vs. 3% per infusion, $P < 0.01$), including peripheral retinal nonperfusion (5% vs. 2% per eye, $P = 0.50$), vitreous hemorrhage (9% vs. 2%, $P = 0.20$), subretinal hemorrhage (0% vs. 2%, $P = 0.99$), branch retinal vein occlusion (5% vs. 0%, $P = 0.29$), choroidal ischemia (14% vs. 4%, $P = 0.14$), and ophthalmic artery spasm/occlusion (27% vs. 0%, $P < 0.01$). Event rates did not correlate with patient age ($P = 0.75$), tumor diameter ($P = 0.32$), tumor thickness ($P = 0.59$), or cumulative dosage of melphalan ($P = 0.13$) or topotecan ($P = 0.59$). There were no IAC-induced vascular events in 72 infusions of 21 consecutively treated eyes in 2016 to 2017. This study shows that the ophthalmic vascular events after IAC have decreased from the early era (2009–2011) through the current era (2012–2017) at this center. Experience performing this highly specialized procedure could be an important factor predicting IAC-related vascular events. There were technical changes made between the two time periods. This includes pulsatile delivery of the infusion, eliminating the guide wire and advancing the catheter only to the ostium of the ophthalmic artery. This alone does not explain the observed change. The later time period also eliminated the use of carboplatin but it does not show more toxicity compared to melphalan in non-human primate studies. The authors surmise that the technique and experience is what accounts for the reduced rate of the ophthalmic vascular events.

High-Risk Intraocular Retinoblastoma: Comparison Between Asian Indians and Americans From Two Major Referral Centers

Swathi Kaliki, Carol Shields, Ralph Eagle Sadiya Iram, et al. *Retina* October 2018; 38:2023-2029.

This retrospective study sought to identify the differences in the clinical and histopathologic features in eyes with advanced intraocular retinoblastoma in a developing country (India) versus a developed country (USA). 524 patients with retinoblastoma who underwent primary enucleation were included in the study, 331 from India and 193 from the USA. Asian Indians were older at presentation (35 months vs 29 months) and had thicker tumors (13.8 mm vs 12.4 mm) compared

to Americans. There was a 2-fold greater risk of high-risk intraocular retinoblastoma in Asian Indians. There were significant differences in the histopathologic features of tumors in Asian Indians versus Americans: massive (>/= 3 mm) choroidal infiltration (17% vs 6%) and optic nerve infiltration (48% vs 15%). Asian Indians had a 5-fold greater risk of having optic nerve invasion and a 3-fold greater risk of massive choroidal invasion compared to Americans. With appropriate use of adjuvant systemic chemotherapy, the difference in rates of systemic metastasis (5% vs 2%) and related death (5% vs 0%) were not statistically significant.

This study demonstrates that high-risk intraocular retinoblastoma is more common in India than in the USA, but with appropriate adjuvant systemic chemotherapy the metastatic rate and death due to metastasis were not statistically different. However, this study includes only advanced intraocular retinoblastoma and/or cases with microscopic extraocular extension and not advanced cases with overt orbital extension. Therefore the results cannot be extrapolated to the overall rate of systemic metastasis and survival of children with retinoblastoma in India versus the USA.

Trefoil Factor Family 1 Expression Correlates with Clinical Outcome in Patients with Retinoblastoma

Maike Busch, Klaus Metz, Manfred Beier, Eva Biewald, et al. *Retina* December 2018; 38:2422-2428.

This retrospective study sought to correlate trefoil factor 1 (TFF1) expression in retinoblastoma tumors with different clinical parameters to evaluate potential involvement of TFF1 in tumor development and progression. A representative cohort of 59 enucleated eyes from patients with retinoblastoma was analyzed for TFF1 expression profile by immunostaining and real-time PCR. TFF1 expression was correlated with demographics, laterality, tumor-node-metastasis (TNM) stage, International Classification of Retinoblastoma, tumor differentiation level, and treatment. Increased TFF1 expression was found to significantly correlate with unilateral tumors diagnosed in older children and with poorly differentiated tumors and higher TNM stages. The exact pathophysiologic role of TFF1 in RB tumor progression is not well understood, and its role as a tumor-suppressor versus an oncogene requires further investigation. There may be potential value of TFF1 as a pharmacologic treatment option for RB tumors. At minimum, this study indicates that TFF1 expression levels are potentially useful markers in the classification of tumor staging and prognosis of patients with RB.

Strabismus in retinoblastoma survivors with long-term follow-up

Fabian ID, Stacey AW, Naeem Z, Onadin Z, et al. *J AAPOS*. Aug 2018;22(4):276.e1–276.e7

The goal of this paper was to report the long-term strabismus rate in salvaged retinoblastoma (Rb) patients and investigate possible risk factors leading to strabismus in these patients. The medical records of patients with Rb presenting at a single institution over a 9-year period were reviewed retrospectively with regard to ocular alignment outcomes after long-term follow-up. A total of 64 eyes of 42 patients (22 bilateral cases which consisted of 52% of the patients) were included, presenting with International Intraocular Retinoblastoma Classification (IIRC) in the worse eye as follows: group A (n = 1), B (n = 16), C (n = 12), D (n = 11), no Rb (n = 2). Fifteen patients (36%) were initially referred because they had no family history of Rb. Mean age at presentation was 8.2 months (range, 0.3-58.3 months). Overall treatments in this group of patients included intravenous chemotherapy (62 eyes), intraophthalmic artery chemotherapy (10 eyes), brachytherapy (11 eyes), transpupillary thermotherapy (22 eyes), cryotherapy (47 eyes), and external beam radiotherapy (4 eyes). At final follow-up (mean, 93.7 months), 69% of patients had strabismus, with exotropia being the most common type (n = 18), followed by esotropia (n = 8), and alternate exotropia/esotropia (n = 3). On univariate analysis, the worse eye group IIRC and cTNMH, sporadic cases, strabismus, and foveal tumor at presentation were found to be significantly associated with the presence of strabismus at the final follow-up ($P \leq 0.043$). On multivariate analysis, only foveal involvement was found to be significant ($P < 0.001$). The authors find that strabismus, exotropia in particular, is a common adverse sequela following successful conservative treatment for Rb, with 69% of the present cohort having some type of deviation after long-term follow-up, for which foveal tumor at presentation was found to be a significant risk factor. This information can be helpful in guiding parental expectations in this group of patients.

Retinoblastoma in the United States:A 40-Year Incidence and Survival Analysis.

Arthur Gustavo Fernandes, Benjamin D.Pollock, Felicia A. Rabito
J of Ped Ophth & Strabismus. 2018; 55(3):182-188

The purpose of this study is to determine the incidence of retinoblastoma in the United States from 1973 to 2012 (40 years) and characterize the 5-year overall survival rate of the included patients. The patient data came form the Surveillance, Epidemiology, and End Results (SEER) Program(national Cancer Institute, Rockville, MD). A total of 879 cases of retinoblastoma were derived from the SEER database**.** Incidence rates were calculated using U.S. Census Bureau data as the standard population, and trends over time were determined using the chi-square test. Hazard ratios with a 95% confidence interval (CI) were estimated for variables associated with mortality using Cox regression models. Survival rates were calculated using the Kaplan–Meier method and compared
The study showed that the annual incidence rates of retinoblastoma for a period of 40 years were 12.14 (95% CI: 11.32 to 12.96) cases per 1 million children 4 years or younger and 0.49 (95% CI: 0.36 to 0.65) cases per 1 million children between the ages of 5 and 9 years. There was no significant trend for children 4

years or younger (*P* = .6324) or between the ages of 5 and 9 years (*P* = .7695). The 5-year overall survival rates were 97.6%, 92.7%, 91.1%, and 96.4% for children diagnosed at the first, second, third, and after the third year of life, respectively (*P* = .0136). The 5-year overall survival rates were 92.5% for bilateral and 96.3% for unilateral cases (*P* = .0116). The 5-year overall survival rates were 90.8%, 92.5%, 97.6%, 97.3% for increasing time intervals (1973 to 1979, 1980 to 1989, 1990 to 1999, and 2000 to 2012, respectively; *P* = .0017). The authors concluded that the incidence rate of retinoblastoma in the United States has remained stable for the past 40 years. Survival rate analysis indicates a significant effect of laterality of tumor, age at diagnosis, and decade of diagnosis.

NON-RETINOBLASTOMA

20.ORBIT

Computed tomography-based 3D modelling to provide custom 3D-printed glasses for children with craniofacial abnormalities.

Brodie FL, Nattagh K, Shah V, Swarnakar V, et al. *JAAPOS* 2019 June; 23(3): 165-167.e1.

Children with craniofacial malformations frequently require spectacles but have difficulty finding an acceptable fit with current offerings of pediatric spectacle frames. The authors describe a novel method for creating custom 3D-printed spectacle frames based on a 3D reconstruction of a prior computed tomography scan. This method offers the ability to create better-fitting spectacles to children who are not served by "off the rack" frames. The authors suggest that some improvements are still warranted with the current design. They are working to automate the design process and have also begun exploring other methods for digitizing patient anatomy, such as photogrammetry (measurement of relative distances using multiple photographs from varying perspectives), which will decrease our reliance on existing and potentially outdated imaging.

Delayed surgical treatment of orbital trapdoor fracture in paediatric patients

Su Y, Shen Q, Bi X, Lin M, et al. *Br J Ophthalmol.* April 2019;103:523-526

Trapdoor orbital fractures can lead to extraocular muscle entrapment and ocular motility restriction. In general early surgery is recommended when there is motility restriction, positive forced duction testing, diplopia, and confirming findings on CT scan. However, due to some concerns of availability of urgent surgery (including the authors' area in China), this study aimed to evaluate outcomes after delayed treatment or orbital trapdoor fractures. Thirty patients (age 3 to 14 years,

mean 7.63 years) who underwent delayed surgery for trapdoor fractures were evaluated. Of those, 17 had muscle entrapment and 13 had soft-tissue entrapment. The mean time to surgery in the muscle entrapment group was 16.7 days (delayed due to a variety of reasons including non-medical reasons). The mean time to surgery for the soft-tissue group was 24.2 days. Mean follow-up time was 16.4 months. In the muscle group, 13/17 totally recovered from diplopia, compared to 7/13 in the soft-tissue group. Overall 10/30 patients had persistent diplopia after surgery. This included 4/17 in the muscle group, all of which had severe motility restriction before surgery, and 6/13 in the soft-tissue group. Overall severe motility restriction was found to have a higher incidence of persistent diplopia compared to mild restrictions. However persistent diplopia can still occur after mild restriction if surgery is delayed longer (>30 days). In conclusion, the authors recommend prompt surgical repair if there is muscle entrapment or significant restriction in soft-tissue entrapment.

Long-term Methimazole Therapy in Juvenile Graves' Disease: A Randomized Trial

Fereidoun Azizi, Miralireza Takyar, Elham Madreseh, and Atieh Amouzegar

Pediatrics May 2019; 143 (5) e:20183034

Hyperthyroidism is not a common disease in children and adolescence. For a majority of these patients, it is caused by a toxic goiter. The three standard treatment modalities have been suboptimal because of significant side effects and a high relapse rate. There have been a few studies that report long-term therapy of antithyroid drugs as effective and safe in curing hyperthyroidism. The study aimed to compare short and long term usage of methimazole treatment in juvenile Graves' as well as variables associated with remission of hyperthyroidism. In a randomized, parallel group trial, 66 consecutive patients with untreated Graves' were enrolled. After a medial of 22 months of methimazole treatment, the group was randomized to either receive low-dose methimazole treatment or to discontinue the treatment. The long-term group completed 96-120 months of methimazole treatment. At baseline, the short and long term treatment groups had similar profiles (age, sex, goiter degree, ophthalmopathy. fT4, T3, and thyrotopin levels). After 48 months, 16 patients in the short-term group (67%) and 3 patients in the long-term group (12.5%) relapsed ($p < 0.001$). Side effects only occurred in the first stage of methimazole treatment when all patients were being treatment and these were cutaneous reactions (3 patients). No serious complications occurred in the long-term group on low-dose treatment. In this study, the researchers demonstrate that long-term low-dose methimazole treatment is both effective and safe in treating the hyperthyroidism and preventing relapse. The other benefit of using methimazole is that the other choices of therapy (surgical resection and radioiodine) can lead to other medical issues and life-long hypothyroidism. The limitations of the study include small number of patients, the subjects were only of west Asian descent potentially limiting its applicability to other

populations, and that the study was not double-blinded possibly creating selection bias. In summary, this study suggests that long-term methimazole is safe and effective treatment for juvenile Graves' hyperthyroidism with higher recovery rates than the short term treatment.

Spontaneous Orbital Hemorrhage Related to the Extraocular Muscles

Helen H. L. Chan, Thomas G. Hardy, Alan A. McNab *Ophthalmic Plast Reconstr Surg* May/June 2019;35:256–261

The authors present the largest series of patients to date of spontaneous hemorrhage in relation to extraocular muscles (EOMs). This was an observational retrospective case series. Eighteen patients with a mean age of 71 years presented with 20 episodes of spontaneous orbital hemorrhage closely related to an EOM. Most patients woke with unilateral proptosis, pain, and diplopia. Vision was impaired in 25%. Imaging identified a characteristic well-circumscribed hematoma arising within the muscle sheath or intermuscular septum. Three episodes required surgical drainage. All patients had good recovery of vision. The authors describe a distinct clinical entity of idiopathic hemorrhages related to EOMs. No patient had an underlying vascular malformation or other lesion. The authors demonstrate that a proportion of these patients have vascular risk factors, namely, hypertension, hyperlipidemia, and antiplatelet use. This study suggests that inferior rectus is the most commonly affected EOM and shows that it is the muscle sheath or intermuscular septum of inferior rectus that is involved, rather than the muscle belly. Most patients can be managed conservatively with good visual outcomes. However, there were 3 exceptional cases that required surgical intervention. The findings that spontaneous orbital hemorrhages related to EOMs have certain predisposing factors, a characteristic radiological appearance, and a typically benign course will be helpful for clinicians in the management of this condition.

Distinguishing IgG4-Related Ophthalmic Disease From Graves Orbitopathy

Andrea A. Tooley, Diva R. Salomao, Elizabeth A. Bradley, James A. Garrity.

Ophthalmic Plast Reconstr Surg Mar/Apr 2019;35:170–176

Purpose: The authors aimed to determine key features of IgG4-related ophthalmic disease (IgG4-ROD) and Graves orbitopathy (GO) to aid in diagnosis.

The authors retrospectively identified ophthalmology patients seen between June 2009 and November 2013 with clinical overlap of GO and IgG4-ROD. Patient findings were reviewed to characterize the 2 conditions. Among 8 patients (7 male and 1 female), the mean age was 45.8 years. Time between diagnoses of GO and IgG4- ROD ranged from 1 month to 8 years. Imaging showed enlarged extraocular muscles in all patients. Enlarged infraorbital nerves were seen in 4 patients. Tissue biopsy showed CD20+ lymphocytes with a large proportion of

IgG4 plasma cells in 7 of 8 orbital specimens. Six patients had a ratio of IgG4:IgG cells >40%. No pathognomonic clinical findings for GO or IgG4-ROD have been reported, but some key features can help distinguish the conditions. GO is likely if findings include increased thyrotropin receptor antibodies, lid retraction/lid lag, and enlarged extraocular muscles with typical tendon-sparing morphology. Findings suggestive of IgG4-ROD include history of asthma and progressive orbital disease in patients with previous diagnosis of GO, disproportionately large lateral rectus muscle, and enlarged infraorbital nerves. Increased serum IgG4 level and biopsy showing >10 IgG4+ plasma cells/high-power field and IgG4:IgG ratio >40% will support the diagnosis of IgG4-ROD. GO and IgG4-ROD are complicated inflammatory processes affecting the orbit and present diagnostic challenges. The authors recommend biopsy for patients who do not follow the usual clinical course of GO or have clinical characteristics of IgG4-ROD.

Comparison of optic canal Diameter in Children with Malignant Osteopetrosis and Normal Children and the effects of Hematopoietic Stem Cell Transplantation on the Optic Canal Diameter.

Wnhong Cao, Wenbin Wei, Gang Yu, Qian Wu et al.*J Ped Ophth & Strabismus.*2019;56(1):35-42

The purpose of this study is to investigate the difference in the optic canal diameter between children with autosomal recessive malignant infantile osteopetrosis and normal children, and to assess the influence of hematopoietic stem cell transplantation (HSCT) on the optic canal diameter. Twenty pediatric patients with malignant infantile osteopetrosis and 22 normal control children were included in this study. Eleven patients with malignant infantile osteopetrosis underwent hematopoietic stem cell transplantation. The measurements included optical canal diameter and flash visual evoked potential. Comparisons of these measurements between patients with malignant infantile osteopetrosis and normal controls as well as before and after hematopoietic stem cell transplantation were performed. The correlation between age and optic canal diameter was analyzed using Pearson correlation analysis. The study showed that the mean optic canal diameter before hematopoietic stem cell transplantation was 1.65 ± 0.54 mm in patients with malignant infantile osteopetrosis and 3.38 ± 0.60 mm in the control group ($P < .001$). The mean optic canal diameter after hematopoietic stem cell transplantation was 2.72 ± 0.66 mm, which was significantly different from the pre-transplantation measurement ($P < .001$). The P2 latency for the flash visual evoked potential after hematopoietic stem cell transplantation (152.3 ± 36.4 ms) was significantly less than that before transplantation (165.5 ± 27.7 ms; $P = .051$). Pearson correlation analysis revealed a significant correlation between age and optic canal diameter ($r = 0.722$, $P < .001$). The authors concluded that the optic canal in patients with malignant infantile osteopetrosis is significantly narrower than that in normal children, and successful HSCT can relieve the progressive optic canal stenosis and control the deterioration of visual function impairment. Early HSCT is associated with favorable prognosis. Orbital

3DCT reconstruction and visual electrophysiological examination are effective methods for assessing the optic nerve damage in malignant infantile osteopetrosis and also helpful in the evaluation of the optic nerve before and after transplantation.

Radiographic Course of Medically Managed Pediatric Orbital Subperiosteal Abscesses.

Matthew T. Cossack, Samantha P.Herretes, Abdourahman Cham, Matthew C. Sniegowski et al. *J Ped Ophth & Strabismus*. 2018;55(6):387-392

The purpose of this retrospective case review was to describe the natural radiographic course of subperiosteal orbital abscesses that were managed medically in pediatric patients. Out of the 418 patients identified as having orbital cellulitis or subperiosteal abscess, 15 patients had repeat imaging and did not undergo surgery prior to the second scan. The initial size of the empyema, size of the empyema on repeat imaging, and clinical course were recorded for each patient. The study showed that the size of the empyemas increased 240% on average in the first 2 to 3 days. Imaging up to 11 days after the diagnosis showed that 9 cases persisted; meanwhile, 4 cases had radiographic resolution, with the earliest by 21 days. Two cases recurred months later. The largest increase in size was 500% over 3 days, but the initial empyema was only 0.3 cm^3. The results suggest a time between 11 and 21 days, but the sample size was limited. However, children who are improving clinically are rarely reimaged because there is no indication for a follow-up study and radiation exposure should be limited.The authors conclude that the natural radiographic course of medically managed subperiosteal empyemas in children includes initial enlargement for 2 to 3 days prior to radiographic resolution over 2 to 3 weeks. Interpretation of the size of the empyema should not guide management but, in the face of repeat imaging, this study can provide context for a normal radiographic course. Limitations of this study are the small sample size and its retrospective nature. The small sample size was a result of two factors: the frequency of surgical intervention and the infrequent nature of repeat imaging; only 15 of 418 patients had repeat imaging on our review. The retrospective nature of the study predisposes the series to a selection bias. Naturally, cases with clinical resolution would rarely undergo repeat imaging, whereas cases with a worsened clinical picture would be more likely to prompt repeat imaging. Similarly, this may explain the large proportion of cases that went on to eventual surgical management. Only one case with persistence on imaging was managed only medically.

Optical coherence tomography Thickness Measurements of the Extraocular Rectus Muscle Tendons in Graves' Ophthalmopathy

Lucia De-Pablo-Gomez-DE-Liano, Jose Ignacio Fernandez-Vigo, Nestor Ventura-Abreu, Juan Troyano-Rivas et al. *J Ped Ophth & Strabismus.*2018;55(6):356-362.

The purpose of this cross-sectional observational study is to examine the extra-ocular muscle tendons in patients with Graves' ophthalmolopathy using optical coherebnce tomography(OCT). Fifty five healthy control, fourty five patients with inactive clinically Graves' ophthalmopathy, and twelve patietns with clinically active disease were enrolled. Scanning was performed at 3 and 9 o'clock position. The medial rectus tendon thickness was measured at 7.2 mm and 9.2 mm from the limbus and the lateral rectus tendon thickness was measured at 8.5 and 10.00 m from the limbus. The study showed that the 9.2-mm medial rectus, 8.5-mm lateral rectus, and 10.5-mm lateral rectus tendons were thicker in the inactive Graves' ophthalmopathy group than the control group (240 ± 70, 231 ± 63, and 228 ± 54 μm vs 201 ± 71, 199 ± 53, and 200 ± 32 μm, respectively; $P \leq .011$), whereas the 8.5-mm lateral rectus and 9.2-mm medial rectus tendons were thicker in patients with active Graves' ophthalmopathy than patients with inactive Graves' ophthalmopathy (274 ± 77 and 283 ± 68 μm vs 231 ± 63 and 240 ± 70 μm, respectively; $P \leq .048$). A correlation was detected between lateral rectus and medial rectus tendon thicknesses and the Graves' ophthalmopathy clinical activity score ($R = 0.252$, $P = .035$; and $R = 0.291$, $P = .013$, respectively. The authors concluded that OCT is an accurate method for measuring medial rectus and lateral rectus tendon thicknesses in patients with Graves' ophthalmopathy. The imaging tool was able to detect thicker horizontal rectus tendons in patients with inactive Graves' ophthalmopathy than in controls, and in patients with active compared to inactive disease. The study has several limitations. OCT allows visualization of the anterior part of the muscle but not of the muscle belly, making it especially difficult to examine in patients with motility restrictions. The vertical rectus muscles are also difficult to examine because of interference from the eyelids and motility restrictions, mainly in the inferior rectus. In addition, because muscle insertion distances vary between individuals, the muscle measurement points used here may not have been equivalent. Future studies are needed to explore the inferior rectus in patients with Graves' ophthalmopathy because it is the most affected extraocular muscle, and also to compare OCT findings with MRI findings. Further limitations of our study were the relatively small number of patients with active Graves' ophthalmopathy, and the fact that the posterior portion of the lateral rectus could be measured only in a few cases. Accordingly, studies including larger patient populations are needed to confirm the results of the current study.

Embryologic and Fetal Development of the Human Orbit

Hatem A. Tawfik and Jonathan J. Dutton *Ophthal Plast Reconstr Surg* Sep/Oct 2018;34:405–421

This paper aimed to review the recent data about orbital development and sort out the controversies from the very early stages during embryonic life till final maturation of the orbit late in fetal life, and to appreciate the morphogenesis of all the definitive structures in the orbit in a methodical and timely fashion. The authors extensively review major studies detailing every aspect of human embryologic and fetal orbital morphogenesis including the development of extraocular

muscles, orbital fat, vessels, nerves, and the supportive connective tissue framework as well as bone. These interdisciplinary studies span almost a century and a half, and include some significant controversial opposing points of view which the authors hopefully sort out. The authors also highlight a few of the most noteworthy molecular biologic studies regarding the multiple and interacting signaling pathways involved in regulating normal orbital morphogenesis. Orbital morphogenesis involves a successive series of subtle yet tightly regulated morphogenetic events that could only be explained through the chronological narrative used by the authors. The processes that trigger and contribute to the formation of the orbits are complex and seem to be intricately regulated by multifaceted interactions and bidirectional crosstalk between a multitude of cellular building raw materials including the developing optic vesicles, neuroectoderm, cranial neural crest cells and mesoderm. Development of the orbit is a collective enterprise necessitating interactions between, as well as contributions from different cell populations both within and beyond the realm of the orbit. A basic understanding of the processes underlying orbital ontogenesis is a crucial first step toward establishing a genetic basis or an embryologic link with orbital disease.

Extraocular Muscle Enlargement and Thyroid Eye Disease-like Orbital Inflammation Associated with Immune Checkpoint Inhibitor Therapy in Cancer Patients

Oded Sagiv, Thomas J. Kandl, Sudip D. Thakar, et al. *Ophthal Plast Reconstr Surg* Jan/Feb 2019;35:50–52

The goal of the paper to describe thyroid eye disease (TED)-like orbital inflammatory syndrome in 3 cancer patients treated with immune checkpoint inhibitors. All consecutive patients treated by the senior author who were receiving immune checkpoint inhibitors and developed TED-like orbital inflammation were included. Three cancer patients treated with immune checkpoint inhibitors developed orbital inflammation. The first patient was treated with a combination of a cytotoxic T-lymphocyte antigen-4 inhibitor and a programmed cell death protein 1 inhibitor and developed TED-like orbital inflammation with normal thyroid function and antibody levels. The second patient had a previous diagnosis of Graves disease without TED, and developed TED soon after initiating treatment with a programmed cell death protein 1 inhibitor. The third patient developed acute hyperthyroidism with symptomatic TED following treatment with an investigational cytotoxic T-lymphocyte antigen-4 inhibitor agent. All 3 patients were managed with either systemic steroids or observation, with resolution of their symptoms and without the need to halt immune checkpoint inhibitor treatment for their cancer. TED-like orbital inflammation may occur as a side effect of immune checkpoint inhibitor therapy with anti–cytotoxic T-lymphocyte antigen-4 or anti- PD-1 inhibitors. To the best of their knowledge, this is the first reported case of TED as a result of programmed cell death protein 1 inhibitor monotherapy. All 3 patients were treated with systemic steroids and responded quickly while continuing treatment with immune checkpoint inhibitors for their cancer. With increasing use of this

class of drugs, clinicians should be familiar with the clinical manifestations and treatments for this adverse reaction.

Efficacy of Propranolol Between 6 and 12 Months of Age in High-Risk Infantile Hemangioma

Eulalia Baselga, Bozenna Dembowska-Baginska, Przemyslaw Przewratil et. al *Pediatrics* September 2018; 142 (3): e20173866.

Infantile hemangiomas (IHs) are benign vascular tumors with an estimated prevalence of 4-5% of children with 24% of these individuals experiencing complications (ulcerations, vision loss, and airway obstruction). A multi-center trial in Spain and Poland was conducted for infants ranging from 35 to 150 days with high-risk IH in the proliferative phase to determine the success and side effects of oral propranolol. High risk IHs were defined as those that were life-threatening, at risk for functional impact, or ulcerated hemangiomas, nonresponsive to standard wound care measures. The babies were treated for 6 months with 3 mg/kg per day of oral propranolol. If success had been achieved, then the propranolol was stopped and observation began. If there was re-growth of the IH, then treatment was re-initiated. If there was no success at 6 months, then treatment was continued for a total of 12 months before stopping medication. Success was defined as resolution of target IH (IH disappearance with minimal degree of telangiectasias, erythema, skin thickening, soft tissue swelling, and/or palpable component) and absence of functional impact (using Hemangioma Severity and Hemangioma Dynamic Complication scales). 45 patients were enrolled in the study. The success rate after 6 months was 47% and increased to 76% at one year. Of the patients that achieved success, 24% required retreatment. Adverse events occurred in 80% of children which included 13 treatment-emergent serious adverse events. The authors do not attribute the propranolol usage only to some of the documented infectious illnesses but 18% of the children experienced bradycardia which was most likely associated with the propranolol. None of these bradycardic children required new medications or termination of propranolol. The primary limitation of the study is the lack of a control group. In conclusion, treatment of high risk IH with 3 mg/kg per day of propranolol is an efficacious treatment modality with a satisfactory safety profile.

Clinico-radiological features and treatment outcomes in children with traumatic orbital subperiosteal hematoma

Sing M, Seth, N, Zadeng Z, Kar M, et al. *JAAPOS*. Dec 2018;22:6 416-420.

The goal of this paper was to look at the clinical findings, imaging features, and treatment outcomes in children diagnosed with traumatic orbital subperiosteal hematoma (OspH). The study involved 10 children who had a history of blunt trauma (mean age, 6.8 years; 8 males). The medical records of eligible OSpH

children treated either via needle aspiration or open surgical drainage were reviewed retrospectively. Three anatomical factors (inferior globe displacement, superior orbital sulcus fullness, extraocular movements) and two functional parameters (visual acuity, pupillary reactions) were used to determine overall success. All included patients had a history of blunt trauma, unilateral presentation, inferior globe displacement, fullness of superior orbital sulcus, and raised retrobulbar resistance. Diminution of vision and restricted elevation was noted in 7 children, and 4 had a relative afferent pupillary defect. Computed tomography (CT) revealed superior OSpH in all 10 children and, additionally, orbital wall fracture in 4. Needle aspiration of the OSpH was performed in 8 children; 2 underwent open surgical drainage. At a mean follow-up of 8.5 months, all children showed satisfactory improvement in both anatomical and functional parameters:1 child had a persistent nebulomacular corneal opacity, and 1 had minimal upper eyelid edema. The authors confirmed that the most significant anatomic factor contributing to OSpH is the presence of subperiosteal space, which is why the superior quadrant of the orbit is the most common location for OSpH. A high index of suspicion, appropriate radiology (CT of orbits), and early management through needle aspiration of OSpH may help in early intervention and therefore to increase satisfactory anatomical and functional outcomes.

Orbital fractures in children: clinical features and management outcomes

Barh A, Swaminathan M, Mukherjee B. *J AAPOS*. Dec 2018;28(6)415.e1-415.e7

This paper's purpose was to report the clinical characteristics and management outcomes of orbital fractures in children. The medical records of pediatric patients (<18 years of age) who presented with orbital fractures over a 15-year period (January 2001-December 2015) were reviewed retrospectively. The cause of injury, imaging findings, clinical features, management, and outcomes were noted. A total of 52 patients (39 males) were included in this study. Mean age at presentation was 10.9 years (range, 2-18). Road traffic accidents (18/52 [35%]) were the most common cause of the fractures with sports being the second most common cause, with the orbital floor (42/52 [81%]) being the most common fracture site with frequency occurring then in the medial, lateral, and roof in that order. The most common complaint in the patients was double vision (52%). Most patients were managed conservatively, however thirty-eight patients underwent surgical intervention, and extraocular muscle entrapment (56%) was the most common indication for surgery. Early surgical intervention within 15 days of injury resulted in complete resolution of diplopia in all the patients underwent surgery in this time frame. The authors conclude that orbital floor fracture was most common. The trapdoor type of fracture was seen in almost half of the patients, with diplopia being the most common presenting complaint. Early surgical intervention (within 15 days) was associated with complete resolution of ocular motility limitation and diplopia.

Pediatric Orbital Primitive Neuroectodermal Tumors

Tayyab Afgani, Hassan Mansoor, Syed Naeem Raza Hamdani *J of Ped Ophth & Strabismus*.2018; 55(2): 128-134

The purpose of this retrospective study is to present the clinical, radiological, histopathological, immunohistochemical features and the follow-up of orbital primitive neuroectodermal tumors (PNETs) in pediatric patients along with a review of the literature. Patients' demographic characteristics, ophthalmic findings, imaging, immunohistochemistry, metastatic work-up, treatment, globe salvation, and survival were documented and a mini literature review of orbital PNET was done. Complete remission, partial remission, and progression were diagnosed according to the Response Evaluation Criteria In Solid Tumors (RECIST) criteria.Four diagnosed cases of orbital PNET presented with proptosis and visual impairment were treated during the study period. The radiological imaging showed primary orbital involvement. There were three males and one female with a mean age of 63.75 months (range: 3 to 244 months). Histopathology of all studied patients showed round malignant cells with hyperchromatic nuclei, increased nuclear cytoplasmic ratio, and positive test results for CD99 and FLI-1. The studied patients underwent orbital surgery for excision of tumors followed by chemotherapy. One of the patients also had external radiation in addition to chemotherapy after a second recurrence. The follow-up period of these patients varied from 1 to 5 years. Only one child who had recurrence twice was followed up to 5 years, but was lost to follow-up after that. The authors believe that most orbital peripheral PNET tumors present as well-defined masses on both imaging and perioperatively and are easily removed surgically. The apparently disguised “benign profile” of orbital PNET may prove deceptive and the shorter duration of symptoms remains a strong reminder of the malignant nature of the lesion.

Intravenous Steroids With Antibiotics on Admission for Children With Orbital Cellulitis

Lena Chen, Nora Silverman, Andrew Wu, Roman Shinder *Ophthal Plast Reconstr Surg* 2018;34:205–208

This prospective comparative interventional study compared the outcomes of children with orbital cellulitis treated with intravenous (IV) dexamethasone and antibiotics on admission to patients treated with antibiotics alone. The study looked at forty-three children admitted to a tertiary institution with orbital cellulitis. On admission, all patients were started on broad spectrum IV antibiotics and parents were offered IV dexamethasone (0.3 mg/kg/d every 6 hours for 3 days). Patients whose parents refused steroid treatment served as the control group. Twenty-eight (65%) patients received IV steroids and antibiotics on admission while 15 (35%) received IV antibiotics alone. Children who received IV steroids had significantly shorter hospital stays than those who did not receive steroids (3.8 ± 0.2 days vs. 6.7 ± 0.3 days; $p < 0.001$). This was true both for children who underwent surgery for subperiosteal abscess (5/28 with steroids, 3/15 without; 5.0 ± 0.7 days vs. 7.3 ± 1.2 days; $p = 0.011$) and for those who did not require

surgical intervention (23/28 with steroids, 12/15 without; 3.6 ± 0.6 and 6.5 ± 1.0 days; $p < 0.001$). Side effects of steroid treatment were considered mild (hyperactivity and insomnia) and did not require termination of therapy. Children who received steroids had a shorter hospital stay than those who did not. During follow up, all study patients had returned to their baseline health without any cases of decreased vision or disease recurrence. The results of the current study give additional evidence to the relative safety and efficacy of systemic steroid use concurrently with IV antibiotics in children with orbital cellulitis. This is the first study to recommend IV steroids on hospital admission and a standardized dosing regimen.

Lateral Rectus Muscle Expands More Than Medial Rectus Following Maximal Deep Balanced Orbital Decompression

Adit Gupta, Alex Nobori, Yi Wang, Daniel Rootman, et al *Ophthal Plast Reconstr Surg,* 2018;34(2): 140-142

It has been reported that extraocular muscles can enlarge following orbital decompression in thyroid eye disease. In this article, the authors studied the changes in extraocular muscles size following maximal deep lateral and medial balanced decompression in a large sample of thyroid eye disease patients. Imaging data were reviewed preoperatively and postoperatively 48 consecutive patients (75 orbits). Radiologic proptosis was assessed. Maximal axial muscle width of the medial and lateral recti was measured. Results: Data from 48 consecutive patients (75 orbits) were included. There was a significant increase in the width of both the lateral and medial recti after decompression ($p < 0.01$). The mean (standard deviation [SD]) change was less for the medial rectus (0.7 mm) than for the lateral (2.7 mm). This difference was significant ($p < 0.01$). For the lateral rectus, 80% of all decompression surgeries were associated with an increase in width of >1 mm. Mean (SD) proptosis reduction was 8.2 mm (3.4 mm). These results suggest that the extraocular muscles enlarge in the most deep lateral wall decompressions. The authors postulate that the expanded muscles may be in a relatively stretched position preoperatively and with postoperative changes in globe position and the resultant altered vector pathway of the muscle, the central belly may appear more greatly expanded. In conclusion, for decompression as performed in this article, expansion tends to be more commonly found and of a greater magnitude in the lateral rectus compared with medial.

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

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

J of Ped Ophth & Strabismus.2018;55(1);37-42

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

21.OCULOPLASTICS

Risk factors for Poor Surgical Outcome of Pediatric Nasolacrimal Duct Obstruction.

Jamie Dietze, Donny Suh. *J of Ped Ophth & Strabismus*.2019; 56(4): 261-264

The purpose of this retrospective, observational case control clinical study was to determine whether there are common factors that might help predict if a child is at a higher risk for surgical failure for nasolacrimal duct obstruction. A pediatric ophthalmologist identified patients who required surgical correction based on symptom history refractory to conservative management. Patients were grouped by the need for multiple surgical interventions versus single surgery. Patient factors hypothesized to predispose patients to an unsuccessful initial procedure were compared via odds ratio analysis. Patient success was based on symptom resolution 6 months postoperatively. The study showed that patient factors with statistically significant increased odds ratios were trisomy 21, allergic rhinitis/seasonal allergies, history of an upper respiratory tract infection within 1 month, and obstructive sleep apnea. This study suggests that patients with trisomy 21 or a history of recent upper respiratory tract infection may be correlated with a higher

risk of failure with a probing and irrigation surgery only. Patients with trisomy 21 may benefit from an initial balloon dilation procedure rather than probing and irrigation, due to an increased risk profile. Patients with a recent upper respiratory tract infection may benefit from postponing surgery until symptom treatment or resolution. Limitations of our study include relatively small population sizes and lack of standardization of nasolacrimal duct obstructions among the various clinicians prior to referral. A large standardized, prospective, randomized study would be beneficial to address these limitations.

Surgical outcome of External Dacryocystorhinostomy with silicone Intubation for Recurrent Lacrimal Abscess in children younger than 6 years

Pradhnya Sen,MS, Elesh Jain, DOMS,Amit Mohan, MS, Amit Kumar MD

J of Ped Ophth & Strab.2019;56(3):188-193

The purpose of this single-center retrospective analysis was to assess the success rate of external dacryocystorhinostomy(DCR) with silicone intubation for recurrent lacrimal abscess in children younger than 6 years.Forty-six eyes of forty cidlren who underwent DCR were included in the study.Probing done previously in these cases was unsuccessful. Only those children who underwent incision and drainage of the abscess at least once with antibiotic treatment were included in the study. In all cases, silicone tube removal was done after 3 months. A successful outcome was defined as the absence of subjective complaints of pain and swelling over the medial canthal area and watering and discharge at 6 months postoperatively. Objective assessment of patency of the lacrimal apparatus was done by sac syringing at 6 months postoperatively. The mean age at surgery was 4.93 ± 0.93 years (range: 3 to 6 years) and the mean follow-up duration was 11.80 ± 11.87 months (range: 6 to 84 months). Intraoperative difficulties encountered were excessive peri- sac adhesion (n = 28) and severe bleeding/hemorrhage (n = 24). A total of 82.61% cases had a successful outcome after DCR with silicon tube intubation. One child had granuloma formation at the wound. Spontaneous tube extrusion occurred in three children. The authors conclude that external DCR with silicone tube intubation is a safe and effective surgical approach for treating dacryocystitis with recurrent lacrimal abscess in children younger than 6 years with failed attempts on probing to avoid unnecessary frequent use of systemic and topical antibiotics and risk of serious complications. Being retrospective in nature, this study has inherent limitations, although the number of cases is satisfactory for pediatric population. It is difficult to compare the results of this study with those of others because this study included children with recurrent lacrimal abscess who were younger than 6 years exclusively, both of which are risk factors for failure of DCR. However, based on the authors' findings, DCR with intubation is satisfactory in these high risk cases of lacrimal abscess. Future studies are warranted exclusively in the same age group with uncomplicated NLDO to prove its efficacy in total.

Effect of probing in Congenital Nasolacrimal Duct Obstruction in Children older than two years.

Vaishali Lalit Une, Sushma Subhash Kulkarni, Varsha Sharad Nandekarh. *J Ped Ophth & Strabismus* 2019; 56(3):141-145

The purpose of this prospective interventional case series is to determine the effect of probing for congenital nasolacrimal duct obstruction in children older than 2 years. One hundred ten eyes (n=110) of 94 patients with congenital nasolacrimal duct obstruction (CNLDO) aged 2 years or older, with no previous intervention were included in the study. The diagnosis was based on clinical findings (epiphora, discharge, regurgitation test, and fluorescein dye disappearance test). The children were divided into two groups: 2 to 5 years and 6 to 8 years. Probing of the nasolacrimal duct under general anesthesia was done. Success was predefined as resolution of symptoms and signs that persisted 3 months postoperatively. Another probing was done at 4 to 6 weeks when necessary before considering the final outcome as a failure. The chi-square test was used to analyze the result. Patients' ages ranged from 2 to 8 years (average age: 55 months).The study showed that twenty-six (28%) patients needed a second probing. The overall success rate was 80%-85% in the 2 to 5 years group and 73% in the 6 to 8 years group. The success rate was significantly lower in patients with complex obstruction (33.3%). The outcome of probing was not affected by the age of the patients (*P* = .2305). The authors concluded that probing is a viable primary surgical option in CNLDO in older children and hence should not be withheld in children who are referred late.

Conservative management of congenital dacryocystocele: resolution and complications

Lee M, Park J, Kim N, Choung H, et al. *Can J Ophthalmol.* August 2019;54(4):421-425

Incidence of congenital dacryocystocele varies from 0.02% to 0.1% of newborns. The best treatment approach is controversial. Some people recommend early surgical intervention to reduce risks of infection and avoid further complex surgery. Others recommend monitoring due to high rates of spontaneous resolution. The authors of this study looked at a population of Asian children to evaluate the outcomes of conservative management for congenital dacryocystocele. 30 dacryocystoceles (28 infants) were retrospectively reviewed. Conservative treatment included digital massage four times daily and antibiotic eye drops if needed. 27 cases did not develop infection. Of these, 20/27 (74%) resolved spontaneously after conservative treatment. The mean duration of this treatment was 27.5 days. In 5 cases probing was needed due to persistent dacryocystoceles after 1 month

of massage. 5 total cases developed infection including 3 at presentation. 2 cases became infected during the period of conservative management. These all received systemic antibiotic treatment, and 3 cases required external incision and drainage. All of these resolved without needing additional procedures. The authors conclude that uninfected cases of congenital dacryocystocele could be managed conservatively in a majority of cases. Vigilance is still needed to detect infection, but after infection is controlled conservative management is still an option.

Incidence and clinical characteristics of congenital nasolacrimal duct obstruction

Sathiamoorthi S, Frank R, and Mohney B. *Br J* Ophthalmol. April 2019;103:527-529.

Congenital nasolacrimal duct obstruction (CNLDO) occurs in 5-20% of newborns. Reports on the incidence and demographics of this disorder are uncommon and old. This study reviewed over 17 thousand newborns during a 10-year period in Minnesota (through the Rochester Epidemiology Project). Out of the 17,713 newborns born from 1995 to 2004, 1998 were diagnosed with CNLDO, giving a prevalence of 1/9 live births. The median age at diagnosis was 5 weeks, and 90% of the diagnoses were made by a primary care physician. CNLDO was associated with premature birth and Caucasians. Two-thirds of cases presented with discharge alone, while tearing was observed in one-third. Previous studies report tearing as the most common presenting symptom. This study may have found discharge as the most presenting symptom due to the younger age ay presentation for the group compared to other studies, in which case tear production is not fully developed. One third of cases were bilateral. The authors do mention that there may be a significant number of infants with CNLDO that are asymptomatic and ultimately not diagnosed, and that this population (a relatively homogenous Caucasian group) does not generalize to other populations.

Surgical Timing for Congenital Ptosis Should Not Be Determined Solely by the Presence of Anisometropia

Chisholm SAM, Costakos DM, and Harris GJ *Ophthalmic Plast Reconstr Surg* July-Aug 2019;35:374–377

Timing of surgery in children with congenital ptosis is a critical component of care, and anisometropia is frequently cited as an indication for early intervention. The purpose of this study is to evaluate the change in refractive error following surgery for congenital ptosis to better inform decisions regarding the timing of surgery. A retrospective review of clinical records was performed on patients who underwent surgical correction of congenital ptosis in an academic oculoplastic surgery practice from 2002 to 2017. Patients with complete preoperative and postoperative refractive data were included in the study. Changes in refractive error following surgery were analyzed. Among 184 pediatric patients who

underwent ptosis surgery during the study period, 56 patients (71 eyes) met inclusion criteria. The mean age at surgery was 5.1 years. Mean refractive error change in all the operated eyes was a 0.82D decrease in spherical equivalent ($p = 0.1920$) and a 0.40 D increase in cylinder ($p = 0.0255$). There were no statistically significant changes in spherical equivalent or cylinder in the control eyes. The authors data did not show movement toward normalization of refractive error following ptosis surgery. In fact, it showed a statistically significant worsening of astigmatism following surgery. Because refractive error does not improve following surgery, anisometropia should not be the sole indication for early surgery in congenital ptosis.

Anthropometric Analysis on the Ocular Region Morphology of Children and Young Adults in Chinese Han Population

Cai X, Chen Y, Li Q, Ma H, et al.

Ophthalmic Plast Reconstr Surg July-Aug 2019;35:326–332

The periocular features vary in different age groups and ethnic populations. In this study, the authors sought to determine whether age-related differences exist for certain periocular parameters between children and young adults of Chinese Han population. Both eyes of 310 children (aged 7–10 years) and 301 young adults (aged 20–30 years) were evaluated by 2-dimensional photogrammetry. All the subjects were of Chinese Han population. The eyelid crease profiles were classified according to their morphology. Periocular measurements, including 11 linear and 3 angular parameters were acquired from standardized photographs, 3 indices were further derived. The presence of epicanthal fold was also recorded. Each of the parameters was compared between the age groups. A statistical difference was found between the 2 age groups for the distribution of eyelid crease types. Statistical significances existed between the age groups for various parameters, these include palpebral fissure height and width, margin reflex distance, intercanthal and outercanthal width, distance from the medial end of the eyebrow to the medial canthus, distance from the lateral end of the brow to the lateral canthus, crease height and eyebrow height, angle of endocanthion and exocanthion, palpebral fissure inclination, palpebrae fissure index, canthal index, and angular index ($p < 0.05$). The incidence of epicanthal fold tended to decrease with increase of age. Age differences exist in periocular features between children and young adults of Chinese Han population. Standards of periocular measurements based on age and race could provide reliable guidelines for clinical examination and planning periocular surgery.

Congenital Dacryocystocele: A Major Review

Singh S, Ali MJ *Ophthalmic Plast Reconstr Surg* July- Aug 2019;35:309–317

The paper aimed to provide a systematic review of the literature on congenital dacryocystoceles (CDCs) and summarize their presentations, investigations, management, and outcomes. The authors performed a PubMed search of all articles published in English on CDCs. Data captured include demographics, clinical

presentations, investigations, management modalities, complications, and outcomes. Fourteen major series (10 or more than 10 cases) and 89 isolated case reports/series on CDCs with a collective patient pool of 1,063 were studied in detail. Specific emphasis was laid on addressing the controversial issues including initial conservative versus surgical management and the role of endoscopic evaluation. Numerous terminologies have been used to describe CDC. Congenital dacryocystoceles are rare variants of congenital nasolacrimal duct obstructions and comprise of 0.1% to 0.3% of all such cases. There is a female predilection (64.2%, 683/1,063) and the mean age at presentation is at 7 days of birth. Initial conservative treatment can be a viable option in the absence of an acute dacryocystitis or a respiratory distress. Endoscopy-assisted probing appears to have better outcomes as compared with the in-office probing. Congenital dacryocystoceles with acute dacryocystitis are preferably managed with intravenous antibiotics and an early probing under endoscopy guidance to avoid missing intranasal cysts. Marsupialization is the preferred technique in the management of intranasal cysts. Silicone intubation was rarely used and has no definitive indications. Dacryocystorhinostomy is very rarely needed in the management of CDC. Congenital dacryocystocele is a commonly accepted term and its use should be advocated to enhance uniformity in reporting. Endoscopic evaluation of CDC is useful in the diagnosis and treatment of associated intranasal cysts and enhances the rates of successful outcomes.

The Role of Inferior Turbinate Fracture in the Management of Congenital Nasolacrimal Duct Obstruction

Mohammad Taher Rajabi, Bahman Inanloo, Mirataollah Salabati, et al.

Ophthalmic Plast Reconstr Surg May/June 2019;35:269–271

To evaluate the effect of inferior turbinate fracture in the treatment of congenital nasolacrimal obstruction combined with first attempt probing in children younger than 36 months. This prospective case–control study was conducted on 230 eyes from 176 children aged 12 to 36 months with congenital nasolacrimal duct obstruction. All patients underwent simple probing under general anesthesia. Inferior turbinate fracture was performed in case group combined with first probing. Patients were followed up 1, 3, and 6 months after surgery. Total success rate was 91.2% for patients with turbinate fracture and 86.4% for patients without turbinate fracture. The difference between success rates was not statistically significant ($p = 0.269$). The authors did not find significant difference between cases and controls in age subgroups. Success rate in combined case and control groups in patients younger than 24 months (success rate: 91.7%) was significantly higher than those older than 24 months (success rate: 71.9%; $p = 0.001$). In univariate logistic regression analysis, age ≥24 months showed a negative association with the success rate (odds ratio = 0.232; 95% confidence interval: 0.91–0.59; $p = 0.002$). Other factors like sex, bilaterality of nasolacrimal duct obstruction, method of probing were not significantly associated with response to treatment. Inferior turbinate fracture does not improve the outcomes of simple

probing and is not recommended during the first attempt in treatment of congenital nasolacrimal duct obstruction. Late probing (after 24 months of age) may have a higher failure rate, and increased age is the important factor that predicts failure in probing simple congenital nasolacrimal duct obstruction.

Outcomes of Frontalis Sling Versus Levator Resection in Patients With Monocular Elevation Deficiency Associated Ptosis

Tarjani Vivek Dave, Pranjali Sharma, Arpita Nayak, et. al. *Ophthalmic Plast Reconstr Surg* May/June 2019;35:251–255

To compare outcomes of frontalis sling (FS) silicone and levator resection (LR) in ptosis associated with monocular elevation deficiency. Retrospective interventional comparative case series of FS and LR in monocular elevation deficiency associated ptosis. Favorable outcome was defined as difference in margin reflex distance 1 of ≤1mm between the 2 eyes in unilateral cases and margin reflex distance 1 of 4 mm in bilateral cases at last follow-up visit. One hundred four eyes of 95 patients were included. Median age at surgery was 14 years, and the mean follow- up period was 19.75±34.55 months. Ptosis was severe in 91 (87.5%) patients. Associated Marcus Gunn jaw-winking (MGJW) phenomenon was seen in 43 (42%) patients. Frontalis sling was performed in 76 (73%) and LR in 28 (27%). Mean pre- and postoperative margin reflex distance 1 were −1.27 ± 2.17 mm and 2.18±1.49mm ($p < 0.0001$). The mean improvement in margin reflex distance 1 was significantly more with FS (4.46 ± 2.19) compared with LR (1.85 + 2.5) ($p < 0.0001$). There were no cases of exposure keratopathy requiring reversal of surgery in either group. The number of resurgeries required was 42 (55%) in the FS group and 10 (36%) ($p = 0.08$) in the LR group. Favorable outcome was seen in 54 (71%) in FS group and 16 (57%) ($p = 0.17$) in LR group. When compared with levator resection, frontalis suspension with silicone gives a better eyelid elevation but has greater regression requiring more resurgeries. In spite of a poor Bells phenomenon, exposure keratopathy is not a concern.

Selection of surgical intervention for congenital dacryocystocele

Zhang Y, Fan Y, Fan J, Cui Y *EJO* March 2019, 29(2):158–164

The purpose was to evaluate the surgical intervention and its effect on congenital dacryocystocele. A total of 531 children with congenital dacryocystocele admitted to the Department of Ophthalmology of Beijing Children's Hospital, Shanghai Aier Eye Hospital, Nanjing Aier Eye Hospital, and the First Affiliated Hospital of Jinzhou Medical University between January 2007 and January 2017 were retrospectively analyzed. The patients were followed up for 3–24 months, with an average of 13.3 months. No serious intraoperative complications (such as bleeding and tissue damage) and postoperative complications (bleeding, infection, and hole atresia) were found. We classified the outcomes into three categories based on the signs (overflowing tears and empyema) and objective routine follow-up by endoscopy. Cure indicated that mass, overflow of tears, and breathing difficulties disappeared, and 81.5% cases (433/531) were postoperatively cured. Improvement indicated disappearance of mass, overflow empyema, and the presence of

residual tears (due to trocar and tears puncture), and 18.5% cases (98/531) were postoperatively improved. Unhealed indicated overflowing pus and tears, and 0% cases did not heal after surgery. It was concluded that nasal endoscopic surgery is relatively safe, with high success rate for treatment of congenital dacryocystocele. Systematic training is required to promote the application of nasal endoscopy, so that more ophthalmologists can learn this technique.

Efficacy of Office-Based Nasolacrimal Duct Probing.

Austin Bach, Elizabeth Ann Vanner, Roberto Warman. *JPOS*.2019;56(1):50-54

The purpose of this study is to analyze the efficacy of nasolacrimal duct probing conducted in the office for nasolacrimal duct obstruction. A retrospective chart review was conducted of 1,294 patients. Of those, 1,227 patients who underwent office-based nasolacrimal probings of the nasolacrimal duct at a single tertiary care center were included. A total of 82 (6.7%) patients needed reprobing. Of the 82 patients who underwent a second procedure, 35 (43%) underwent a second in-office probing with a success rate of 77%. The 8 (22%) patients who failed the second in-office probing underwent probing and Crawford stent placement in the operating room and their symptoms resolved. For the 47 (57%) patients who failed the primary in-office probing and underwent operating room probing and stent placement, only 1 (2%) needed a second operating room probing and stent placement. Logistic regression analyses indicated an increased likelihood of needing a secondary procedure with increased age at the time of the first probing. Our results showed an overall 93.3% success rate of first in-office probing and a success rate of 77% for a repeat in-office probing. We have also shown an 88.8% success rate for in-office probings for patients older than 12 months. These results are at the upper end of successful treatment when looking at both in-office probings and probings in the operating room for patients of any age in prior studies. This review of in-office probings shows the efficacy of a minimally invasive procedure on all children younger than 24 months. With proper training of staff, nasolacrimal duct obstruction can be treated quickly and safely in the office. This will save time and money for the family, ophthalmologist and his or her staff, and the insurance companies, both public and private. The study has multiple limitations: some of the patients were not observed for more than one or two follow-up appointments after the in-office probing. The failure rate only included those patients without resolution of symptoms who underwent a secondary probing performed by the same pediatric ophthalmology group and it may have missed patients who went elsewhere for further treatment. The statistics may then include patients who failed probing but went elsewhere for further treatment or who spontaneously resolved months after probing. Also, because the logistic regression analyses do not show the strongest correlation between increasing age and need for reprobing, there are likely other factors that need to be understood that were not addressed in this study. Because the data were de-identified, the logistic regression could not account for possible correlation between the bilateral probings of a single patient, but because these were only 20 of the 1,227 total probings, this is unlikely materially to affect the results.

Association between congenital nasolacrimal duct obstruction and mode of delivery at birth.

Tavakoli M, Osigian CJ, Saksiriwutto P, Reyes-Capo DP, et al. *J AAPOS*. Oct 2018; 22(5): 381-385.

The purpose of this retrospective study was to investigate the association between mode of delivery, incidence of congenital nasolacrimal duct obstruction (CNLDO), and treatment outcomes. A total of 104 children diagnosed with CNLDO at a tertiary referral center between 2012 and 2017 were included. Patient demographics, pregnancy and birth history, clinical characteristics of CNLDO, and treatment outcomes were compared in patients delivered via cesarean section (CS) versus vaginal delivery (VD). The rates of CS, as well as full-term and premature births, were also compared to Miami-Dade County normative values to eliminate the confounding effects of prematurity. A significantly higher percentage of patients with CNLDO (61%) were delivered via CS ($P < 0.0001$). The authors state that among full-term babies, there was 55% greater risk (OR = 1.55; 95% CI, 0.98-2.43; $P = 0.067$) of CNLDO for CS birth compared to all other babies. However, this is *not statistically significant*. Among preterm babies, there were no significantly greater odds of CNLDO for CS compared to VD births ($P = 0.575$). CNLDO did not resolve spontaneously in 50 patients, including 37 CS (74%) and 13 VD (26%) patients ($P = 0.007$). Among those patients who failed first-line probing, 86.2% were born via CS, whereas 13.8% were born via VD ($P = 0.0009$).The authors concluded that CS is a risk factor for CNLDO, independent of gestational age. Children born via CS also tend to have a more complicated clinical course requiring additional surgical interventions. Despite some misinterpertations this study highlights an interesting observation.

Congenital dacryocystocele: sonographic evaluation of 11 cases.

Miranda-Rivas A, Villegas VM, Nieves-Melendez JR, De La Vega A. *J AAPOS*. Oct 2018; 22(5): 390-392.

The purpose of this retrospective case series was to describe the prenatal sonographic findings of congenital dacryocystocele. Eleven cases of congenital dacryocystocele diagnosed at a tertiary care center from 2003 to 2015 were included . No accompanying fetal anatomic anomalies where detected. Mean maternal age at evaluation was 22 years of age (range, 17-32 years). Four cases were primigravidas. The mean gestational age at evaluation was 32.6 weeks' gestational age (range, 27.2-37.4 weeks). Ten out of 11 cases occurred in female fetuses (91%). Ten cases were unilateral and 1 was bilateral. The mean diameter at evaluation was 5.1 mm (range 1- 14/2 mm). Spontaneous resolution occurred in 2 cases (18%). In the remaining 9 fetuses, postnatal diagnosis of dacryocystocele were confirmed by an ophthalmological evaluation. The authors concluded that prenatally diagnosed congenital dacryocystocele may undergo spontaneous resolution before birth; However, referral to a pediatrician and pediatric ophthal-

mologist should be considered for complete evaluation and postnatal management. The article concentrates mainly on the prenatal diagnosis of dacryocystocele and would probably be more of interest to fetal-maternal-medicine physicians. It discusses nicely the approach and possible differential diagnosis of cystic lesions near the orbit.

Balloon Dacryoplasty for Congenital Nasolacrimal Duct Obstruction: A Report by the American Academy of Ophthalmology: Ophthalmic Technology Assessment

Wladis EJ, Aakalu VK, Yen MT, Bilyk JR, Sobel RK et al. *Ophthalmology* 125; 10 Oct 2018: 1654-1657.

Balloon dacryoplasty has emerged as a popular option to address recalcitrant nasolacrimal duct obstructions. This technique involves passing a lubricated, inflatable balloon along a guide wire into the nasolacrimal duct and through the level of obstruction. The balloon is then inflated for 90 seconds to dilate the obstruction, deflated, and reinflated a second time, or removed. The goal of this study was to determine the efficacy and adverse events of balloon dacryoplasty. A literature search was last performed in September 2017 in the PubMed database to identify all reports of balloon dacryoplasty. All searches up to and including the last search were limited to the English language, and they yielded 104 articles that were assessed for relevancy. Thirty-six articles were selected for full review, and 8 of these were selected for inclusion in this assessment and assigned a quality of evidence rating by the panel methodologist. Three of the 8 studies included in this assessment were rated level II, and 5 were rated level III. Success rates varied from 75% to 100%. Only 2 complications were identified, and these were cases of self-limited postoperative emesis. The 2 studies that compared balloon dacryoplasty with lacrimal stenting reported that outcomes were comparable between the 2 techniques. Although level I evidence was not available, the studies that were included in the literature review indicate that balloon dacryoplasty is a safe, effective procedure to address congenital nasolacrimal duct obstruction that persists after standard probings. The outcomes of this intervention are similar to those of lacrimal stenting, and the absence of an implanted stent theoretically reduces the risk of complications. This review did not examine the age at initial probing or balloon dacryoplasty. The optimal time for balloon dacryoplasty is also not addressed. It is important to note that there was no level 1 evidence in the literature for this review.

Spontaneous Resolution and Timing of Intervention in Congenital Nasolacrimal Duct Obstruction.

Saraniya Sathiamoorthi, Ryan D. Frank, Brian G. Mohney. *JAMA Ophthalmology*. November 2018; 136 (11); 1281-1286.

This study was a retrospective medical chart review of a large cohort of 1998 consecutive infants diagnosed with congenital nasolacrimal duct obstruction (CNLDO) from 1995 through 2004 at Mayo Clinic in Rochester, MN regarding the gender and the rate of spontaneous resolution of CNLDO. This cohort had a mean age of diagnosis at 1.2 months and 48% were girls and 89% white. Of the 1998 pediatric cases, 1669 (83.5%) spontaneously resolved, 289 (14.5%) underwent treatment, and the remaining 40 (2.0%) children were lost to follow up. By three months old, nearly half (47.3%) had spontaneously resolved and by 9 months old, 75.7% had spontaneously resolved and 78.4% had spontaneously resolved by 12 months old. Of note, CNLDO resolved in boys 0.5 months faster than girls and unilateral resolved 0.2 months faster than bilateral CNLDO. Regarding resolution after NLD probing, children probed at 15 months or older had decreased odds of resolution (odds ratio, 0.11, 95% CI, P=.04) compared to children with NLDO probing between 12 to 14 months old. Limitations of this study include the retrospective analysis of medical records over 20 years in Olmstead county of a semiurban white population. The authors suggest that the rate of spontaneous resolution of CNLDO tends to plateau after 9 months of age and successful NLD probing declines after 15 months old, and therefore, it is reasonable to perform NLDO probing between 9 to 12 months old. In comparison to the current general practice of probing for CNLDO after 12 months of age, the authors present a narrower and earlier time frame for consideration of surgical intervention in children with CNLDO.

Revision Surgery for Undercorrected Blepharoptosis After Frontalis Sling Operation Using Autogenous Fascia Lata

Ju-Hyang Lee, Kyung In Woo, and Yoon-Duck Kim

Ophthal Plast Reconstr Surg Sep/Oct 2018;34:487–490

Undercorrected blepharoptosis can be encountered after frontalis sling operation. Revision surgery for undercorrection has commonly involved introducing a new sling material. We describe and evaluate a simple surgical technique to correct undercorrection by adjusting preexisting fascia. This is a retrospective interventional case series of patients undergoing sling revision between February 2010 and February 2017. Skin incision was made on the previous incision line. Careful dissection was performed superiorly to identify a preexisting fascia, and the dissected fascia was reattached to the tarsal plate using nonabsorbable sutures with adjustments for eyelid height and contour. The success of the procedure was defined as less than 1 mm of difference in the marginal reflex distance 1 of both eyes without any contour deformity. Twenty-one eyelids in 18 patients were included with a mean follow-up of 17.5 months (range 6–48) and a mean age of 14.7 years (range 5–57). All patients had undergone frontalis sling with autogenous fascia lata for congenital ptosis. Undercorrection due to recurrent ptosis was found in 12 eyelids, and contour deformity such as temporal ptosis was found in 9 eyelids. The mean time interval between previous frontalis sling operation and sling revision was 6.8 years. Nineteen patients (90.5%) achieved surgi-

cal success and a cosmetically acceptable appearance. Sling revision is a simple and effective method with low perioperative morbidity for cases of undercorrection or contour deformity following frontalis sling operation using autogenous fascia lata, even long after the primary procedure.

Improving Outcomes of Posterior Approach Levatorpexy for Congenital Ptosis With Reduced Levator Function

Ilan Feldman, Lucas Brusasco, and Raman Malhotra *Ophthal Plast Reconstr Surg* Sep/Oct 2018;34:460–462)

The authors present a new series of our experience using posterior approach levatorpexy for congenital ptosis with poorer levator function (LF) in comparison with our first published report. This technique avoids a skin incision or any resection in addition to no excision of tissue. A consecutive series of 16 patients was subject to a retrospective review of levatorpexy for congenital ptosis. Data included eyelid margin reflex distance 1, pretarsal show, contour, and complications, including nocturnal lagophthalmos, eyelid lag on downgaze, and dry eye. Surgery was considered successful if the following 4 criteria were simultaneously met: a postoperative margin reflex distance 1 of ≥2 mm and ≤4.5 mm, intereyelid height asymmetry of ≤1 mm, no overcorrection compare to opposite eye, and satisfactory eyelid contour. Mean age was 10.3 years (range 1–26 years). Mean LF was 7.3 mm (2–14 mm), while 66% (12) had LF ≤7 mm. Preoperative phenylephrine test was positive in 87.5% of patients. Mean preoperative and postoperative margin reflex distance 1 was 1.34 mm and 3.2 mm, respectively. Fourteen patients (87%) achieved the desired eyelid height and fulfilled our criteria set of success. Among 10 patients with LF ≤7 mm, 9 (90%) achieved the desired eyelid height and fulfilled our criteria set of success. Ninety-four percent did not report nocturnal lagophthalmos. Three patients needed a further levatorpexy procedure due to undercorrection. Mean postoperative follow up was up 11.2 (range 6–36) months. Posterior approach levatorpexy is an useful first-line choice for congenital ptosis for all ranges of LF. It is popular among parents due to its avoidance of a skin incision or any resection or excision of tissue.

Symmetry of Upper Eyelid Contour After Unilateral Blepharoptosis Repair With a Single-strip Frontalis Suspension Technique

Patricia Akaishi, Alicia Galindo-Ferreiro, and Antonio A. V. Cruz

Ophthal Plast Reconstr Surg Sep/Oct 2018;34:436–439

The goal of the paper was to analyze the upper eyelid contour of patients with unilateral congenital ptosis who underwent single-strip frontalis suspension. The authors compared the upper eyelid shape of the right and left eyes of 10 patients who underwent unilateral frontalis suspension with a single strip of autogenous fascia. At a mean postoperative time of 10.1 ± 4.01 months, the image J software was used to measure the ratio between the nasal and temporal areas of the upper half of the palpebral fissure. The midpupil upper eyelid distance (MRD1) was

also measured on the photos with the same software. The nonparametric Wilcoxon signed-rank test was used to compare the data. Postoperative MRD1 ranged from 2.5 to 4.7 mm (median = 3.8) on the affected side. The MRD1 for nonoperated eyelid ranged from 1.8 to 5.0 mm (median = 3.5). On the operated side, the temporal areas ranged from 50.3 to 85.7 mm2 (median 65.2) and nasal areas ranged from 41.5 to 72.3 (the median was 60.1). In the contralateral, nonoperated palpebral fissures, the temporal areas ranged from 42.7 to 94.3 mm2 (median = 54.5) and the nasal areas ranged from 36.8 to 86.1 mm2 (median 52.3). The T/N ratio distributions were almost identical between groups, ranging from 0.9 to 1.2 (median = 1.1) in the operated eyes and from 0.9 to 1.3 (median = 1.1) in the fellow eyes. In autogenous fascia frontalis suspension procedures, the upper eyelid contour of the ptotic eyelids can be adequately normalized with a single area of traction on the tarsal plate.

Ophthalmic Pyogenic Granulomas Treated With Topical Timolol—Clinical Features of 17 Cases

Lauren N. DeMaria, Nora K. Silverman, Roman Shinder *Ophthal Plast Reconstr Surg* Nov/ Dec 2018;34:579–582

Topical timolol has been increasingly demonstrated to be an effective treatment for pyogenic granulomas (PG). The authors review the treatment outcomes of 17 patients with ocular PG treated with topical timolol. Retrospective interventional study of 17 patients with ocular PGs treated with timolol 0.5% solution. Patient demographics, clinical features, treatment response, and recurrence were noted. Nine females and 8 males with a mean age of 23 years (range, 3–67 years) were included. Mean duration of disease prior to treatment was 3.81 months (range, 0.25–11 months). Etiologies included chalazia (12 cases, 71%), postsurgical (4, 24%) and trauma (1, 6%). Five patients (29%) had treatment with topical steroids prior to presentation. Fifteen patients (88%) had PG located on the palpebral conjunctiva and 2 (12%) involving the bulbar conjunctiva. Mean lesion size was 5.06 × 6.06 mm (range, 3–8 × 3–18 mm). Fifteen patients (88%) had complete lesion resolution with a mean treatment duration of 3.07 weeks (range, 2–5 weeks) and no adverse events or recurrences with a mean follow up of 9.47 months (range, 6–27 months). Two patients (12%) underwent lesion excision after 6 weeks of timolol failed to yield resolution. Topical timolol appears to be a well-tolerated nonsurgical treatment of ocular PG in both children and adults. Clinicians may wish to consider topical timolol to treat PG as opposed to topical steroids, given the inherent risk of steroid response ocular hypertension and the difficulty to measure intraocular pressure in younger children who require general anesthesia for excision.

Frontalis Muscle Flap Versus Maximal Anterior Levator Resection as First Option for Patients With Severe Congenital Ptosis

Ramón Medel, Salvador Molina, Luz Maria Vasquez, Josep Visa, et al.

Ophthal Plast Reconstr Surg Nov/Dec 2018;34:565–569

The paper aimed to compare 2 surgical techniques (frontalis flap versus maximal anterior levator resection) as first surgical options for the treatment of congenital ptosis with poor levator function in patients younger than 2 years of age with a follow up of 10 years. This was a retrospective study of 58 patients (71 eyelids) with severe ptosis and poor levator function who underwent frontalis muscle flap (FMF = 47) or maximal anterior levator resection (ALR = 24) for correction of their ptosis. Eyelid measurements were taken at baseline, 1, 5, and 10 years after surgery. The presence of complications, need for reoperations, and palpebral contour were evaluated. Most patients in both groups required only one surgical procedure with a stable average margin-reflex distance 1 over the 10-year follow-up period in both groups, with no statistically significant difference between the 2 techniques in achieving an adequate palpebral height after one single procedure. Eleven eyelids treated with FMF (23%) and 12 treated with ALR (50%) needed a reoperation, with a statistically significant difference between the 2 techniques. Five ALR patients (21%) and 6 FMF patients (13%) had alterations of eyelid contour. Pop-eyelid and eyelash ptosis were observed in 8% of patients operated with FMF. Good functional and aesthetic results were obtained with both surgical techniques. FMF required fewer reoperations compared with maximal ALR, offering a better long-term result without residual ptosis.

Current Management of Childhood Ptosis

Daniel T. Weaver *Curr Opin Opthalmol* 2018, 29:395-400

Ptosis in the pediatric population has an incidence of 7.9/100,000 children. Most often it is congenital and unilateral as well as isolated but it can occur in association with syndromes. It is classified into four subtypes: aponeurotic- usually due to trauma, myogenic- usually due to primary levator muscle dysgenesis, neurogenic- such as Horner's syndrome or myasthenia, and mechanical- due to a mass in the orbit or upper eyelid. Preoperative evaluation should include the assessment of the MRD, photographic documentation, measurement of the palpebral fissure before and after surgery as well as levator function. Surgical timing is dictated by the presence of amblyogenic ptosis which usually dictates repair prior to 6 months of age. The timing of nonamblyogenic ptosis is controversial. One study found that repair in children aged 2-4 was associated with no recurrence compared to 22% in other age groups. Techniques for repair include Muller's muscle resection for Horner's syndrome and mild cases of congenital ptosis. Levator muscle resection is usually performed in patients with moderate levator muscle function and mild-moderate ptosis. Maximal levator resection and frontalis suspension can be used in patients with poor levator function but an lead to overcorrection or corneal exposure. Materials used for frontalis suspension include sutures, as well as silicone rods, and fascia lata. Newer techniques such as the double rhomboid and two point suspension have been studied and various configurations for the sling have been suggested.

The paper discusses the timing and techniques for ptosis repair in children and reviews different techniques for repair with particular attention paid to frontalis suspension.

Perioperative use of intravenous dexamethasone in the management of congenital nasolacrimal duct obstruction with balloon dacryoplasty

Hussein MA, Lopez P. *JAAPOS*. Dec 2018;22(6):449-451.

This paper's purpose is to evaluate the effect of perioperative dexamethasone, presumed to reduce edema, on the success rate of nasolacrimal duct obstruction (NLDO) treatment by balloon dacryoplasty. The medical records of patients treated for NLDO using balloon dacryoplasty were reviewed retrospectively. Infants with <6 months' follow-up, genetic diseases, prior NLDO surgery, or anomalous nasolacrimal duct system were excluded. Patients either received intravenous dexamethasone perioperatively at a dose of 0.50 mg/kg (steroid group) or no dexamethasone (control group). Surgery was considered successful if there was no tearing or mucus discharge 1 month after surgery. A total of 74 patients were included in this study. In 71 eyes of 61 patients, dexamethasone was used; in 18 eyes of 13 patients, no dexamethasone was used. The mean age at treatment was 23.3 ± 15.6 months for the steroid group and was 22.5 ± 14.9 for the control group, with no difference between groups (P = 0.84). In the steroid group, 6 eyes (8.5%) had residual symptoms after surgery; in the control group 5 eyes (27.8%) had residual symptoms after surgery. There was a statistically significant higher success rate in the steroid group compared with the control group (P = 0.045; RR = 0.31 [95% CI, 0.11-0.9]). In this study cohort, use of perioperative dexamethasone was associated with a reduced rate of failure in children treated for NLDO using balloon dacryoplasty.

Congenital Nasolacrimal Duct Obstruction and Its Association With the Mode of Birth.

Mansha Palo, Shweta Gupta, Millind N.Naik, Mohammad Javed Ali
JPOS.2018; 55(4): 266-268

The purpose of this prospective interventional case series is to assess the association of congenital nasolacrimal duct obstruction (CNLDO) with mode of birth (vaginal or cesarean). Data from two hundred consecutive cases of CNLDO were analyzed including demographics, mode of delivery, elective or emergency cesarean section, primary or secondary cesarean sections, type of CNLDO (simple or complex), management and outcomes. Of the 200 consecutive patients, 97 (48.5%) were vaginal deliveries and 103 (51.5%) were cesarean sections. Of the 103 cesarean section patients, 57 (55.3%) were primary cesarean sections and the remaining were secondary cesarean sections. Based on the type of CNLDO, 172 (86%) were simple CNLDO. In general, the current study did

not find any significant association between the incidence of CNLDO and mode of delivery. Among the complex CNLDO cohort (n = 28), a significant association was found with cesarean section delivery (*P* = .016); however, no such association was noted when the patients were analyzed with regard to their age at presentation. The authors conclude that there is no overall significant association between CNLDO and the mode of delivery; however, the subset of patients with complex CNLDO showed a significant association with cesarean section. This study has several limitations such as lack of comparison with the general population and a smaller sample size within certain subgroups.

Pediatric Frontalis Suspension With Braided Polyester: A comparison of Two Techniques.

Andrea Molinari, Daniel T.Weaver, Todd A. Goldblum, David Silbert et al
JPOS.2018; 55(4):229-233

The purpose of this retrospective, non-randomized study is to demonstrate the benefits of using braided polyester in the management of severe or recurrent ptosis in children and young adults and to compare the efficacy of the two surgical techniques. The records of 30 patients (43 eyelid procedures) affected by congenital or acquired severe ptosis who underwent frontalis suspension with braided polyester from 2008 to 2016 were reviewed. Two surgical techniques were compared: the base-down triangle and the Fox pentagon, both of which were performed using a closed technique. Functional success was defined as clearing of the visual axis. Complications and results were examined including over/under corrections, granuloma formation, and localized cellulitis. The postoperative effectiveness of braided polyester in elevating the upper eyelid was evaluated by determining the eyelid fissure height, the MRD1, and the recurrence of ptosis. Functional success was defined as clearing of the central visual axis resulting in a postoperative MRD1 of at least 1mm without chin-up position. The study showed that functional success was obtained in 39 eyes of 43 procedures. Marginal reflex distance increased an average of 2.51 mm with the base-down triangle technique and 1.70 mm with the Fox pentagon technique (*P* = .05). The vertical palpebral fissure height increased an average of 4.60 mm with the base-down triangle technique and 2.45 mm with the Fox pentagon technique (*P* <.001). Mean follow-up duration was 38.6 months. Complications included untied suture (n = 2), suture dehiscence (n = 1), cellulitis (n = 2), and granuloma (n = 1). The authors concluded that Braided polyester was found to be a safe, effective, easy-to-handle, and low-cost sling material for frontalis suspension and should be considered for clinical use, especially in developing countries where the cost and availability of other materials represents a significant barrier to treatment. In the authors' experience, the base-down triangle technique appeared superior to the Fox pentagon technique. Weakness of the current study included retrospective nature, non-masked observers, and different surgeons. Although ptosis etiology was different in all cases, levator function was uniformly poor. Delayed undercorrection could also potentially occur with more prolonged follow-up.

Double rhomboid Suture Technique for Congenital Ptosis.

Austin Bach, Marcos Snachez-Gonzalez, Roberto Warman
J POS.2018; 55(2): 117-121

The purpose of this retrospective chart review was to evaluate the reoperation and complication rates of the double rhomboid suture technique for congenital ptosis. Records of 69 patients who were operated on between 2002 and 2016 were reviewed. All patients received the same operation of a double rhomboid frontalis sling[1] using a 1-0 Supramid (S. Jackson, Inc., Alexandria, VA) (nylon) suture on patients 36 months of age and older and a 3-0 Supramid suture on patients younger than 36 months. The 3-0 suture on a Ski needle was used instead of a Wright needle because the 3-0 suture is preloaded on the Ski needle. Four patients were excluded due to missing information in their charts and 27 patients were excluded due to having less than 6 months of follow-up.
For patients with more than 6 months of follow-up, there were 38 patients with 46 primary surgeries (22 [58%] males and 16 [42%] females). The average age at the first surgery was 39.34 ± 33.18 months. There was a mean follow-up time of 51.87 ± 53.79 months. There were 7 children who needed one revision and 1 child who needed a second revision, equaling a 23.9% rate of revision. Patients who had surgery before the age of 3 years had a statistically significant likelihood of needing a second surgery (chi-square test = 7.246, $P = .007$, 95% confidence interval = 0.027 to 0.687). It was also statistically significant ($P < .05$) that, throughout childhood, older patients were less likely to need a revision.
The authors conclude that the double rhomboid frontalis sling using a nylon suture is an effective technique to treat congenital ptosis. This technique is easy to master and has a low cost compared to techniques involving autografts and allografts. The authors also suggest that it is important to advise the family of the likelihood of a second surgery if there is a need to operate at a young age. This study is limited by its retrospective nature.

Simultaneous Versus Sequential Ptosis and Strabismus Surgery in Children

Karen E. Revere, Gil Binenbaum, Jonathan Li, Monte D. Mills, et al. *Ophthal Plast Reconstr Surg* 2018;34:280–283

The authors sought to compare the clinical outcomes of simultaneous versus sequential ptosis and strabismus surgery in children in a retrospective, single-center cohort study of children requiring both ptosis and strabismus surgery on the same eye. This is the first comparative study of simultaneous versus sequential ptosis and strabismus surgery. Simultaneous surgeries were performed during a single anesthetic event; sequential surgeries were performed at least 7 weeks apart. Outcomes were ptosis surgery success (margin reflex distance 1 ≥ 2 mm, good eyelid contour, and good eyelid crease); strabismus surgery success (ocular alignment within 10 prism diopters of orthophoria and/or improved head position); surgical complications; and reoperations. Fifty-six children were studied. The majority of patients had simple congenital ptosis and comitant strabismus. Of

these patients, 38 had simultaneous surgery and 18 sequential. Strabismus surgery was performed first in 38/38 simultaneous and 6/18 sequential cases. Mean age at first surgery was 64 months, with mean follow up 27 months. A total of 75% of children had congenital ptosis; 64% had comitant strabismus. The majority of ptosis surgeries were frontalis sling (59%) or Fasanella-Servat (30%) procedures. There were no significant differences between simultaneous and sequential groups with regards to surgical success rates, complications, or reoperations (all $p > 0.28$). The authors conclude that no advantage for sequential surgery was seen. Despite a theoretical risk of postoperative eyelid malposition or complications when surgeries were performed in a combined manner, the rate of such outcomes was not increased with simultaneous surgeries. As a result, the authors feel that performing ptosis and strabismus surgery together appears to be clinically effective and safe, and reduces anesthesia exposure during childhood.

Ophthalmic Manifestations of Facial Dog Bites in Children

Bratton EM, Golas L, Wei LA, Davies BW, et al. *Ophthal Plast Reconstr Surg.* 2018;34(2):106-109

This retrospective study characterizes the ophthalmic manifestations and periocular injuries of pediatric facial dog bites. The authors report the clinical features and management on the largest series of ophthalmic and periocular injuries associated with pediatric facial dog bites. These injuries occur in about 1 in 6 dog bites to the face and primarily involve the ocular adnexa. The study included all children younger than 18 years who sought medical attention after a dog bite to the face between January 1, 2003 and May 22, 2014 at a large tertiary pediatric hospital. A total of 1,989 children aged 0.19 to 17 years who had dog bites were identified. The average age was 4.3 years. Dog bites to the face occurred in most patients (n = 1, 414 [71%]). Of those children with facial dog bite injuries, 230 (16%) suffered ophthalmic manifestations. Eyelid injuries occurred in 227 (99%) of children, 47 (20%) sustained canalicular system injuries, 3 (1.3%) suffered corneal abrasions, and 2 patients sustained facial nerve injury resulting in lagophthalmos. No patients suffered vision loss. Complications occurred in 32 patients (14%), with the most common being epiphora in 9 patients (28%), upper eyelid ptosis in 8 (25%), and prominent scar formation in 4 patients (13%). Thirteen children (5.7%) needed one or more secondary procedure to correct complications. The incidence of infection was also high at 11.8% with the majority of these patients requiring intravenous antibiotics and hospitalization. In summary, despite early and appropriate surgical management in pediatric facial dog bites, complications and the need for revision surgery are relatively common.

22. INFECTIONS

Cortical Visual Impairment in Congenital Cytomegalovirus Infection.

Haoxing Douglas Jin, MD; Gail J.Demmler-Harrison, MD; Jerry Miller, MS, PhD; Jane C.Edmond, MD et al. *J of Ped Ophth & Strabismus*.2019; 56(3): 194-202

The purpose of this study is to describe the presentation, evolution and long-term outcome of cortical visual impairment (CVI) in patients with symptomatic congenital cytomegalovirus (CMV) infection, and to identify risk factors for the development of CVI in patients with symptomatic congenital CMV. In this retrospective subanalysis of a long-term prospective cohort study eleven of seventy-seven (14.3%) patients had symptomatic CMV, zero of a hundred nine had asymptomatic CMV and fifty-one control patients had CVI. Overall, patients with symptomatic CMV had worse vision than patients with asymptomatic CMV, who in turn had worse vision than control patients. Microcephaly, intracranial calcification, dilatation of ventricles, encephalomalacia, seizure at birth, optic atrophy, chorioretinitis/retinal scars, strabismus, and neonatal onset of sensorineural hearing loss were risk factors associated with CVI. The study concluded that CVI may result from symptomatic congenital CMV infection. CVI may be suspected when one or more classic CMV symptoms present at birth. Microcephaly, intracranial calcification, dilatation of ventricles, encephalomalacia, seizure at birth, optic atrophy, chorioretinitis/retinal scars, strabismus, and neonatal onset of sensorineural hearing loss are risk factors for CVI. The relationship of CVI and its risk factors in patients with CMV suggests the potential to predict the development of CVI through predictive modeling in future research. Early screening of CVI in children born with symptomatic congenital CMV can facilitate educational, social, and developmental interventions.

Measles

Strebel PM, Orenstein WA. *N Engl J Med*. July 2019;381:349-357

This article reviews the clinical features, management and epidemiology of measles in light of three measles outbreaks that took place in three under-vaccinated United States communities in late 2018-2019. Pediatric ophthalmologists may encounter measles patients because conjunctivitis can accompany cough, coryza (nasal drainage) and rash. The following are key points from the review article:

• Clinicians should suspect measles in persons who have a febrile illness with rash, especially if they lack documentation of measles vaccination, have recently traveled overseas, or are part of a community with low vaccine acceptance.
• Clinical specimens (e.g., serum and nasopharyngeal swab) for laboratory confirmation should be obtained from all patients suspected to have measles at their first contact with a health care provider.
• All suspected cases of measles should be reported immediately to the local or state health department without waiting for diagnostic test results.

• U.S. travelers to other countries account for a high proportion of imported cases of measles, which emphasizes the importance of measles vaccination before international travel.
• Serious adverse events after measles–mumps–rubella vaccination are rare and much less common than those associated with natural measles infection.

- Clinicians play a critical role in managing parental concerns about vaccination and in maintaining trust in vaccines.
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Randomized, Controlled, Phase 2 Trial of Povidone-Iodine /Dexamethasone Ophthalmic Suspension for Treatment of Adenoviral Conjunctivitis

Pepose JS, Ahuja A, Liu E, et al. *Am J Ophthalmol.* 2018 October;194:7-15.

The authors of this multicenter, randomized, vehicle-controlled, double-masked trial aimed to evaluate the efficacy and safety of a 0.6% povidone-iodine (PVP-I) and 0.1% dexamethasone suspension in patients with acute adenoviral conjunctivitis. Adults with a positive rapid adenovirus screening test were randomized to PVP-I 0.6%/dexamethasone 0.1%, PVP-I 0.6% alone, or vehicle, bilaterally, four times per day for 5 days. Patients were examined on days 3, 6, and 12 with the end points of clinical resolution and adenoviral eradication. The authors found that that the proportion of eyes with adenoviral eradication at day 3 and day 6 were higher in the PVP-I/dexamethasone group than in the other two groups. Additionally, the PVP-I/dexamethasone group had a higher proportion of clinical resolution at day 6 than the other two groups (31.3% vs. 10.9 % (vehicle) and 18.0% (PVP-I)). The authors concluded that the PVP-I /dexamethasone treatment was safe and improved eradication of the adenovirus and clinical resolution. They discussed that the drop tolerability was as good in the PVP-I dexamethasone group compared to the vehicle group. And one of the major limitations of this study is that it was only tested on adults (though included here because it certainly is relevant to the pediatric ophthalmologist).

Neurodevelopment in Infants Exposed to Zika Virus In Utero.

Lopes Moreira ME, Nielsen-Saines K, Brasil P, et al. *N Engl J Med*. 2018 Dec; 379:2377-9.

182 pregnant women with confirmed Zika virus were recruited for a prospective study; their babies were followed longitudinally until age 12-18 months, when they underwent neuroimaging, eye and hearing evaluations, and developmental assessments using the Bayley scale. Abnormal findings on neuroimaging were found in 37%. Among children with abnormal findings on brain imaging, 7 of 112 (6%) had an abnormal eye examination and 6 of 49 (12%) had an abnormal hearing assessment. Among 131 children who were exposed to Zika virus in utero and who underwent imaging, neurodevelopmental assessment, sensory or-

gan assessment, or all of these tests, 19 (14%) were found to have severe neurodevelopmental delay (2 SD below the mean score), sensory organ dysfunction, or both. The corollary is perhaps surprising, in that the majority of infants exposed to Zika virus in utero actually fared okay, without severe neurodevelopmental delay, ocular abnormalities or hearing loss.

Eye Findings in Infants with Suspected or Confirmed Antenatal Zika Virus Exposure

Irene Tsui, Maria Elisabeth Lopes Moreira, Julia D. Rossetto et al. *Pediatrics* October 2018; 142(4); e20181104

Because of the difficulty in obtaining viral confirmatory testing for Zika virus in pregnant women, the authors wanted to compare ophthalmic findings in patients with known Zika virus with those suspected Zika virus. This information could be used to guide screening recommendations in areas that commonly see patients exposed to Zika virus. After the ZIKA outbreak in Rio de Janeiro in 2015-2016, pediatric ophthalmologists performed complete eye examinations between 2016-2017 on infants known to have Zika exposure and those suspected of it. The five unique features of Zika virus syndrome include 1) severe microcephaly with partially collapsed skull, (2) thin cerebral cortices with subcortical calcifications, (3) macular scarring and focal pigmentary retinal mottling, (4) congenital contractures, and (5) marked early hypertonia and symptoms of extrapyramidal involvement. Two pediatric ophthalmologists examined each infant and were blinded to the RT-PCR results confirming or not confirming the diagnosis of Zika. If there was a discrepancy of the grading of their ophthalmologic findings, a third ophthalmologist evaluated the infants. There were 224 mother-infant pairs with 189 having RT-PCR testing of which 82.5% were positive for the Zika virus and 68 pairs who were diagnosed based on clinical findings. 21.8% of the RT-PCR-positive group and 38.2% of the unconfirmed RT-PCR group had ocular abnormalities. Of the 224 infants, 19.6% had optic nerve abnormalities and16.5% had retinal findings (chorioretinal atrophy or pigment mottling). Uncommon ocular findings included microcornea, iris coloboma, ON coloboma, microphthalmia, retinal vessel attenuation, and optic atrophy. 52% of infants had repeat testing and there was no evidence of worsening , ongoing activity or regression of ophthalmic lesions. Of the 224 evaluable infants, 40.2% had CNS abnormalities including microcephaly. Eye abnormalities were found in 54.4% of the patients with CNS abnormalities suggesting that there may be a correlation between ophthalmic and neurologic changes. The RT-PCR positive group and the RT-PCR unconfirmed group differed in their frequency of eye abnormalities and CNS abnormalities; with higher incidence of eye findings observed in the suspected, laboratory unconfirmed group. This difference likely reflects the referral pattern with more affected infants in the RT-PCR unconfirmed group being referred for findings consistent with ZIKA virus. Given the findings of the study, the authors highly recommend universal newborn eye screening in infants with potential antenatal ZIKV

exposure. The early identification of eye abnormalities will facilitate early low-vision interventions to improve visual function and outcomes in these children.

Visual function in infants with antenatal Zika virus exposure

Zin A, Tsui I, Rosetto JD, Gaw SL, et al. *JAAPOS*. Dec 2018;22(6):452-456.e1

The purpose of this paper is to report the findings of a cross-sectional study of visual function in infants with confirmed or suspected antenatal Zika virus (ZIKV) infection seen at a single referral center in Rio de Janeiro. Infants were examined following the ZIKV outbreak period at Instituto Fernandes Figueira/FIOCRUZ. Visual function was considered abnormal if an infant could not fix and follow a standardized high-contrast target (10 cm) by 3-6 months of age. Visual function and associations with structural eye abnormalities, central nervous system (CNS) abnormalities, microcephaly, and nystagmus were assessed. Sensitivity and specificity of screening criteria for structural eye abnormalities was assessed. A total of 173 infants met inclusion criteria for this study. 85 (49.1%) of the infants had abnormal CNS findings. Abnormal visual function was found in 52 infants (30.0%) and was significantly associated with eye abnormalities (40/52; OR = 44.2; 95% CI, 16.6-117.6), CNS abnormalities (50/52; OR = 64.0; 95% CI, 14.7-277.6), microcephaly (44/52; OR = 31.5; 95% CI, 12.7-77.8), and nystagmus (26/52; OR = 120.0; 95% CI, 15.6-924.5). Using microcephaly as screening criteria for the detection of eye abnormalities provided a sensitivity of 88.9% (95% CI, 76.0-96.3) and specificity of 82.8% (95% CI, 75.1-88.9). Using both abnormal visual function and microcephaly increased sensitivity to 100% (95% CI, 92.1-100.0) and decreased specificity to 80.5% (95% CI, 72.5-86.9). The authors recommend that infants with suspected antenatal ZIKV infection and reduced visual function should be referred to an ophthalmologist. The authors conclude that visual function assessments are helpful in screening for antenatal ZIKV exposure in resource-limited settings and can identify infants who may benefit from visual habilitation.

Resistant Infantile Bacterial Conjunctivitis in Egypt: A microbiology Study.

Aiman Abdeltawwab Hashish, Molham Abdelhafez Elbakary, Waleed Abdelhady Allam *J of Ped Ophth & Strabismus*.2018; 55(2): 135-139

The purpose of this study is to investigate the microbiological aspects of infantile bacterial conjunctivitis resistant to empirical topical antibiotic therapy in Egypt. Ninety-two eyes of 86 infants with bacterial conjunctivitis were included in this prospective study. They all failed to show evidence of clinical improvement after 2 weeks of empirical topical antibiotic therapy. Conjunctival swabs were obtained from all patients for bacterial culture and antibiotic sensitivity testing. The age of the participants ranged from 4 to 6 months. Culture results revealed infection with a solitary organism in 48.9% of eyes. Mixed bacterial growth was reported in

47.8% of eyes, whereas 3.3% of eyes showed no bacterial growth. The most commonly isolated organisms were Staphylococcus aureus, Streptococcus pneumoniae, and Pseudomonas aeruginosa. These organisms were highly sensitive to fluoroquinolones (levofloxacin, ciprofloxacin, ofloxacin, and norfloxacin), followed by chloramphenicol, vancomycin, and amikacin, and were resistant to carbapenems (imipenem and meropenem), fusidic acid, and pipracellin. According to the results of antibiotic sensitivity found in this study, it is recommended to change the current empirical antibiotic eye drops used in infantile conjunctivitis in Egypt from tobramycin or fusidic acid to other agents such as chloramphenicol, which is safe, inexpensive, readily available, and more effective. These results also provide strong evidence that fluoroquinolones can be reserved for resistant cases of bacterial conjunctivitis as long as other safe and effective agents are available.

23.PEDIATRICS/ INFANTILE DISEASE/ SYNDROMES

Assessment of corneal and lens clarity in children with Wilson disease.

Doğuizi S, Özateş S, Hoşnut FÖ, Şahin GE, et al. *JAAPOS* 2019 June: 23(3); 147.e1-147.e8

The aim of this multicenter cross-sectional study was to investigate the effect of copper accumulation on corneal and lens clarity in children with Wilson disease (WD) compared to healthy children. A total of 24 subjects with WD and 25 age-matched controls were recruited. Clinical and laboratory characteristics of the WD subjects were recorded. The Pentacam HR imaging system was used both for lens densitometry and corneal densitometry. Corneal densitometry values were higher in the posterior 6-10 mm ($P = 0.021$), posterior 10-12 mm ($P < 0.001$), posterior total diameter ($P = 0.037$), total thickness 10-12 mm ($P = 0.032$), and total thickness 6-10 mm zones and layers ($P = 0.040$) in the WD eyes than in control eyes. The lens densitometry values of zone 1 were higher in WD eyes ($P < 0.001$). There was a significant relationship between corneal densitometry values in the posterior 10-12 mm zones ($P = 0.012$; $r = 0.527$) and the duration of WD and liver copper content ($P = 0.016$; $r = 0.507$). A statistically significant correlation was also detected between lens densitometry values in zone 1 and WD duration ($P = 0.018$; $r = 0.426$). The authors conclude that in this study cohort, children with WD had decreased corneal and lens clarity, regardless of the presence of Kayser-Fleischer rings and sunflower cataracts. This study demonstrates that densitometry measurements using Scheimpflug imaging may detect corneal and lens involvement early in the disease course. These corneal and lenticular changes are very non-specific and can not be used for the diagnosis of Wilson disease. Nonetheless, the study results indicate that they correlate with disease duration and may be used as another parameter to determine response to treatment. This may warrant longitudinal studies.

Anesthesia for pediatric ophthalmologic surgery

Waldschmidt B and Gordon N *JAAPOS* 2019 June; 23(3): 127-131.

This review presents updated recommendations, based on existing clinical research, for anesthetic management of strabismus surgery in children. In children, unlike adults, eye surgery nearly always requires general anesthesia, even for brief procedures. Recommendations for preoperative anxiolysis, fasting guidelines, and management of upper respiratory infections are discussed. Airway considerations and the oculocardiac reflex are highlighted. The prevention of postoperative complications, including those related to opioid prescription therapy, is also addressed. Finally, given the 2016 warning from the Food and Drug Administration about anesthesia neurotoxicity in children, recent studies are also discussed by the authors on anesthetic neurotoxicity in children undergoing general anesthesia. This very important review offers practical approaches to various aspects of pediatric anesthesia and can assist strabismus surgeons in preparing their patients and families for surgery and in managing their patients pre-operatively, during surgery and post-operatively.

Ophthalmologic findings in the Cornelia de Lange syndrome

Angell Shi & Alex V. Levin (2019) Ophthalmologic findings in the Cornelia de Lange syndrome, *Ophthalmic Genetics*, 40:1, 1-6, DOI: 10.1080/13816810.2019.1571617

The authors reviewed 37 articles that were identified through an electronic search in PubMed and through the reference lists of previously conducted reviews. Studies of 30 or more patients were used to report frequencies of common and less common findings. The reviewed articles gave rise to 181 affected individuals demonstrating that ocular anomalies were present in the majority of patients (57%). Current genetic testing allows for genotype-phenotype associations that the authors suggest should heighten concern for certain conditions such as increased ptosis severity in patients with truncating mutations in NIPBL compared to missense mutations, as well as the higher prevalence rates of nystagmus and strabismus in patients with NIPBL mutations. The small number of patients in this rare condition limit the ability to demonstrate if all of the genotype-phenotype associations are statistically significant. The authors suggest an ophthalmologic exam at diagnosis Treatment should be instituted where indicated to avoid permanent vision loss. Difficulty in examination of patients with this syndrome may make it difficult to estimate frequency of ophthalmologic abnormalities. It may be helpful to conduct an examination under anesthesia when a complete examination cannot be accomplished and to combine procedures if the patients is undergoing another surgical intervention when possible.

The authors present a thorough and complete review of Cornelia de Lange Syndrome demonstrating possible genotype-phenotype correlations that could require heightened surveillance and be used to counsel families.

Development of Pediatric Eye Questionnaires for Children with Eye Conditions

Hatt SR, Leske DA, Castaneda YS, et al. *Am J Ophthalmol.* 2019 April; 200: 201-217.

The purpose of this study was to develop a patient-derived Pediatric Eye Questionnaires (PEDEyeQ) to separately assess eye related quality of life (ER-QoL) and functional visual in children. Based on a previous study by the same authors, specific concerns about functional vision and ER-QOL were identified using individual interviews. A large pool of potential questions was created. This study was the second stage of the process where the authors used these items to develop patient reported outcome measures to ensure content validity. The third step in developing these questionnaires (not reported here) will be to determine validity and reliability of the questions. There were a total of 444 children with eye conditions (0 to 18 years old) across 10 diagnostic categories included in this study. The parents of these children and 277 of the children (5 and older) completed the master questionnaires. The authors then used Rasch maps to decide which questions to retain based on reliability indices and item separation indices until there were 10 or fewer items in each domain. The authors hope to validate the questionnaires as their next step with the goal of separately being able to evaluate ER-QoL and functional vision in pediatric patients with a range of eye pathology. The authors point out the major limitation being the lack of diversity in their patient demographics, but this doesn't take away from the need for the rigorous development of pediatric specific ER-QOL scores that can be used for multiple eye conditions.

Ocular Adverse Events Associated with MEK Inhibitors

Silvia Mendez-Martinez, Pilar Calvo, Oscar Ruiz-Moreno, Nieves Pardinas Baron, et al. *Retina.* August 2019 ;39(8):1435-1450

MEK (MAP/ERK kinase) inhibitors act to suppress the mitogen-activated protein kinase (MAPK) pathway, which is involved in a variety of cellular processes and plays a fundamental role in oncogenesis. This medication does have several ocular toxicities. This is a meta-analysis review article reporting these ocular adverse effects (OAE). Reported OAEs include retina vein occlusion and MEK-associated retinopathy (MEKAR), which is subretinal fluid. This is thought to occur since the MAPK pathway participates in the maintenance, protection and repair of the retina and RPE, so its' inhibition leads to OAEs. Other reported OAE include dry eye symptoms, ocular adnexal abnormalities, visual field defects, and panuveitis. The incidence of OAEs is up to 90%. MEKAR and other OAEs are typically self -limited. This article highlights the OAEs seen in this medication, which is now used to treat several pediatric cancers.

Longer-Term Assessment of Azithromycin for Reducing Childhood Mortality in Africa.

Keenan JD, Arzika AM, Maliki R, Boubacar N, et al. *N Engl J Med* June 2019; 380:2264-2265

A previous trial conducted in Niger showed that mass administration of azithromycin twice a year for 2 years resulted in 18% lower childhood mortality than administration of placebo. Whether this benefit could increase with additional azithromycin administration or wane owing to antibiotic resistance was unknown. In the first trial (MORDOR I), 594 communities were randomly assigned to four twice-yearly distributions of either azithromycin or placebo to children 1 to 59 months of age. In this follow up trial (MORDOR II), all these communities received two additional open-label azithromycin distributions. All-cause mortality was assessed twice yearly by census workers who were unaware of participants' original assignments.

In MORDOR II, mortality was 24.0 per 1000 person-years (95% confidence interval [CI], 22.1 to 26.3) in communities that had originally received placebo in the first year and 23.3 per 1000 person-years (95% CI, 21.4 to 25.5) in those that had originally received azithromycin in the first year, with no significant difference between groups (P = 0.55). In communities that had originally received placebo, mortality decreased by 13.3% (95% CI, 5.8 to 20.2) when the communities received azithromycin (P = 0.007). In communities that had originally received azithromycin and continued receiving it for an additional year, the difference in mortality between the third year and the first 2 years was not significant (-3.6%; 95% CI, -12.3 to 4.5; P = 0.50).

The effect of mass administration of azithromycin on childhood mortality in Niger did not wane in the third year of treatment (although there was also not additional benefit to receiving azithromycin for a third year). Childhood mortality decreased when communities that had originally received placebo received azithromycin, which essentially replicated the results of MORDOR I. This study did not address why mortality declined with mass azithromycin administration, but there are other parallel trials investigating the mechanisms.

Why is childhood mortality and mass azithromycin administration of any relevance to pediatric ophthalmologists? This study was designed as a follow up to data coming from trachoma treatment programs: azithromycin given en mass to children in communities w endemic trachoma also ended up improving childhood mortality. It is reminiscent of the studies on vitamin A supplementation in curing corneal blindness and simultaneously (with dietary measures and measles vaccination) reducing childhood mortality. This study is a modern day example of an ophthalmological intervention having a major impact on global health.

Macrolide Resistance in MORDOR I — A Cluster-Randomized Trial in Niger

Doan T, Arzika AM, Hinterwith A, Maliki R, et al. *N Engl J Med* June 2019; 380:2271-2273

The MORDOR I study was a study of childhood mortality in 594 communities in Niger that were randomly assigned to four twice-yearly distributions of either azithromycin or placebo given to children 1 to 59 months of age. Mass administration of azithromycin resulted in 18% lower childhood mortality than administration of placebo. This accompanying study compared proportions of macrolide-resistant pneumococcus in the children in the azithromycin group to those in the placebo group.

Broth dilution assays of pneumococcus isolated from nasopharyngeal swabs collected at 24 months (6 months after the fourth twice-yearly treatment) were used for analysis. Pneumococcus isolation and resistance testing were performed according to standard protocols. Because the intestine is a reservoir for antibiotic resistance genes, the study also evaluated rectal samples collected at 24 months for these genes with the use of metagenomic DNA sequencing.

The proportion of macrolide resistance in nasopharyngeal *S. pneumoniae* was higher in the communities receiving azithromycin (mean, 12.3%; 95% CI, 5.7 to 20.0) than in those receiving placebo (mean, 2.9%; 95% CI, 0 to 6.1; P=0.02). Similarly, genetic determinants of macrolide resistance in the intestinal flora were more prevalent in the communities that received azithromycin (68.0%; 95% CI, 61.3 to 74.0) than in those that did not (46.7%; 95% CI, 36.0 to 54.0; P=0.002).

In conclusion, at 2 years, mass treatment with oral azithromycin in preschool children in Niger twice a year increased resistance to macrolides. The long-term effects of prolonged mass distribution of azithromycin in preschool children remain to be determined. Any policy regarding implementation of mass antibiotic administration should be coupled with careful monitoring for antibiotic resistance.

This manuscript is of relevance to pediatric ophthalmologists because it is an extension of data from trachoma treatment programs: azithromycin given en mass to children in communities w endemic trachoma improved childhood mortality but increased macrolide resistance. Ophthalmological interventions are having an impact on global health (reminiscent of the vitamin A story) and also questioning one of the basic tenets of public health: should we really avoid indiscriminate use of antibiotics?

Hope and Humility for Azithromycin

Bar-Zeev N, Biostat M, Moss MJ. *N Engl J Med* June 2019; 380:2264-2265

This is an editorial accompanying the “Longer-Term Assessment of Azithromycin for Reducing Childhood Mortality in Africa” and “Macrolide Resistance in MORDOR I — A Cluster-Randomized Trial in Niger “ publications. The authors pose the question: is azithromycin the elixir of life? Data from trachoma studies

in Ethiopia and the childhood mortality study in Niger show a decrease in childhood mortality with mass azithromycin administration. The findings in these studies raised more questions than they answered. What mechanism explains these observations? Which groups would it be best to target with azithromycin? And what of the thorny issue of antimicrobial resistance? The data from the aforementioned studies differ from data coming from a study in Mali and Burkina Faso, where azithromycin administration decreased morbidity but did not improve (or perhaps even worsened) childhood mortality. Perhaps our hopes for azithromycin are too high, and the benefit to some children will be eclipsed by harm to others with increase in antibiotic resistance.

Neonatal Herpes Simplex Virus Infection Among Medicaid-Enrolled Children: 2009-2015

Sanjay Mahant, Matt Hall, Amanda Schonodelmeyer, et.al. *Pediatrics* April 2019; 143(4): e20183233

Over the past few decades, experts have anecdotally detected an increase in neonatal HSV incidence over the past decade. This study aimed to evaluate the incidence, mortality, and health care usage related to neonatal HSV infection. It was a retrospective, multistate, longitudinal cohort study of HSV infection over a 7-year period using the IBM MarketScan Medicaid Database (MMD). The study identified 900 neonates with HSV infection out of 2,107,124 births with boys and non-Hispanics having more frequent diagnoses. The incidence rate of infection diagnosis increased from 3.4/10,000 births to 5.3/10,000 births from 2009 to 2015 (an increase of 56%). Of the 900 infants with HSV, 54 died which equates to a 6% hospital mortality rate, but there was no significant change in mortality rate over the study period. The median payment for the index hospitalization was $32,683 and a total cumulative payment for all cases was $54,448,783. Within 6 months of discharge, 46% of neonates with HSV required an ED visit and 16% were re-hospitalized. The increase in HSV rate may be attributable to more susceptibility of adolescents to HSV-1 (determined by another study) and increasing oral sex practices over the past 2 decades. In other similar studies, the research demonstrates higher mortality rates. This difference in mortality may be due to diagnostic differences between Medicaid data and the other sources of information. The study suggests substantial health care utilization after hospitalization supporting the need for comprehensive, coordinated care after diagnosis. There should also be public health initiatives targeting disease prevention to decrease the rate of HSV infection.

Optic coherence tomography appearances of retinal astrocytic hamartoma and systemic features in tuberous sclerosis of Japanese patients

Kato A, Obana A, Gohto Y, Seto T, Sasano H *EJO* May 2019,29(3) 330–337

This retrospective observational case series aimed to describe the optical coherence tomography findings of retinal astrocytic hamartoma of tuberous sclerosis and to confirm the association between the type of retinal astrocytic hamartoma and systemic manifestations in Japanese patients. The medical records of 35 patients with tuberous sclerosis who underwent ophthalmological examination were reviewed. The retinal astrocytic hamartomas were classified into four types based on the optical coherence tomography findings, and their association with systemic disease was evaluated. A total of 40 retinal astrocytic hamartomas in 13 eyes of eight patients aged 4–28 years were identified. Optical coherence tomography images were obtained for 23 lesions in 10 eyes of seven patients. Retinal astrocytic hamartomas were seen as protruding lesions of varying heights (maximum thickness, range between 221 to 1043 μm). Of the 23, 15 lesions showed homogeneous reflectivity; in six lesions, hyper-reflective spots that presumably represented intratumoral calcification were noted. Vitreous changes were noted in 13 lesions; vitreous seeding by retinal astrocytic hamartoma was observed in seven eyes. There were no significant differences in the rates of each systemic feature among the optical coherence tomography types. Retinal astrocytic hamartomas were classified into four types according to the previous reports; however, this classification may be worthless because the extent of protrusion did not correspond to the intratumoral characteristics, and the involved depth of the retina was not same even in the same type. An association between the type of retinal astrocytic hamartoma and systemic manifestations was not confirmed in this small case series. We considered that the classification of retinal astrocytic hamartoma and its association with systemic manifestations need further study.

Ocular manifestations of Marfan syndrome in children and adolescents.

Salchow DJ, Gehle P. *Eur J Ophthalmol.* Jan 2019.

The authors performed a retrospective comparative cohort study to compare ocular findings in 52 patients with confirmed Marfan syndrome versus controls to clarify the salient ocular findings in this condition. Primary findings included flatter cornea, higher astigmatism, thinner central cornea, and higher myopia than controls. Patients with Marfan syndrome had transillumination defects in 19.6% of patients and ectopia lentis was defected in 49% of patients. This study serves to further highlight eye findings in children with Marfan syndrome.

The Phenotypic Spectrum of Albinism.

Kruijt CC, de Wit GC, Bergen AA, Florijn RJ et al. *Ophthalmology*. 2018 Dec;125(12):1953-1960.

This retrospective cohort study aims to describe the phenotypic spectrum of a large cohort of albino patients, to investigate the relationship between the ocular

abnormalities and the visual acuity (VA), and to define diagnostic criteria for the white population. The authors also estimated the prevalence of albinism in The Netherlands. They investigated the phenotype of 522 patients with albinism from the databases of Bartiméus (452 patients), Leiden University Medical Center (44 patients), and the Academic Medical Center Amsterdam (26 patients).

Collected data included clinical, genetic, and electrophysiologic data of patients with albinism. Grading schemes for iris translucency, fundus hypopigmentation, and foveal hypoplasia were utilized. The main outcome measures were visual acuity, nystagmus, iris translucency, fundus pigmentation, foveal hypoplasia, and misrouting.

Nystagmus was absent in 7.7% (40/521), iris translucency could not be detected in 8.9% (44/492), 3.8% (19/496) had completely normal fundus pigmentation, 0.7% (3/455) had no foveal hypoplasia, and misrouting was not established in 16.1% (49/304). The VA varied from -0.1 to 1.3 logarithm of the minimum of angle of resolution (logMAR). The foveal hypoplasia grading correlated best with the VA ($r = 0.69$, $P < 0.001$), whereas iris translucency, fundus pigmentation, and misrouting did not predict the VA significantly. The authors estimated a prevalence of albinism in The Netherlands of at least 1:12 000.

The authors conclude that none of the characteristics of albinism were consistently present in this cohort. To be able to distinguish albinism from other conditions with similar ocular features, especially in northern and western European countries, they propose major and minor clinical criteria. Major criteria would be (1) foveal hypoplasia grade 2 or more, (2) misrouting, and (3) ocular hypopigmentation, either iris translucency or fundus hypopigmentation grade 2 or more. Minor criteria would be (1) nystagmus, (2) hypopigmentation of skin and hair, (3) grade 1 fundus hypopigmentation, and (4) foveal hypoplasia grade 1. They propose that 3 major criteria or 2 major and 2 minor criteria are necessary for the diagnosis. In the presence of a molecular diagnosis, 1 major criterion or 2 minor criteria will be sufficient.

Joubert Syndrome: Ophthalmological Findings in Correlation with Genotype and Hepatorenal Disease in 99 Patients Prospectively Evaluated at a Single Center

Brooks, BP, Zein, WM, Thompson AH, Mokhtarzadeh M, et al. *Ophthalmology* 125; 12 December 2018: 1937-1952.

Ocular involvement in Joubert Syndrome (JS) varies from mild to severe, often depending on genetic cause; sometimes, variability can be noted even within the same genotype. Ocular involvement can be developmental (e.g., coloboma) or degenerative (e.g., retinal dystrophy). This variability makes it difficult to predict the functional visual trajectory for individual patients. This study describes the varying ocular phenotypes in JS patients, with correlation to systemic findings and genotype. All patients were systematically and prospectively examined at the National Institutes of Health (NIH) Clinical Center in the setting of a dedicated

natural history clinical trial. All ninety-nine patients underwent genotyping for JS, followed by complete age-appropriate ophthalmic examinations. Color and fundus autofluorescence imaging, Optos wide-field photography (Dunfermline, Scotland, UK), and electroretinography (ERG) were performed when possible. The VA (with longitudinal follow-up where possible), ptosis, extraocular muscle function, retinal and optic nerve status, and retinal function as measured by ERG. Among patients with JS with quantifiable VA (68/99), values ranged from 0 logarithm of the minimum angle of resolution (logMAR) (Snellen 20/20) to 1.5 logMAR (Snellen 20/632). Strabismus (71/98), nystagmus (66/99), oculomotor apraxia (60/77), ptosis (30/98), coloboma (28/99), retinal degeneration (20/83), and optic nerve atrophy (8/86) were identified. Based on the findings, the authors recommend regular monitoring for ophthalmological manifestations of JS beginning soon after birth or diagnosis. We demonstrate delayed visual development and note that the amblyogenic time frame may last significantly longer in JS than is typical. In general, patients with coloboma were less likely to display retinal degeneration, and those with retinal degeneration did not have coloboma. Severe retinal degeneration that is early and aggressive is seen in disease caused by specific genes, such as *CEP290*- and *AHI1*-associated JS. Retinal degeneration in *INPP5E-, MKS1-,* and *NPHP1*-associated JS was generally milder. Finally, ptosis surgery can be helpful in a subset of patients with JS; decisions as to timing and benefit/risk ratio need to be made on an individual basis according to expert consultation. Because this study required a week-long, on-site evaluation, this may had led to sampling bias toward families who were able to make accommodation. Very severely affected JS patients, who require intensive care, including as mechanical ventilation, may be under represented in this study.

Adrenal Suppression in Infants Treated with Topical Ocular Glucocorticoids

Bangsgaard R, Main KM, Boberg-Ans G, Monten La Cour et al. *Ophthalmology* 125; 10 Oct 2018: 1638-1643.

Increasingly, clinical evidence suggests that the any treatment with glucocorticoids (GC) may suppress adrenal function and cause Cushing's syndrome irrespective of administration route. Adrenal suppression after topical ocular GCs is not well documented. The main objective of the study was to analyze the incidence of adrenal suppression and the glucocorticoid (GC) dose per kilogram body weight in infants treated with standard protocol for topical ophthalmic GCs after congenital cataract surgery. The authors analyzed retrospectively collected data from patients younger than 2 years of age who underwent operation for congenital cataract between January 2011 and May 2015 in a single center. Standard regimen after cataract surgery was subconjunctival injection at the time of surgery 0.5 to 1.0 mL methylprednisolone acetate 40 mg/ml (Depo-Medrol, Pfizer, Belgium). This was followed by topical administration of dexamethasone 1 mg/ml (Maxidex, Alcon, UK) eye drops 6-8 x/day for the first week, then 4 to 6 drops for the second week then tapering by one drop per week, hence up to 6

weeks of administration of drops. A standard ACTH provocation test was scheduled approximately 1 month post-operatively whenever possible. Among 26 consecutive infants, 15 (58%) were tested while they were still on GC treatment. Ten of these 15 infants (67%) had adrenal suppression, 2 of whom had obvious clinical signs of Cushing's syndrome and 1 of whom had signs of Addisonian crises during general anesthesia. Eleven of the 26 infants (42%) were tested at a median time of 21 days (range, 6–89) after treatment cessation, and they all had normal test results. Infants with suppressed adrenal function had received cumulative GC doses per body weight that were significantly higher the last 5 days before testing compared with children with normal test results. Infants with adrenal suppression were treated with hydrocortisone replacement therapy. Adrenal function recovered after a median of 3.1 months (range, 2.3 months to 2.3 years). In conclusion two thirds of the infants tested during treatment with a standard GC protocol after congenital cataract surgery showed adrenal suppression. There was a significant association between the cumulative daily dose of GCs and the test result. Because adrenal suppression is a serious but treatable condition, the authors recommend a systematic assessment of adrenal function in infants treated with doses of topical ocular GCs comparable to our regimen and careful evaluations of other treatment regimens.

Macular and Retinal Nerve Fibre Layer Thinning in Xeroderma Pigmentosum: A Cross-sectional Study

Anna M. Gruener and Ana M. S. Morley *Neuro-ophth* Dec 2018, 42(6), 356–366

The purpose of this study was to evaluate retinal thickness in different Xeroderma Pigmentosum (XP) complementation groups using spectral-domain optical coherence tomography (SD-OCT). This was a cross-sectional pilot study of 40 patients with XP. All patients had healthy-looking retinae and optic nerves on slit lamp biomicroscopy, and subtle or no neurological deficits. Patients were divided into two groups based on the known tendency for neurodegeneration associated with certain XP complementation groups. A third control group was obtained from a normative database. Using SD-OCT, we compared peripapillary retinal nerve fibre layer (pRNFL) and macular thickness between the groups. XP patients with a known tendency for neurodegeneration were found to have a statistically significant reduction in both pRNFL ($p < 0.01$) and macular thickness ($p < 0.001$) compared withhealthy controls. In contrast, there was no statistically significant difference between pRNFL and macular thickness in XP patients not expected to develop neurodegeneration compared to the same control group. When both XP groups were compared, a statistically significant reduction in total pRNFL ($p = 0.02$) and macular thickness ($p = 0.002$) was found in XP patients predisposed to neurodegeneration.Our results suggest that pRNFL and macular thickness are reduced in XP patients with a known tendency for neurodegeneration, even before any marked neurological deficits become manifest. These findings demonstrate the potential role of retinal thickness as an anatomic biomarker and prognostic indicator for XP neurodegeneration.

Functional and cognitive vision assessment in children with autism spectrum disorder

Bhaskaran S, Lawrence L, Flora J, Perumalsamy V. *JAAPOS*. Aug 2018;22(4):304-308.

This paper's goal is to assess functional vision in children with autism spectrum disorder (ASD) with a cognitive visual function battery in addition to standard ophthalmic examinations. For this study, subjects were recruited from a school for children with ASD. In addition to a comprehensive ophthalmic examination, all children underwent cognitive vision assessment at a tertiary ophthalmological care center in India. A total of 30 children were included in the study. The distribution of the number of children with mild to moderate versus severe ASD was nearly equal based on CARS autism scores. The majority of subjects had normal color vision (16/18), contrast (24), shape discrimination (26), and perception of directionality (28). Most were not able to identify optical illusions or differentiate tests of emotions. Ocular pursuits, saccades, and recognition of size differences were often abnormal. Poor visual closure was noted in (11) subjects. The duration of fixation to Heidi face target was inversely proportional to the severity of ASD. The study further established that cognitive visual impairment was present in children with ASD irrespective of their severity of ASD. In examining autism patients, it is important that many of these patients will have some form of cognitive visual impairment independent of ASD severity.

Changes in refractive errors in albinism: a longitudinal study over the first decade of life

Schweigert A, Lunos S, Connett J, Summers CG. *JAAPOS*. Dec 2018;22(6): 462-466.

The goal of this study is to analyze longitudinal changes in refraction in patients with albinism. The medical records of 481 patients were reviewed retrospectively to identify patients who had cycloplegic refractions at three ages: visit A, 0-18 months old; visit B, 4-6 years old; visit C, 8-10 years old. The authors recorded refraction, type of albinism, glasses wear, and best-corrected visual acuity at visit C. Only right eyes were analyzed. A total of 75 patients were included in this study. Of these, 73 wore glasses and 73 presented with nystagmus. Mean best-corrected visual acuity at visit C was 20/72 (range, 20/25-20/200). Mean spherical equivalent was 2.81 ± 2.4 D at visit A, 2.53 ± 3.4 D at visit B, and 2.15 ± 4.0 D at visit C. These values did not differ significantly from visits A to C ($P = 0.0578$). Mean astigmatism for the three time points was 1.60 ± 1.00 D, 2.50 ± 1.14 D, and 2.87 ± 1.45 D; these values did differ significantly from A to C ($P < 0.0001$). Subgroup analysis for OCA1A (16 eyes), OCA1B (20 eyes), and OCA2 (30 eyes) showed an increase in astigmatism from A to C, with a significant difference in means ($P < 0.0001$, $P < 0.0001$, and $P = 0.0001$, resp.). Worse best-corrected visual acuity and higher mean astigmatism at visit C were found

for OCA1A (20/104 and +4.08 ± 1.34) compared to OCA1B (20/59 and +2.30 ± 1.36; P < 0.0001) and OCA2 (20/66 and +2.53 ±1.21; P < 0.0001); OCA1A patients also had the highest rate of increase of astigmatism with age. The authors note that their results corroborate the presence of impaired emmetropization in patients with albinism and recommend that children with albinism require periodic cycloplegic refraction, because astigmatism often increases within the first 10 years of life. They conclude that the refractive error in the first 10 years of life in persons with albinism follows a unique trend with increasing hyperopia with WTR that increases wit little change in the spherical equivalent and axis. The most severe type of albinism (OCA1A) has higher astigmatism and worse visual acuity compared to the other types.

Patient-derived questionnaire items for patient-reported outcome measures in pediatric eye conditions

Hatt SR, Leske DA, Castaneda YS, Wernimont SZ, et al. *JAAPOS*. Dec 2018;22(6):445-448.e2.

The purpose of this paper is to identify specific health-related quality of life (HRQOL) and functional vision concerns of children with eye conditions, and create comprehensive lists of potential questionnaire items as a first step in developing patient-reported outcome measures. Children experiencing a range of pediatric eye conditions, along with one of their parents, were interviewed to identify specific concerns. Transcribed interviews were reviewed, and specific HRQOL and functional vision concerns were coded independently by two reviewers. Coded concerns were reviewed to formulate questions to address specific child concerns (derived from child and parent interviews) and specific parent concerns. Questions were grouped into bins of like questions. Two comprehensive lists of questions were formulated, one addressing child-related concerns and one addressing parent-related concerns. This study included 180 children and 328 parents. A total of 614 individual child questions were grouped into 36 bins (eg, appearance, coordination, glasses, learning), and 589 parent questions were formulated and grouped into 61 bins (eg, having to assist the child, worry about deterioration, time off work, safety). Using rigorous methods based on individual interviews, we identified a comprehensive list of patient- and parent-derived questionnaire items that address functional vision and HRQOL concerns of children with eye conditions and of their parents. The authors plan to use this large pool of potential questionnaire items to develop a formal set of pediatric outcome measures, and this pool of questions may also be a resource for future research. The authors will be presenting the future stages of creating and testing these questionnaires in future studies.

Functional vision and quality of life in children with microphthalmia/anophthalmia/coloboma—a cross-sectional study

Dahlmann-Noor A, Tailor V, Abou-Rayyah Y, Adams G, et al. *JAAPOS.* Aug 2018;22(4):281–285.e1

The goal of this study was to determine the child's and parental perception of functional visual ability (FVA), vision-related and health-related quality of life (VR-QoL, HR-QoL) in children with microphthalmia/anophthalmia/coloboma (MAC).Between June 25, 2014, and June 3, 2015, the authors carried out a cross-sectional observational study at Moorfields Eye Hospital, London, UK, enrolling 45 children 2-16 years of age with MAC attending our clinics, and their parents. To assess FVA, VR-QoL, and HR-QoL they asked participants to complete three validated tools, the Cardiff Visual Ability Questionnaire for Children (CVAQC), the Impact of Vision Impairment for Children (IVI-C) instrument, and the PedsQL V 4.0. The main outcome measures were the FVA, VR-QoL, and HR-QoL scores, reported by children and parents. In children with MAC, FVA is moderately reduced, with a median CVAQC score of −1.4 (IQR, −2.4 to 0.4; range, −3.0 [higher FVA] to +2.8 [lower FVA]). VR-QoL and HR-QoL are greatly reduced, with an IVI-C median score of 63 (IQR, 52-66; normal VR-QoL, 96), a median self-reported PedsQL score of 77 (IQR, 71-90; normal HR-QoL, 100) and parental score of 79 (IQR, 61-93), and a family impact score of 81 (67-93). A greater number of surgeries was found to be associated with worse HR-QoL scores reported by both children and parents. Psychosocial well-being scores are lower than physical well-being scores in this group of patients. Additionally, parents and children have a different perception of the impact of the condition on the child's HR-QoL. MAC has a significant impact on a child's FVA and QoL, similar to that described by children with acute lymphoblastic leukaemia and chronic systemic conditions. Physicians should consider that children and families with microphthalmia/anopthalmia/coloboma may benefit from psychosocial support.

The Eye Examination in the Evaluation of Child Abuse

Cindy W. Christian, Alex V. Levin, Council on Child Abuse and Neglect, Section on Ophthalmology, American Association of Certified Orthoptists, American Association for Pediatric Ophthalmology and Strabismus, American Academy of Ophthalmology *Pediatrics*. August 2018; 142(2): e20181411.

In this clinical report, the authors outline the current knowledge regarding retinal hemorrhages (RHs) in abusive head trauma (AHT) as well as provide recommendations for the examination of children suspected of AHT. Because RHs occur in approximately 75% of victims of AHT and can lead to significant visual loss, it is imperative that ophthalmologists examine these children in a timely fashion and report their findings to the medical team and state agencies. Injuries related to child abuse may be external such as periorbital ecchymoses, frontal and orbital roof fractures, and subconjunctival hemorrhages. Internal injuries can include corneal abrasions/lacerations, traumatic hyphemas, traumatic cataracts, and ruptured globes. For more than 30 years, the key ocular indicator of abuse has been known to be RHs. Approximately 25% of victims of AHT have no RH, and one-third of all cases have mild to moderate RH. In general, the number and severity of RHs correlate with the severity of neurologic injury and are infrequently

found in neurologically normal children. RHs that are too numerous to count, multilayered, bilateral, and extend to the ora serrata are highly specific for AHT. Retinal folds, retinoschisis, and retinal detachments can also be observed in AHT. The timing of the RHs cannot be accurately timed. Intra-retinal hemorrhages resolve more quickly than pre-retinal hemorrhages and may last only a few days. Therefore, it is advisable for an ophthalmologic exam to optimally occur within 24 hours of suspicion. The differential diagnosis for RHs include meningitis, leukemia, coagulopathy, and retinal disorders but these are often confined to the posterior pole of the retina. The birth process also can result in RHs (vacuum assisted delivery >70% and routine cesarean delivery at <20%). The flame hemorrhages related to birth resolve by 2 weeks and the dot or blot hemorrhages resolve by 6 weeks. Research shows that the RHs in ART are related to the vitreoretinal traction sustained during the repetitive acceleration and deceleration mechanism. These forces cause the RHs and macular retinoschisis. 40% of AHT victims have visual problems that are most often related to the occipital cortical damage and/or optic nerve injury. The RHs generally resolve without sequelae but in more severe cases can lead to macular scarring or fibrosis, retinal detachment, and amblyopia. Because of the key information found in an ophthalmologic exam in cases of AHT, it is critical that a child suspected of abuse undergo as thorough of an ocular examination as possible.

Ocular findings in Loeys-Dietz syndrome.

Busch C, Voitl R, Goergen B, et al. *Br J Ophthalmol.* 2018 Aug;102(8):1036-1040.

Loeys-Dietz syndrome (LDS), an autosomal-dominant connective tissue disorder, is characterized by systemic manifestations including arterial aneurysm and craniofacial dysmorphologies. Although ocular involvement in LDS has been reported, detailed information on those manifestations is lacking. This is a retrospective chart review of patients with diagnosed LDS and comparison with age-matched control patients. The authors found atients with LDS less frequently had iris transillumination, cataract and glaucoma compared with controls. Scleral and retinal vascular abnormalities were not found in any of the LDS eyes. Ectopia lentis was found in one patient with LDS. The eyes of patients with LDS tended to be more myopic and longer. Central corneal thickness was significantly reduced in LDS eyes. Corneal curvature and interpupillary distance did not differ significantly between both groups. Visual acuity was similar between both groups. This paper revealed that decreased central corneal thickness and a tendency towards mild myopia and increased axial length were most characteristic findings in LDS. In contrast to previous reports, hypertelorism, scleral discoloration and retinal vascular abnormalities were not associated with LDS.

24.<u>UVEITIS/ SYSTEMIC</u>

Successful treatment with infliximab after adalimumab failure in pediatric noninfectious uveitis.

Ashkenazy N, Saboo US, Abraham A, Ronconi C et al. *J AAPOS*. 2019 May 4.

This study describes the use of infliximab after adalimumab failure in the treatment of pediatric noninfectious uveitis.
A retrospective analysis was performed on the medical records of pediatric patients with noninfectious uveitis treated with infliximab for a minimum of 6 months after previously failing to achieve steroid-free remission using adalimumab at the University of Texas Medical School and Children's Medical Center between September 2015 and March 2018. Rates of achieving disease activity quiescence and steroid-free remission as well as incidence of adverse events were calculated. A total of 13 patients with noninfectious uveitis refractory to treatment with adalimumab met inclusion criteria. Three (23%) had anterior uveitis, 4 (31%) had pars planitis, and 6 (46%) had panuveitis. Eleven (85%) patients had preexisting ocular comorbidities. Of these, 4 (31%) had retinal vasculitis, and 1 (7.7%) had cystoid macular edema. There was a 100% response rate to treatment with infliximab following failure to achieve disease quiescence on adalimumab. At mean follow-up time of 21 months (range, 8-31) from initiation of infliximab, there was a reduction in steroid dependence from 100% to 15% after transitioning from adalimumab to infliximab ($P < 0.001$). Nine patients (69%) had achieved steroid-free remission on infliximab therapy. The mean time to steroid-free remission was 8.7 months. In this study cohort, infliximab was used successfully in all cases of recalcitrant pediatric noninfectious uveitis that previously failed adalimumab therapy.

Treatment of presumed trematode-induced granulomatous anterior uveitis among children in rural areas of Egypt.

El Nokrashy A, Abou Samra W, Sobeih D, Lamin A, et al. *Eye* (Lond). 2019 Apr 3.

This study evaluates the efficacy of systemic antiparasitic medications alone or in combination with surgical aspiration in management of presumed trematode-induced anterior uveitis in children.
The design is a prospective case series. Children who presented with anterior chamber (AC) granuloma were included in the study. All patients received antiparasitic treatment and after 2 weeks; patients were divided based on their clinical improvement in terms of the baseline granuloma area into two groups: group A (<2.5 mm2) who continued on antiparasitic medications only ($n = 15$) and group B (≥ 2.5 mm2) who underwent surgical aspiration ($n = 15$). Basic demographics data, visual acuity (VA), corneal thickness, granuloma area and AC activity (cells and flare) were recorded and analyzed. Systemic work-up including stool and urine analysis, full blood count, chest X-ray and schistosomiasis titres were performed. Thirty eyes of 30 patients were included in the study with a mean age of

13.4 ± 2.42 years. All patients were male. Patients were examined and followed at Mansoura Ophthalmic Center, Mansoura University. Both groups showed statistically significant improvement in VA, AC activity, corneal thickness and granuloma area (p-value < 0.001), which was achieved with medical treatment only in group A. However, in group B granuloma required aspiration and did not recur after that. Presumed trematode-induced AC granuloma is common among children living in the rural areas of Egypt. Antiparasitic medication alone was found to be effective for small-sized granulomas. Surgical aspiration is an effective adjuvant procedure to treat large-sized ones.

Post-streptococcal uveitis syndrome in a Caucasian population: a case series.

Curragh DS, McAvoy CE, Rooney M, McLoone E. *Eye* (Lond). 2019 Mar;33(3):380-384.

Uveitis is an uncommon manifestation of post-streptococcal syndrome (PSUS). Despite reports, the condition is often not well recognized. This retrospective study reports a case series of children with post-streptococcal uveitis.
All cases of PSUS were identified from all new pediatric patients diagnosed with uveitis over a 6-year period. Diagnosis of PSUS was based on the following diagnostic criteria:
unilateral or bilateral uveitis with positive anti-streptolysin O titres (ASOT) or anti-deoxyribonuclease (anti-DNase) titers, and negative routine investigations for other causes of uveitis.
Eleven Caucasian pediatric patients were diagnosed with PSUS. One had a novel finding of peripheral corneal endotheliopathy, 73% of patients presented in Spring or Winter months and 88% of eyes had a final VA of better than or equal to 6/12 at a mean follow-up of 22 months. Systemic immunosuppressant treatment was used in 36% of patients. Adalimumab was used in 18% of patient's refractory to other treatment.
This is the largest consecutive series of Caucasian patients under 16 years of age with PSUS. The study demonstrates a seasonal preponderance with presentation typically in Winter or Spring. A novel finding of corneal endotheliopathy in one PSUS patient is reported. The authors also report on the benefit of adalimumab in the management of severe cases of PSUS; use of biologics in this particular cohort of uveitis patients has not previously been reported.

Symptoms in noninfectious uveitis in a pediatric cohort: initial presentation versus recurrences.

Marino A, Weiss PF, Davidson SL, Lerman MA. *J AAPOS*. 2019 Jun 26.

This study aims to describe the prevalence of symptoms with noninfectious uveitis (NIU) in a pediatric cohort and to assess the association between the presence of symptoms with first episode of uveitis (first-U) compared to symptoms at

uveitis recurrence. The medical records of patients with NIU treated at a tertiary referral hospital from March 2008 to November 2107 were reviewed retrospectively. Symptomaticity (eye pain, eye redness, photosensitivity) was captured at initial uveitis activation and subsequent episodes. Univariate logistic regression modeling was used to identify clinical features associated with symptomatic first-U. Ordinal regression identified patient characteristics associated with symptomatic recurrence.
A total of 118 cases were reviewed; of these, 92 were followed for at least 6 months and had at least 1 reactivation. Juvenile idiopathic arthritis-related uveitis (JIAU) was the most common diagnosis (67/118 [57%]), followed by idiopathic uveitis (33%). In the majority, uveitis was restricted to the anterior chamber (82%). Of the 118 cases, 58 patients (49%) had symptomatic first-U, 34% JIA versus 69% non-JIA. Non-JIAU, age ≥7 years, and negative antinuclear antibody (ANA) test were significantly associated with symptomatic first-U; spondyloarthritis was not. With recurrence, half had symptoms: 41% JIA versus 66% non-JIA. Of those who had symptomatic first-U, 35% were asymptomatic at recurrence. Those with JIA had 50% or less odds of symptomaticity at reactivation. Complications did not vary based on having had symptoms at first-U.
The authors conclude that non-JIA diagnosis, older age, and ANA-negativity were associated with symptomatic first-U in our study cohort, but no patient characteristics were significantly associated with symptomatic recurrence. Clinical patterns may change during disease course, with uveitis switching from symptomatic to
asymptomatic, which has implications for uveitis monitoring recommendations.

Visual and Clinical Outcome of Macular Edema Complicating Pediatric Noninfectious Uveitis

Eiger-Moscovich M, Tomkins-Netzer O, Amer R, et al. *Am J Ophthalmol.* 2019 June; 202: 72-78.

A retrospective case series of 25 children (33 eyes) was performed with the purpose of better understanding the clinical course and visual outcomes of pediatric patients with chronic noninfectious uveitis and macular edema (ME). The patients from this study were from four academic institutions in Israel and the UK over a 10-year period. The mean follow up was 48 months. They authors found that the most common diagnosis was intermediate uveitis, that most patients had active uveitis at the time of ME diagnosis, that it took a median of 6 months for the ME to resolve, and that baseline visual acuity was worse than 20/40 in 75% of patients but that decreased to 50% of patients by 3 months after diagnosis. ME resolved in 75% of patients during the 24 month follow up. They could not find any correlation between treatment strategy or structural characteristics on the ME and the visual outcomes. The conclusion was that despite the chronic course of ME in pediatric patients, the prognosis is favorable, which is in contrast to adult studies. This is the largest study of pediatric macular edema and is an important contribution to the pediatric uveitis literature.

Therapeutic Advances in juvenile idiopathic arthritis- associated uveitis.

Julie Gueudry, Sara Touhami, Pierre Quartier et al. *Curr Opin Ophthalmol* May 2019, 30 179-186

The authors undertake a review of JIA associated uveitis and current treatment modalities. The prevalence of uveitis is between 11.6-30% and its incidence is 2.8% per year. Usually presents as asymptomatic chronic anterior uveitis. Risk factors include young age at onset, female sex, ANA+, oligoarticular disease, however a large multivariate analysis found that independent predictive risk is young age at diagnosis and ANA+ only. Screening is recommended at diagnosis and then in 3-12 month intervals based on different risk factors (table 1 in the paper). The authors then go through different therapeutic agents including, corticosteroids, methotrexate, and biologics with emphasis on the fact that adalimumab is now approved as a second line treatment and is being used earlier in the disease process. A new class of agents known as JAK inhibitors are being investigated. The SHARE network has attempted to put together a treatment algorithm which is provided in the article. The authors then conclude with a discussion of the difficulties with tapering medications and the complications associated with uveitis such as glaucoma and cataract. Of note is the change in attitude towards the absolute contraindication to IOL implantation in those patients and more dependent on the specific case and the level of disease activity.

Cost-Effectiveness Analysis of Adalimumab for the Treatment of Uveitis Associated with Juvenile Idiopathic Arthritis.

Hughes DA, Culeddu G, Plumpton CO, Wood E, et al. *Ophthalmology*. 2019 Mar;126(3):415-424.

This study investigates the cost effectiveness of adalimumab in combination with methotrexate, compared with methotrexate alone, for the management of uveitis associated with juvenile idiopathic arthritis (JIA). A cost-utility analysis based on a clinical trial and decision analytic model. The participants are children and adolescents 2 to 18 years of age with persistently active uveitis associated with JIA, despite optimized methotrexate treatment for at least 12 weeks.
The SYCAMORE (Randomized controlled trial of the clinical effectiveness, SafetY and Cost effectiveness of Adalimumab in combination with MethOtRExate for the treatment of juvenile idiopathic arthritis associated uveitis) trial (identifier, ISRCTN10065623) of methotrexate (up to 25 mg weekly) with or without fortnightly administered adalimumab (20 or 40 mg, according to body weight) provided data on resource use (based on patient self-report and electronic records) and health utilities (from the Health Utilities Index questionnaire). Surgical event rates and long-term outcomes were based on data from a 10-year longitudinal cohort. A Markov model was used to extrapolate the effects of treatment based on visual impairment.

The main outcome measures were medical costs to the National Health Service in the United Kingdom, utility of defined health states, quality-adjusted life-years (QALYs), and incremental cost per QALY.
Adalimumab in combination with methotrexate resulted in additional costs of £39 316, with a 0.30 QALY gain compared with methotrexate alone, resulting in an incremental cost-effectiveness ratio of £129 025 per QALY gained. The probability of cost effectiveness at a threshold of £30 000 per QALY was less than 1%. Based on a threshold analysis, a price reduction of 84% would be necessary for adalimumab to be cost effective.
The authors conclude that Adalimumab is clinically effective in uveitis associated with JIA; however, its cost effectiveness is not demonstrated compared with methotrexate alone in the United Kingdom setting.

Incidence, management and outcome of raised intraocular pressure in childhood-onset uveitis at a tertiary referral centre

Tan S, Yau K, Steeples L, Ashworth J, et al. *Br J* Ophthalmol. June 2019;103:748-752.
Incidence rates of secondary glaucoma in children with uveitis range from 10.3% to 42.0%. These patients can be particularly challenging to manage. This retrospective study aims to review the incidence, management, and outcome of uveitis and elevated IOP in children at a tertiary center in the UK. 320 children were included with mean age of 8.2 years at uveitis diagnosis. 55 patients (17.2%) were found to have raised IOP requiring treatment. The median duration from time of diagnosis of uveitis to raised IOP was 12 months. Pre-treatment IOP was 32.3 mmHg, and IOP at last visit was 15.5 mmHg (over medial follow-up of 43.7 months). 44.0% of eyes required systemic acetazolamide during their treatment period. 37.3% required glaucoma drainage surgery. Overall 11.5% of eyes required surgery at 1 year after diagnosis of high IOP, increasing to 50.0% at 5 years. At time of diagnosis, mean BCVA was 0.26 logMAR which was stable at 0.28 logMAR at final follow-up. Finally, the mean cup-to-disc ratio at final follow-up was 0.4, although 10.7% of eyes were 0.8 or worse. The overall incidence of high IOP in this study was within limits of other studies. The rate of surgical intervention was found to be much higher than adults. There were 8 eyes that underwent cyclodiode laser treatment, and all required later filtration surgery. This study did show that the majority of children had good visual outcomes, and that perhaps early surgical intervention can prevent loss of vision.

Clinical features of paediatric uveitis at a tertiary referral centre in São Paulo, SP, Brazil

Souto F, Giampietro B, Takiuti J, Campos L, et al. *Br J* Ophthalmol. May 2019;103:636-640.

There is limited data on pediatric uveitis in Brazil, so the authors of this study sought to evaluate the clinical features, systemic associations, and visual outcomes of uveitis in children at a university based tertiary referral center in São Paulo, Brazil. They conducted a retrospective, observational study of patients less than 16 years old diagnosed with uveitis and with a minimal follow-up of 6 months. 39 patients were included with a mean age of 10.7 years. Mean age at uveitis diagnosis was 6.3 years. Mean follow-up was 47.7 months. 89.7% were bilateral, 56.4% were asymptomatic, and 84.6% were recurrent/chronic. Anterior uveitis was most common (46%), followed by intermediate (26%), posterior (15%), panuveitis (10%), and retinal vasculitis (3%). JIA-associated (41%) was the most common disease association. Ocular toxoplasmosis was found in 3 patients and toxocariasis in 2 patients. 84% of patients had improvement or preservation of visual acuity over the study. Legal blindness at last visit was found in 9.7% of patients. Ocular complications were found in 46% of patients at the first visit and 90% at the final visit. Cataract was the most common complication, followed by posterior synechia, ocular hypertension, and band keratopathy. Prednisone, immunosuppressive therapy or biologic medications were used in all non-infectious cases. The visual preservation or improvement in visual acuity in a large percentage of patients was encouraging despite patients presenting with severe disease and secondary complications

What is New in Paediatric Uveitis

Kara C. LaMattina and Anjum F. Koreishi *Curr Opin Ophthalmol* 2018, 29:412-418 (Sept 2018)

Pediatric uveitis is most commonly an anterior, nongranulomatous, chronic uveitis that is noninfectious (67.2-93.8% of cases). JIA is the most common systemic association with VKH, Behcet disease and TINU common in Asian and European studies. Pars planitis is common in the Middle East. Infection uveitis is less common (6.2-32.9 % of cases) with toxoplasmosis one of the most widely reported. In addition toxocariasis, viral and TB infections occur.
Treatment includes a number of modalities. Steroids should be used in the initial control of uveitis, flares and as a bridge to steroid sparing agents (SSAs). Topical prednisolone acetate 1% most commonly used. Chronic use of steroids can lead to cataract and glaucoma. The use of steroid implants has been shown in some case reports to provide good control although there is an increased risk of glaucoma and cataract. Antimetabolites such as methotrexate have been used for a long time with good long-term data on safety and efficacy. Mycophenolate sodium is also effective at controlling inflammation. Biologic agents such as TNF-alpha are another class of medication. Adalimumab is 80% effective in controlling refractory uveitis although adverse events such as infection were a concern. Interleukin-1 and interleukin-6 blockade is a newer area of treatment but there are only small number of studies looking at the efficacy. This paper reviews the different treatment modalities currently being used for the management of pediatric uveitis.

Blau Syndrome – Associated Uveitis: Preliminary Results from an International Prospective Interventional Case Series

Sarens IL, Casteels I, Anton J, et *Am J Ophthalmol.* 2018; 187:158-166.

The authors of this study sought to look at baseline and follow up eye findings in a large multi centered trial of the rare disease Blau Syndrome. There were 25 centers worldwide who provided baseline data for 50 patients. These patients were also followed for 1, 2, or 3 years after enrollment and their data recorded, when available. The median age of the onset of eye disease was 60 months and most of these patients had uveitis (78%) (almost always bilateral) and 21% of patients had moderate to severe visual impairment. Over half of patients had panuveitis with multifocal choroidal infiltrates. Other findings included optic disc pallor, peripapillary nodules, and anterior chamber inflammation. Patients who had panuveitis had a longer disease duration. Most patients were on topical steroid and most received systemic steroids and immunomodulatory therapies. A large percentage of patients had complications of chronic inflammation (band keratopathy, cataract, synechiae, retinal detachment, macular edema, etc). Many patients had persistent eye inflammation despite topical and systemic treatments. The authors point out the important conclusion with this paper is that the uveitis in this rare disease is found frequently and is very severe, warranting close eye follow up.

25.PRACTICE MANAGEMENT/ HEALTH CARE SYSTEM

Tropicamide has limited clinical effect on cycloplegia and mydriasis when combined with cyclopentolate and phenylephrine .

Sherman AE, Shaw MM, Ralay-Ranaivo H and Rahmani B *JAAPOS* 2019 Feb;23(1):30. e1-30. e5.

This prospective cross-sectional study examined the cycloplegic and mydriatic effect of tropicamide omission from a common pediatric eye drop combination. A total of 75 consecutive children (4-11 years of age) who were examined at the Ann & Robert H. Lurie Children's Hospital of Chicago from June 8, 2017 to September 6, 2017 were enrolled prospectively . Tropicamide, cyclopentolate, and phenylephrine (TCP) was instilled in one eye; cyclopentolate and phenylephrine (CP), in the other. Spherical equivalent, maximum pupil size, and pupillary constriction in response to photo-stimulation were measured before and 30 minutes after instillation using an autorefractor and pupillometer. Iris pigmentation was examined as a between-subjects variable. Mean differences in spherical equivalent between TCP and CP were not statistically significant ($P = 0.95$). Significant interactions between eye drop regimen and iris pigmentation were observed for pupil size ($P = 0.001$) and constriction percentage ($P = 0.02$). Among only patients with dark

irides, TCP yielded slightly larger pupils (7.70 vs 7.31 mm [P < 0.001]) that were less responsive to light (5.75% vs 8.07% [P = 0.002]). All pupils dilated to ≥6.0 mm, with equivalent proportions achieving ≥7.0 mm for TCP and CP (P = 0.18). The authors conclude that both regimens elicited equivalent cycloplegic effects. Mydriatic differences between the two combinations, although statistically significant in dark irides, were of limited clinical magnitude, and all pupils achieved sufficient dilation for funduscopy. However, tropicamide did have a discernible mydriatic effect when combined with cyclopentolate and phenylephrine in dark irides and may be considered in certain clinical situations. Within-subjects design enabled participants to serve as their own controls, allowing the authors to compare the two regimens without the influence of pharmacodynamic confounders that may exist between patients of various refractive errors, pupil reactivities, and iris shades. A limitation of this design, however, is the possibility of tropicamide exerting a contralateral effect on the eye receiving CP It could be informative to compare the time courses of TCP and CP to see whether their onset and duration of actions differ.

Ophthalmologists on Smartphones: Image-Based Teleconsultation

Mohan, Amit; Gajraj, Manju; et al. *Br Ir Orthopt J* 2019; 15(1): 3-7

Teleophthalmology has the potential of providing wider access to expert. The studies purpose was to compare image quality between hand held devices, smartphones and tablets, to those viewed on computer screens. Smartphones were found to have higher ratings for subjective image quality by ophthalmologists compared to tablets and computers. The ratings were higher for fundus images and extraocular images than anterior segment images. The use of smartphones in teleophthalmology not only provides excellent image quality but faster turnaround time in areas with minimal to no access to expert care.

Positive results bias in pediatric ophthalmology scientific publications.

Gershoni A, Ben Ishai M, Vainer I, Mimouni M, et al. *J AAPOS.* Oct 2018; 22(5): 394-395.e391.

Positive results bias is a type of publication bias, in which editors are more likely to accept studies that exhibit positive results than negative ones. An association was previously demonstrated in several fields of medicine, including general ophthalmology, between the results of a trial and the impact factor (IF) of the journal in which it was published. The authors hypothesized that randomized clinical studies in pediatric ophthalmology with positive results have a greater chance of publication in journals with a higher IF than those with negative results. They analysed 174 randomized, controlled trials conducted in the field of pediatric ophthalmology, which were published between January 1, 1997, and January 1, 2017 and appeared on Pubmed. Each study was classified as having either a positive or a negative result. A positive result was defined as a study in which

there was a statistically significant difference between groups ($P < 0.05$). No difference in IF was found between negative and positive outcomes, after statistically adjusting for the number of subjects and year of publication. The authors concluded that, unlike general ophthalmology, positive results bias probably does not occur in the field of pediatric ophthalmology. The study included only RCTs; Therefore, its conclusion might not be relevant to other study types in pediatric ophthalmology.

Outbreak of Adenovirus in a Neonatal Intensive Care Unit: Critical Importance of Equipment Cleaning During Inpatient Ophthalmologic Examinations.

Sammons JS, Graf EH, Townsend S, Hoegg CL, et al. *Ophthalmlogy* 2019. Jan;126(1):137-143.

Adenovirus is a common cause of respiratory infections and conjunctivitis in children and adults. Although these infections are often benign and self-limited, they can have severe complications and even death in vulnerable populations. In this report, the authors describe an outbreak of adenovirus in neonatal intensive care units (NICUs) due to contaminated handheld ophthalmologic equipment used during retinopathy of prematurity (ROP) screening and describe the investigation, response, and successful containment of an adenovirus outbreak in a NICU. A total of 23 hospitalized neonates, as well as NICU staff and parents of affected infants were included in this epidemiologic investigation. In August 2016, a routine surveillance identified an adenovirus outbreak in a level IV NICU. Epidemiologic investigation followed, including chart review, staff interviews, and observations. Cases were defined as hospital-acquired adenovirus identified from any clinical specimen (NICU patient or employee) or compatible illness in a family member. Real-time polymerase chain reaction (PCR) and partial- and whole-genome sequencing assays were used for testing of clinical and environmental specimens. A total of 23 primary neonatal cases and 9 secondary cases (6 employees and 3 parents) were identified. All neonatal case-patients had respiratory symptoms. Of these, 5 developed pneumonia and 12 required increased respiratory support. Less than half (48%) had ocular symptoms. All neonatal case-patients (100%) had undergone a recent ophthalmologic examination, and 54% of neonates undergoing examinations developed adenovirus infection. All affected employees and parents had direct contact with infected neonates. Observations revealed inconsistent disinfection of bedside ophthalmologic equipment and limited glove use. Sampling of 2 handheld lenses and 2 indirect ophthalmoscopes revealed adenovirus serotype-3 DNA on each device. Sequence analysis of 16 neonatal cases, 2 employees, and 2 lenses showed that cases and equipment shared 100% identity across the entire adenovirus genome. Infection control interventions included strict hand hygiene, including glove use; isolation precautions; enhanced cleaning of lenses and ophthalmoscopes between all examinations; and staff furlough. The authors recommended that ophthalmologists performing inpatient examinations take measures to avoid adenoviral spread from contaminated handheld equipment.

Trends in US Emergency Department Visits for Pediatric Acute Ocular Injury

E Matsa, J Shi, KK Wheeler, et al. *JAMA Ophthalmol*. August 2018; 136(8): 895-903.

This was a retrospective cohort study of care in emergency departments (EDs) from 2006 to 2014 at the Nationwide ED sample, with a total of 376 040 children ages 0 to 17 years with acute traumatic ocular injuries. Between 2006 and 2014, pediatric acute ocular injuries decreased by 26.1% (95% CI, -27.0 to -25.0). This decline existed across all patient demographic characteristics, injury patterns, and vision loss categories and for most mechanisms of injury. There were increases during the study in injuries related to sports (12.8%; 95% CI, 5.4-20.2) and household/domestic activities (20.7%; 95% CI, 16.2-25.2). The greatest decrease in high-risk injuries occurred with motor vehicle crashes (-79.8%; 95% CI, -85.8 to -74.9) and guns (-68.5%; 95% CI, -73.5 to -63.6).
This study showed a decline in pediatric acute ocular injuries in the United States between 2006 and 2014. Understanding these trends can help establish future prevention strategies regarding pediatric ocular trauma.

Wrong site surgery in Pediatric ophthalmology.

Lauren Maloly, Linda A. Morgan, Robin High, Donny W. Suh *JPOS*. 2018; 55(3): 152-158

The purpose of this study is to determine the prevalence of pediatric oph- thalmologists who have performed wrong-site surgery, propose risk factors leading to these errors, and assess the effectiveness of the Universal Protocol in preventing them. Approximately 1,000 listserv members of the Pediatric Ophthalmology Interest Group were invited from June to July 2015 to complete an anonymous 10 questions survey. Respondents were divided into two groups: those who performed or attempted wrong-site surgery (wrong-site surgery group) and those who had never performed a wrong-site surgery (intended surgical site group). The risk factors (ie, marking procedure, years in practice, surgical experience, adherence to the Universal Protocol time-out, and operating room factors) were compared between groups. Of the 156 respondents, 56.4% never performed, 9% attempted, and 34.6% performed a wrong- site surgery. The use of any procedure to mark the eye decreased the likelihood of a wrong-site surgery by 61% (odds ratio [OR] = 0.39; *P* = .069). A lower likelihood of error occurred when a single individual led the time-out and multiple individuals participated in checking the accuracy of the time-out. Surgeons in practice for less than 15 years had a lower likelihood of performing a wrong- site surgery (OR = 0.37; 95% confidence interval [CI] = 0.19 to 0.72; *P* = .003). Factors not signicantly associated with wrong-site surgeries were the number of surgeries performed per year (OR = 0.66; 95% CI = 0.35 to 1.24; *P* = .20) and the number of operating rooms used. The authors conclude that marking the surgical site, direct involvement in the time-out by the surgeon, active engagement of multiple individuals in check-

ing the time-out for accuracy, and indicating procedure type and laterality can potentially decrease the risk of surgical error as evidenced by the current study. The current study is limited in that data were self-reported and subject to recall bias. Also, many of the interpretations may have been statistically significant had there been a higher response rate. The authors did not isolate the types of errors committed (eg, wrong eye vs wrong muscle vs wrong procedure) and their relation to the safety factors analyzed. Future studies need to be planned that will incorporate additional questions such as when in the physician's practice did the wrong-site surgery occur. Additionally, the response rate was not as high as it was anticipated in this study.
Additional factors not addressed that may contribute to wrong-site surgeries and warrant further review include surgeons' emphasis on efficiency, less contact time with patients, and unfamiliarity with electronic medical record systems.

Chloral Hydrate Administered by a Dedicated Sedation Service Can Be Used Safely and Effectively for Pediatric Ophthalmic Examination

Karaoui M, Varadaraj V, Munoz B, et al. *Am J Ophthalmol.* 2018; 192: 39-46.

The goal of this study is to determine the safety and efficacy of oral choral hydrate sedation in the outpatient pediatric ophthalmology setting for procedures. This is a prospective interventional case series of 324 children aged 1 month to 5 years who were undergoing choral hydrate sedation (CHS) for ocular imaging or evaluations. The authors excluded patients whose weight was <3kg or greater than 20kg, who had ocular surface disease or infection, or who had a medical contraindication to CHS including patients who were ill. There was one ophthalmologist and one pediatrician who reviewed the records prior to enrollment and a "dedicated sedation provider" who administered the medication and monitored the patient. The patients did have NPO requirements similar to those used for general anesthesia. Patients less than 6 months received 50mg/kg dose and the other patients received 100mg/kg. Patients vital signs were monitored every 10 minutes for a mean of 85 minutes total. 300 children (92.9%) had all of the planned procedures completed during the sedation. There was a decrease in heart rate by a mean of 13.8 beats/minutes, respiratory rate 1.2 breaths/minutes, and oxygen saturation 0.9%. The median time between CHS and discharge was 90 minutes. There were no serious adverse effects. The authors discuss the fact that this study was performed on a Saudi Arabian population and thus the results may not be generalizable to a different population. Importantly, CHS is not approved by the FDA for use in children because of the potential of potentially severe side effects. However, the authors of this paper propose CHS is safe and effective when administered by a dedicated sedation service in a select group of patients for outpatient pediatric ophthalmology procedures.

Guidelines for the cleaning and sterilization of intraocular surgical instruments (Review/ Update)

David F. Chang, MD, Nick Mamalis, MD, Ophthalmic Instrument Cleaning and Sterilization Task Force *Journal of Cataract and Refractive Surgery*;2018;44(6):765-773.

Postoperative infectious endophthalmitis and toxic anterior segment syndrome are rare but potentially sight-threatening complications of intraocular surgery. The small volume of the eye and its sensitivity to minute amounts of chemical or microbial contaminants means that improper instrument cleaning or sterilization practices might pose a significant risk to patients. A 3-year collaborative effort by the Ophthalmic Instrument Cleaning and Sterilization (OICS) Task Force recently produced evidence-based, specialty-specific guidelines for the cleaning and sterilization of intraocular instruments. A large outbreak of toxic anterior segment syndrome (TASS) in 2006 was the impetus for these updated guidelines as was subsequent regulatory pressure on high-volume cataract surgeons in adult ambulatory surgery centers. The OICS designed a study that established the safety and acceptability of short-cycle ophthalmic instrument processing for sequential same-day surgery, even when the dry cycle is interrupted, if allowed by the instructions for use for the sterilizer. The use of enzymatic detergents to clean intraocular instruments was also studied as enzymatic detergents have been associated with TASS outbreaks. Thorough rinsing reduced but did not eliminate enzymatic residue on phaco tips in one study. Therefore, the new guidelines state that if intraocular surgical instruments are thoroughly rinsed with critical water promptly after each use, the routine use of enzymatic detergents is unnecessary and should not be required for the routine decontamination of intraocular instruments. The findings of these studies and resulting OICS guidelines are relevant for instruments used in other intraocular surgical procedures and may be useful to pediatric ophthalmologists in educating and assisting surgical staff in implementing appropriate practices for the cleaning and sterilization of intraocular surgical instruments.

Routine Orthoptic-led Paediatric Fundus Digital Imaging: Benefits to Patients and Healthcare System

Ramm, L.B., et al. *Br Ir Orthopt* J 2018; 14(1): 1-5

Ocular fundus digital imaging is a widely used screening modality in many areas of ophthalmology including diabetic retinopathy, retinopathy of prematurity, retinoblastoma, and non-accidental abusive head trauma. The authors demonstrate the effectiveness and safety of orthoptic-led non-mydriatic fundus digital imaging which can be both time and cost effective. Imaging was obtained in 97% of the 616 patients it was attempted on, 87% of which did not require dilation prior to imaging. The authors conclude that fundus imaging is a safe, speedy, and accurate way to examine children without distressing the patient. The authors note that fundus imaging does not bypass the need for cycloplegic refraction, detailed ophthalmoscopy, or peripheral retinal examination.

What's New and Important in Pediatric Ophthalmology and Strabismus for 2019

The All-star abridged handout

AAPOS, San Francisco, CA, USA

October 14, 2019

Presented by the

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1.AMBLYOPIA

Retinal Microvasculature in Amblyopic Children and the Quantitative Relationship Between Retinal Perfusion and Thickness

Wuhe Chen, Jiangtao Lou, Frank Thom, Yingjie Mao, et al *Invest Ophthalmol Vis Sci*. March 2019;60:1185–1191.

This study evaluated retinal vessel density in both amblyopic and non-amblyopic eyes using OCT-Angiography. They compared 85 amblyopic patients with bilateral, anisometropic, or strabismic amblyopia to 66 age-controlled participants. Foveal, parafoveal, and sectoral quadrants in both the superficial capillary plexus (SCP) and deep capillary plexus were examined. No significant differences in retinal vascular density were noted in the deep capillary plexus. There was a decreased capillary density in amblyopic eyes when compared to control eyes. This was shown to be the case only in anisometropic amblyopic eyes. This difference was also seen in the fellow eyes of the amblyopic eyes when compared to the control eyes. As stated by the authors, there is relevant differences of capillary density when comparing amblyopic to control eyes, though the significance and and causality of this difference is yet to be defined.

Multiple-Choice Answer Form Completion Time in Children With Amblyopia and Strabismus

KR Kelly, RM Jost, A DeLaCruz, EE Birch. *JAMA Ophthalmol*. August 2018 136(8):938-41.

In this cross-sectional study completed between 2014 and 2017 at a nonprofit eye research institute to assess for a time difference in academic tasks in children with amblyopia and/or strabismus. At the research institute, there were enrollment of 47 children with amblyopia treated for strabismus, anisometropia, or both, 18 children with non-amblyopic strabismus, and 20 normal controls. In particular, children were asked to transfer the correct answers from a standardized reading achievement test booklet to a multiple-choice answer form as quickly as possible without making mistakes or reading the text. Of the 85 included children, 40 (47%) were female, the mean (SD) age was 10.09 (0.91) years, and the last mean (SD) grade completed was 3.42 (0.92). Compared with children in the control group (mean [SD] time to completion, 230 [63] seconds), children with amblyopia (mean [SD] time to completion, 297 [97] seconds; difference, 63 seconds; 95% CI, 24-102; P = .001) and children with non-amblyopic strabismus (mean [SD] time to completion, 293 [53] seconds; difference, 68 seconds; 95% CI, 21-

115; P = .002) required approximately 28% (95% CI, 20-37) more time to fill out a multiple-choice answer form. Completion time was not associated with etiology, visual acuity, or stereoacuity. In summary, this study found that longer completion time in children with amblyopia or strabismus may affect a child's performance on tests using multiple-choice answer forms and may hinder academic success.

2.VISION SCREENING

3.REFRACTIVE ERROR

Prevalence and Risk Factors

Environmental Risk Factors Can Reduce Axial Length Elongation and Myopia Incidence in 6- to 9-Year-Old Children

Tideman JWL, Polling JR, Jaddoe, VWV, Vingerling JR, et al. ***Ophthalmology.*** 2019 Jan;126(1):127-136

It is becoming increasingly clear that an important cause of the myopia rise in the world is the changing lifestyles of school children. The goal of this study was to identify the risk factors for eye growth at a young age that may help to characterize children at risk for whom lifestyle advice and interventions could be beneficial. This study was embedded in the Generation R Study, population-based prospective cohort study of pregnant women and their children in Rotterdam the Netherlands. Children born between April 2002 and January 2006 were invited at age 6 and 9 years of age for examination which included axial length (AL) and corneal radius (CR) measured with an IOLMaster 500. Corneal radius was obtained from average of K1 and K2 from IOL master. Also, daily life activities and demographic characteristics were obtained by questionnaire. Among 4,734 children who completed examination at age 6 and 9, 3,362 children (71%) were eligible for cycloplegic refractive error measurements. Of these, 2,175 children had ocular biometry data at 9 years of age and cycloplegic refractive error. Linear regression models on AL elongation were used to create a risk score based on the regression coefficients resulting from environmental and ocular factors. The predictive value of the prediction score for myopia (≤-0.5 diopter) was estimated using receiver operating characteristic curves. To test if regression coefficients differed for baseline AL-to-CR ratio, interaction terms were calculated with baseline AL-to-CR ratio and environmental factors. The results show that from 6 to 9 years of age, average AL elongation was 0.21±0.009 mm/year and myopia developed in 223 of 2,136 children(10.4%), leading to a myopia prevalence at 9 years of age of 12.0%. Seven parameters were associated independently (P <

0.05) with faster AL elongation: parental myopia, 1 or more books read per week, time spent reading, no participation in sports, non-European ethnicity, less time spent outdoors, and baseline AL-to-CR ratio. The discriminative accuracy for incident myopia based on these risk factors was 0.78. Axial length-to-CR ratio at baseline showed statistically significant interaction with number of books read per week ($P < 0.01$) and parental myopia ($P < 0.01$). Almost all predictors showed the highest association with AL elongation in the highest quartile of AL-to-CR ratio; incidental myopia in this group was 24% (124/513). The authors concluded that determination of a risk score can help to identify school children at high risk of myopia and suggest that behavioral changes can offer protection particularly in these children. Also notable in this study is that the highest effect of the environmental factors was found for those children with the highest risk of myopia.

A preliminary study of astigmatism and early childhood development

Harvey EM, McGrath ER, Miller JM, Davis AL, et a.. *J AAPOS*. Aug 2018;22(4):294-298.

The purpose of this paper is to determine whether uncorrected astigmatism in toddlers is associated with poorer performance on the Bayley Scales of Infant and Toddler Development, 3rd edition (BSITD-III). Subjects include were 12- to 35-month-olds who failed an instrument-based vision screening at a well-child check. A cycloplegic eye examination was conducted in all the patients. Full-term children with no known medical or developmental conditions were invited to participate in a BSITD-III assessment conducted by an examiner masked to the child's eye examination results. Independent samples t tests were used to compare Cognitive, Language (Receptive and Expressive), and Motor (Fine and Gross) scores for children with moderate/high astigmatism (>2.00 D) versus children with no/low refractive error (ie, children who had a false-positive vision screening). The sample included 13 children in each group. The groups did not differ on sex or mean age. Children with moderate/high astigmatism had significantly poorer mean scores on the Cognitive and Language scales and the Receptive Communication Language subscale compared to children with no/low refractive error. Children with moderate/high astigmatism had poorer mean scores on the Motor scale, Fine and Gross Motor subscales, and the Expressive Communication subscale, but these differences were not statistically significant. The results suggest that uncorrected astigmatism > 2.00 D in toddlers may be associated with poorer performance on cognitive and language tasks but it does not seem to be associated with poorer performance on gross motor tasks. The results cannot tell whether correcting the astigmatism with spectacles would improve performance. Further studies assessing the effects of uncorrected refractive error on developmental task performance and of spectacle correction of refractive error in toddlers on developmental outcomes are needed to support the development of evidence-based spectacle prescribing guidelines.

Reducing the Progression of Myopia

Recent updates on myopia control: preventing progression 1 diopter at a time

Rebecca S. Weiss and Sunju Park *Curr Opin Ophthalmol* July 2019 30:215-19

The authors review current treatment modalities in myopia control. The prevalence of myopia is increasing worldwide and there is an inverse correlation between time spent outdoors and myopic progression in children in one longitudinal study. Other studies conclude that increased outdoor time may be protective against myopia onset. Bifocals have not shown significant prevention but in one study, contact lenses that are designed for peripheral hyperopic defocus may show some promise for future myopia control. Orthokeratology has been found to have a statistically significant reduction in axial length elongation however there are risks of microbial keratitis. In addition, with discontinuation of use, axial length elongation was faster compared to controls and continued ortho-K users. Lastly, the authors discuss atopine treatment. They mention the ATOM 1 and 2 studies but discuss more in depth the LAMP studies looking at low dose atropine intervention and found that reduction in spherical equivalent and axial elongation decreased as the dose decreased and the next phase will be looking at long term follow up with respect to washout and maintenance of results. Another study looked at dose dependence based on familial history of progressive myopia. Wu et al developed an algorithm based on dose response and adjunctive therapies. The authors discuss that atropine treatment may need to be customized for each patient based on a variety of factors but that it is the most promising of all the modalities.

4.**VISION IMPAIRMENT**

The Impact of Diplopia on Reading

Lijka, Beckie, et al. *Br Ir Orthopt J* 2019; 15(1): 8-14

The impact of strabismus and diplopia on quality of life (QOL) has been well documented. They can have emotional, psychological, and functional negative effects. Reading is a common way to assess the impact of visual conditions which impacts QOL. The Radner Reading Chart (RRC) was used to compare the effect of induced diplopia (small (6Δ) and large (12Δ) separation) on reading speed and accuracy. Reading speed was significantly slower in both the small separation and large separation groups compared to the control group, worse in the small

separation group. The small separation induced vertical diplopia group had significantly reduced accuracy compared to both control and large separation groups. The authors conclude that vertical diplopia has a significant impact of reading function bot in speed and accuracy and the smaller the deviation the greater the impact. When a diplopic patient is unable to fuse their corrected deviation, treatment may include using Fresnel prisms to further separate the images making the angle of deviation higher.

Visual impairment and Eye Disease Among Children of Migrant Farmworkers.

Rebecca Russ Soares, Michael Rothschild, Danny Haddad, Phoebe Lenhart. J *Ped Ophthal & Strabismus*.2019;56(1):28-34

The purpose of this study is to determine the prevalence of reduced visual acuity and ocular disease in the children of migrant farmworkers in Georgia. A retrospective chart review of data acquired by a vision screening was performed on 156 Haitian and Hispanic children of migrant farmworkers attending a summer school in Georgia. Reduced visual acuity at presentation was analyzed and stratified by ethnicity, type of ocular disease, and immediate resolution with refractive correction. The authors found that 20% of migrant farmworker children have a high prevalence of reduced visual acuity in the worse eye. Of those with worse-eye reduced visual acuity, 83% had uncorrected refractive error. The prevalence of uncorrected refractive error from astigmatism and high astigmatism was significantly higher among Hispanics than Haitians. The prevalence of amblyopia suspects among migrant farmworker children was 3%. Of the amblyopia suspects, 80% were anisometropic. The authors concluded that Children of migrant farmworkers in Georgia have a higher rate of reduced visual acuity, largely from uncorrected refractive error, when compared to other Hispanic and African American children in the United States with a prevalence more aligned to children in Asian and Latin American countries than school children in the United States. This illustrates the need for improved access to screening and care in this vulnerable population. The study has certain limitations: Due to the retrospective nature of this analysis, the eye charts in each group were not standardized. As such, visual acuity may have been underestimated in 4 to 5 year olds and over estimated in older children using the HOTV charts. Also, there was no additional follow-up to determine the best-corrected visual acuity of patients once they had been wearing their new correction for a few weeks. Furthermore, although the prevalence of uncorrected refractive error was high, this prevalence only accounts for presenting vision; it may not account for children who had but did not bring their spectacles. Finally, because this was a screening measure, amblyopia suspects were referred to follow-up if needed. However, given the transient na-

ture of the population, we were unable to track follow-up visual acuity or response to penalization therapy. Future studies examining long-term visual outcomes in such patients, while logistically difficult, would be worthwhile.

5. NEURO-OPHTHALMOLOGY

Impaired Visual Search in Children with Rett Syndrome

Susan A. Rose, Sam Wass, Jeffrey J. Jankowski, Judith F. Feldman, Aleksandra Djukic Pediatric *Neurology* 92 (2019) 26-31

Rett Syndrome is a severely disabling neuro-developmental disorder caused by mutations in the X-linked MECP2 gene. Eye tracking technology (Tobii X2-60 infrared eyetracker) was used to investigate selective attention (the ability to focus on or select a particular element or object in the environment) in this population. The study used a search task in conjunction with the eye-tracking technology. The study sample included 28 females with Rett Syndrome and 32 age-matched controls. Each trial included a target (a red apple) and several distractors (blue apples, red cylinders). The distractors varied in number and were different from targets by a single feature (such as color or shape to produce a pop-out effect) or in conjunction of features requiring serial searching. Children searched for the target in arrays containing five or nine objects, and trials ended when the target was fixated, or time expires (4000ms). Children with Rett Syndrome had more difficulty finding the target than controls (50% vs 80%) in both single and with conjunction of features. Success rate for children with Rett Syndrome was not influenced by display size or age. When successful, children with Rett Syndrome took significantly longer to respond (392 to 574ms longer). It is unclear what factors underlie the difficulties in these children, but a few ideas are postulated: 1) they have difficulty shifting and/or engaging attention from the distractors; 2) visual search is impaired in children with Rett Syndrome because they have difficulty distributing attention across the display; 3) efficient search of children with Rett Syndrome is compromised by a tendency to focus on local (rather than global) features. This article provides the first evidence that selective attention is compromised in Rett Syndrome.

Eculizumab in Aquaporin-4-Positive Neuromyelitis Optica Spectrum Disorder

Pittock SJ, Berthele A, Fujihara K, Kim HJ, et al. *N Engl J Med.* May 2019. E-pub ahead of print.

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune, inflammatory disorder characterized by recurrent attacks of optic neuritis and myelitis, from which patients typically do not recover. At least two thirds of NMOSD cases

are associated with aquaporin-4 antibodies (AQP4-IgG) and complement-mediated damage to the central nervous system. Aquaporin-4 (AQP4) is a water channel protein expressed mainly by astrocytes in the central nervous system. AQP4-IgG triggers the complement cascade, which leads to inflammation and the formation of the membrane attack complex and subsequent astrocyte destruction. In a previous small, open-label study involving patients with AQP4-IgG–positive disease, eculizumab, a terminal complement inhibitor, was shown to reduce the frequency of relapse.

In this randomized, double-blind trial, 143 adults were randomly assigned in a 2:1 ratio to receive either intravenous eculizumab or placebo. The eculizumab was given weekly for four weeks at 900 mg per dose and then every two weeks thereafter at 1200 mg per dose. The continued use of stable-dose immunosuppressive therapy was permitted. The primary end point was the first relapse, as defined by a committee of two neurologists and one neuro-ophthalmologist retrospectively reviewing clinical data, masked to treatment type. A secondary outcomes was a disability score on the Expanded Disability Status Scale (EDSS), which ranges from 0 (no disability) to 10 (death).

130 (91%) of the patients were women of mean age 44 +/- 13 years. Relapses occurred in 3 of 96 patients (3%) in the eculizumab group and 20 of 47 (43%) in the placebo group (hazard ratio, 0.06; 95% confidence interval [CI], 0.02 to 0.20; P<0.001). The mean change in the EDSS score was –0.18 in the eculizumab group and 0.12 in the placebo group (least-squares mean difference, –0.29; 95% CI, –0.59 to 0.01). Upper respiratory tract infections and headaches were more common in the eculizumab group. There was one death from pulmonary empyema in the eculizumab group.

Patients with AQP4-IgG–positive NMOSD who received eculizumab had a significantly lower risk of relapse than those who received placebo. There was no significant between-group difference in measures of disability progression. Although this clinical trial involved adults, neuromyelitis optica can also affect children. Pediatric ophthalmologists should be aware of a new medication in a new medication class that can be used for a blinding disease. Of note, this study was funded by Alexion Pharmaceuticals, which makes eculizumab.

Study of Optimal Perimetric Testing in Children (OPTIC): evaluation of kinetic approached in childhood neuro-ophthalmic disease

Patel D, Cumberland P, Walters B, Cortina-Borja M, et al. *Br J* Ophthalmol. August 2019;103:1085-1091.

The purpose of this study was to investigate the differences between Goldmann and Octopus kinetic perimeters for visual fields testing in children. The “gold-standard” Goldmann perimeter is no longer commercially available, so evaluation

of newer equipment is needed. 30 children aged 5-15 (mean 11.1 years) with either neuro-ophthalmic conditions or known neuro-ophthalmic visual field defects were recruited. Goldmann perimetry was performed first, followed by 5 minutes of rest and the Octopus perimetry. Note that test order was not randomized. Overall 90% completed the Goldmann testing vs 72.4% for Octopus. The most common reason for not completing the test was inability to plot the blind spot due to poor cooperation. The testing time was similar between the perimeters. Test quality (using the Examiner Based Assessment of Reliability tool) was deemed similar for the two perimeters for children 8 and older. For children under 8 years better quality was obtained with Goldman testing (4/5) vs Octopus (2/5). Visual field loss severity scores showed broad agreement. The type of field defect matched in 29/42 (69%) tests. The octopus tended to depict more extensive field loss, and the Goldmann depicted a larger blind spot. The Octopus also tended to underestimate severe visual field defects. Overall the authors felt that the outputs of these two perimeters are not directly interchangeable in this group, and it is not recommended to use the perimeters interchangeably when monitoring children longitudinally. This is important for those practitioners transitioning to the Octopus to develop appropriate strategies to interpret findings in their patients.

Prevalence of Strabismus Among Children With Neurofibromatosis Type 1 Disease With and Without Optic Pathway Glioma.

Gad Dotan, Hanya M.Qureshi, Hagit Toledano-Alhadef, Nur Azem et al. *J Ped Ophthalm & Strabismus*.2019;56(1):19-22

The purpose of this study is to evaluate the prevalence of strabismus in Neurofibromatosis type 1(NF-1) by comparing children with normal neuroimaging to those with optic pathway glioma. A retrospective data collection of all children with NF-1 with neuroimaging studies examined at a single medical center between 2000 and 2016. Of the 198 children with NF-1 reviewed, 109 (55%) were male, 121 (61%) had normal neuroimaging, and 77 (39%) had an optic pathway glioma. Mean age at presentation was 6.3 ± 4.7 years and mean follow-up was 4.8 ± 3.1 years. Strabismus was present in 29 (15%) children and was significantly more prevalent in children with NF-1 with optic pathway glioma (21 of 77 [27%]) than in those with normal neuroimaging (8 of 121 [7%], $P < .001$). Sensory strabismus was only found in children with optic pathway glioma, accounting for most cases (12 of 21 [57%]). A strong association between strabismus and optic pathway glioma is demonstrated by an odds ratio of 5.29 ($P < .001$). Children with NF-1 with optic pathway glioma have a 4.13 times higher relative risk of developing strabismus than children with NF-1 without it ($P = .001$). The direction of ocular misalignment in children with NF-1 with optic pathway glioma was not significantly different than that observed in children without optic pathway glioma ($P = .197$, Fisher's exact test). Only 5 (17%) children with NF-1 with strabismus (3 with optic pathway glioma) underwent corrective surgery to align their eyes. The

authors concluded that optic pathway glioma in children with NF-1 is associated with an increased risk of strabismus, especially sensory strabismus. Although exotropia is the most common ocular misalignment associated with optic pathway glioma, the direction of strabismus cannot be used as an accurate predictor for the presence of optic pathway glioma. Many children with NF-1 with strabismus do not undergo corrective surgery. This study's results should be interpreted within the context of its limitations. Because data were collected retrospectively based on chart reviews, it is subject to variability depending on the accuracy and completeness of records. Furthermore, because all children with NF-1 included were examined in a tertiary referral medical center, they may not accurately represent the entire pediatric population of patients with NF-1.

Myasthenia Gravis

Incidence and Ocular Features of Pediatric Myasthenias

Mansukhani SA A, Bothun ED, Diehl NN, et al. *Am J Ophthalmol.* 2019 April; 200: 242-249.

The authors of this study used a retrospective cohort analysis to report the incidence, demographics, and ocular findings of children with ocular myasthenia. They reviewed the medical records of all children at one academic institution under the age of 19 over a 50 year period. A total of 364 children were evaluated and of those 60% had Juvenile myasthenia gravis (JMG), 38% had congenital myasthenia syndrome (CMS) and 2% had Lambert-Eaton syndrome. The median age of diagnosis was 13.5, 5.1, and 12.6 years respectively. The median time to diagnosis was 5 months. The authors calculated the incidence of ocular myasthenia using the information from the Rochester Epidemiology project as 0.35 per 100 000 under 19 years old. Most JMG and CMS had ocular involvement and of those children with at least a year of follow up, most improved and complete remission was achieved in about a third of children with JMG. The authors concluded that MG in children is exceedingly rare, has two major forms (both of which are likely to cause ocular involvement), and that improvement is more common in the juvenile form. The limitations of this study included those related to retrospective studies. Additionally, since the definition of myasthenia gravis has changed over the last 50 years, the authors were applying newer definitions to patients from years ago, which may have underestimated the rate of disease. Additionally, serology was not available on all children. Overall this paper contributes new information about the ocular involvement in pediatric myasthenia and provides a nice summary of myasthenia gravis in children.

Optic Neuritis

Optical coherence tomography is highly sensitive in detecting prior optic neuritis.

Xu SC, Kardon RH, Leavitt JA, Flanagan EP, et al. *Neurology*. Feb 2019;92(6):e527-e535.

In this retrospective study, the authors examined the use of OCT to detect episodes of prior optic neuritis in a cohort of 51 patients. The goal of the study was to evaluate whether OCT was an effective tool for detecting a prior episode of optic neuritis in patients with unilateral optic neuritis. By utilizing interocular differences as measured with OCT, the authors determined that an interocular difference of ≥9 µm for rNFL or ≥6 µm for GCIPL were reflective of prior optic neuritis. The reduction in GCIPL was a more sensitive measure (76% for GCIPL and 37% for RNFL) to reflect prior optic neuritis as compared to age matched controls. This study defines thresholds for interocular differences which may provide a quantitative way of detecting prior optic neuritis and establishes which measure of OCT is most effective in screening when the history is unknown.

6. NYSTAGMUS

Clinical evaluation of graded Anderson's procedure in idiopathic infantile nystagmus.

Ganesh SC, Rao SG, Narendran K. *Strabismus*. 2019 Jun 20:1-4.

The authors investigate the effect of a graded recession of yoke muscles in patients with idiopathic infantile nystagmus based on the initial head turn. They included 37 patients (26 males) with a mean age of 12.3±8.64 years. All patients improved after surgery, with a mean decrease in the head turn from 22.5 degrees to 7.48 degrees ath the post-operative month 1 visit. The binocular visual acuity improved and all patients were orthotropic in primary gaze. The authors conclude that this modification is useful particularly in moderate head turns and overall is helpful as it involves fewer operated muscles, only has recessions and can be revised.

7. PREMATURITY.

Ophthalmic Features of Premature Infants

Relationship between Retinal Thickness Profiles and Visual Outcomes in Young Adults Born Extremely Preterm: The EPICure@19 Study.

Balasubramanian S, Beckmann J, Mehta H, Sadda SR, et al*. Ophthalmology.* 2019 Jan;126(1):107-112.

Children born preterm are at increased risk of developing a range of ocular and vision disorders later in life. It is known that foveal reflex is reduced in premature infants and that several spectral-domain (SD) studies have shown abnormal foveal contour, absence of foveal depression and retention of inner retinal layers at the foveal center and macular edema. This is the first study correlating the retinal findings to visual function in adults born extreme preterm (EP), before 26 weeks of gestation. All data for this study was obtained from EPICure study, large well-characterized study on young adults born before 26 weeks of gestation, as part of a long-term follow-up study called the EPICure@19 study. Extreme preterm participants were aged 18 to 20 years and a full-term born age-matched comparison group was recruited for assessment. A total of 354 eyes (226 eyes of former EP infants and 128 age-matched full-term control eyes) from 177 young adults were evaluated. Among EP participants, 50% of eyes (112/226) were not previously diagnosed with retinopathy of prematurity (ROP), 38% of eyes (84) had ROP not deemed to require treatment in the neonatal period, and 13% of eyes (30) had neonatal cryotherapy or laser ablation for ROP. Subjects underwent eye examinations including best-corrected visual acuity (BCVA) and Heidelberg Spectralis macular SD OCT imaging. Retinal layers were auto-segmented and thickness profiles were computed at the fovea by the instrument software. Compared with control eyes, the inner and outer retinal layers of EP eyes were significantly thicker and BCVA was significantly reduced. Retinal layer thicknesses and BCVA were similar for untreated EP eyes and those without neonatal ROP. In contrast, treated eyes had increased inner and outer retinal layer thickness and decreased vision. Inner retinal layer thickness was moderately correlated with worse BCVA ($r = 0.30$, $P < 0.001$), but outer retinal layer thickness was not ($r = -0.01$, $P = 0.80$). Multivariate regression indicated ganglion cell layer thickness was a significant independent predictor of BCVA. Extremely premature birth influences maturation of the fovea and visual outcomes into early adult life. Increased ganglion cell layer thickness was associated with worse BCVA. Eyes requiring neonatal treatment for ROP had associated worse BCVA at the age of 19 years. Of note, it is interesting that these EPs when compared to full-term controls did not have a significant difference in refractive error.

Prematurity and Outcomes

8.ROP

ROP and Telemedicine/Screening

Factors in Premature Infants Associated With Low Risk of Developing Retinopathy of Prematurity

Wade KC, Ying GS, Baumritter MS; et al. *JAMA Ophthalmology*. February 2019;137(2):160-166.

This study evaluated characteristics of infants at low risk for development of retinopathy of prematurity (ROP) in North American neonatal intensive care units, especially whom post-discharge screening may be of limited value. In addition, the authors did a post hoc analysis of prospectively collected in-hospital ROP examination results among infants enrolled. In order to characterize the infants at low risk for ROP, the authors characterized infants without ROP and performed logistic regression on the subset of infants who were 27 to 33 weeks' gestational age to determine characteristics associated with the absence of ROP during all in-hospital examinations. A total of 1257 infants born at 22 to 35 weeks' gestation with birth weights less than 1251 g underwent 4,113 ROP examinations between 31 and 47 weeks' post-menstrual age. Overall, 1,153 examinations (38%) showed no ROP, and 456 infants (36%) did not have ROP prior to study center discharge or study end point. Among infants without ROP during examinations at 32 and 33 weeks' post-menstrual age, 16 (9.4%) and 14 (5.3%) subsequently underwent ROP treatment, respectively. At hospital discharge, there was no ROP in 59% of infants of 27 to 33 weeks' gestational age, compared with 15% of those who were less than 27 weeks' gestational age ($P \leq .001$). With more than 85% follow-up among infants without ROP by 37 weeks' post-menstrual age, none were treated for ROP. In a multivariate analysis of infants born at 27 to 33 weeks' gestation, larger birth weight and higher gestational age were statistically significantly associated with absence of ROP. In summary, the findings suggest that, for infants of 27 weeks' gestational age or greater and birth weights larger than 750 g, if no ROP has been detected by discharge at near-term post-menstrual age, then further ROP surveillance has limited value.

Implementation of a Critical Prediction Model Using Postnatal Weight Gain, birth Weight, and gestational Age to Risk Stratify ROP.

Kortany McCauley, Anupama Chundu, Helen Song, Robin High et al. *J Ped Ophthal & Strabismus*.2018;55 (5):326-334

The purpose of this study is to develop a simple prognostic model using postnatal weight gain, birth weight, and gestational age to identify infants at risk for developing severe retinopathy of prematurity (ROP). The medical records from two tertiary referral centers with the diagnosis code “Retinopathy of Prematurity” were evaluated. Those with a birth weight of 1,500 g or less, gestational age of 30 weeks or younger, and unstable clinical courses were included. Multivariate regression analysis was applied to transform three independent variables into a growth rate algorithm. Seventeen of 191 neonates had severe ROP. Weight gain of at least 23 g/d was determined as a protective cut-off value against development of severe ROP. This value maintained 100% sensitivity with 62% specificity to ensure all neonates who require treatment would be captured. Overall, the Omaha (OMA)-ROP model calculated a 58% reduction in eye examinations within the cohort. The authors concluded that inclusion of postnatal growth rate in risk stratification will minimize the number of eye examinations performed without increasing adverse visual outcomes. The OMA-ROP model predicts neonates who gain less than 23 g/d are at higher risk for developing severe ROP. Although promising, larger cohort studies may be necessary to validate and implement new screening practices among preterm infants. This study is not without limitations. Similar to previously proposed models, the OMA-ROP model was developed from tertiary academic hospitals where infants have a higher ROP risk profile. Therefore, this cohort may not represent the average demographic of the national at-risk neonatal population. Furthermore, our findings are not applicable to infants in developing nations where differences exist in health care systems, patient demographics, and a cohort of older and larger infants who develop ROP and who may represent a different ROP risk profile. Accurate assessment of gestational age may not even be possible in some regions. Both the CO-ROP model and the OMA-ROP model screen based on lower-than-predicted weight gain. Therefore, an infant with higher-than-average weight gain due to non-physiologic reasons (edema, sepsis, or hydrocephalus) could theoretically be missed. Of the current proposed postnatal weight gain models, the WINROP is unique in its identification of such infants. Similarly, clinical factors that cause weight gain but are not associated with increased IGF-1 may generate false-negative signals and should be further assessed.

Development of Modified Screening Criteria for Retinopathy of Prematurity: Primary Results From the Postnatal Growth and Retinopathy of Prematurity Study.

Gil Binenbaum, Edward F. Bell, Pamela Donohue, Graham Quinn, et al. for the G-ROP Study Group. *JAMA Ophthalmology*. September 2018; 136 (9): 1034-1040.

This is a retrospective multi center cohort study of the incidence and early course of retinopathy of prematurity (ROP) from infants having ROP screening from 29

hospitals in the United States and Canada from 2006 to 2012. The authors performed a secondary analysis of the G-ROP study data. Of note, the data collection was standardized with a rigorous certification process for interpretation of medical records. To be enrolled in the study, the infant had to meet 1 of 2 conditions: (1) either eye met criteria for the ETROP type 1 or type 2 ROP or underwent treatment for ROP or (2) both eyes had mature retinal vasculature, immature vasculature in zone III with no prior ROP, or a regression of ROP of less than type 1 or type 2 ROP. Among the 7,483 infants included, 947 (12.7%) had birth weight (BW) of 1500g or more and 1440 (19.2%) had a gestational age (GA) of older than 30 weeks. Regarding the demographics, almost half the infants were white and more than 30% were African American. The authors reported that 43.1% (3224 infants) developed ROP, 6.1% (459 infants) developed type 1 ROP and 6.3% (472 infants) developed type 2 ROP. Furthermore, only 514 infants (6.9%) underwent treatment in 1 or both eyes and 147 infants (2%) had zone 1 disease. In infants with BW of less than 1251g, most had type 1 or 2 ROP (98.1%) and only approximately half of the eyes (49.4%) had retinal vasculature into zone III by 37 weeks postmenstrual age. One critical finding in this study is that these multi center cohort study involved ROP screenings of all eligible infants and not only high-risk infants. The authors remind us that for infants with BW less than 1251g, there is a higher risk of developing severe ROP and they reported 12.5% of severe ROP from low BW infants. Limitations of the study include the retrospective analysis and retinal photography was not used to confirm ROP zone or the presence of plus disease. However, study strengths include the large sample size from ROP screening programs from 29 hospitals with a rigorous data abstraction procedure. The authors suggest that this study is helpful for ophthalmologist, neonatologists, and care coordinators by providing ROP risk profiles across GA and BW groups for these infants.

ROP and imaging

ROP and Treatment

Systematic review and meta-analysis of the negative outcomes of retinopathy of prematurity treated with laser photocoagulation

Liang J *EJO* March 2019,29(2) 223–228

Retinopathy of prematurity is a leading cause of potentially avertable childhood blindness around the world. And laser photocoagulation is currently performed as a gold standard for retinopathy of prematurity treatment, but it may contribute to elevated myopia and decreased visual field. Therefore, the objective of this meta-analysis is to explore the negative impact of laser photocoagulation for retinopa-

thy of prematurity in terms of anatomic outcomes and structural outcomes. Studies were retrieved through literature searches in PubMed and EMBASE from 1990 to 2017 in English. Case-control studies that reported anatomic and structural changes or significant complications after laser coagulation or cryotherapy for retinopathy of prematurity were eligible. This meta-analysis included eight original studies related to laser treatment for retinopathy of prematurity at any stages. A total of 1422 infants were participated, of which 1156 documented subthreshold or threshold retinopathy of prematurity without laser treatment were selected as comparison group and the rest treated with diode or argon laser coagulation were chosen for experiment group. Taking all included studies into account, spherical equivalent (mean difference −2.53, 95% confidence interval: –5.23 to 0.18, I2 = 96%, P < 0.00001), anterior chamber depth (mean difference −0.52, 95% confidence interval: −0.76 to −0.28, I2 = 55%, P = 0.11), astigmatism (odds ratio 3.19, 95% confidence interval: 1.61 to 6.32, I2 = 0%, P = 0.54), and myopia (odds ratio 8.08, 95% confidence interval: 3.79 to 17.23, I2 = 37%, P = 0.21) were associated with laser treatment for retinopathy of prematurity. Axial length (mean difference −0.01, 95% confidence interval: –0.28 to 0.27, I2 = 0%, P = 0.62) and anisometropia (odds ratio 4.21, 95% confidence interval: 0.54 to 33.17, I2 = 1%, P = 0.31) had no statistical significance on laser coagulation for retinopathy of prematurity. This meta-analysis showed that spherical equivalent, anterior chamber depth, astigmatism, and myopia were associated with the negative outcomes of laser coagulation, while axial length and anisometropia had no statistical importance on the defects of laser coagulation. Therefore, patients treated with laser coagulation should follow periodic cycloplegic refraction and receive early optical correction.

ROP Epidemiology and Outcomes

Neurodevelopmental Outcomes of Preterm Infants with Retinopathy of Prematurity Treatment

Girija Natarajan, Seetha Shankaran, Tracy Nolen, et. al *Pediatrics*. August 2019; 144(2): e20183537.

This study aimed to determine whether there is a difference in adverse outcomes between bevacizumab therapy and surgery for retinopathy of prematurity in extremely pre-term infants. The study was a retrospective analysis of prospective data on preterm infants 22-26 +6/7 weeks gestational age. The primary outcomes were death and severe neurodevelopmental impairment (NDI) at 18-26 months' corrected age (a composite score of Bayley Scales of Infant and Toddler Development Classification Scale greater than or equal to 2, and bilateral blindness or hearing). The study included 405 infants from multiple health centers. The results demonstrated that the bevacizumab group were a sicker cohort with lower median birth weight, longer durations of conventional ventilation, and

longer supplemental oxygen. Rates of death or severe NDI did not differ between the groups. But, the bevacizumab group had a greater odds of death and developmental scores were significantly lower in the bevacizumab group. There may be significant selection bias given that the physicians chose which patients received injection versus laser and that the bevacizumab group was a sicker group of patients. This study was the first to observe that mortality through infancy was significantly higher in the bevacizumab group than the surgery group. Although not conclusive, these results do highlight the need for rigorous appraisal of the risks and benefits of bevacizumab in a large randomized trial with neurodevelopmental follow up.

Incidence and Early Course of Retinopathy of Prematurity: Secondary Analysis of the Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study.

Graham E. Quinn, Gui-shang Ying, Edward F. Bell, Pamela K. Donohue, et al. for the G-ROP Study Group. *JAMA Ophthalmology*. December 2018; 136 (12): 1383-1389.

This was a large retrospective cohort study of 7483 infants who had serial retinopathy of prematurity (ROP) examinations in 29 hospitals in the United States and Canada between 2006 and 2011. Of note, this article has some overlap of findings and data points and collection in the earlier article from JAMA Ophthalmology September 2018. The authors sought to establish the incidence, onset, and early ROP course in infants undergoing ROP screening. Of note, this study includes all eligible infants for ROP screening, not only high-risk infants for ROP. Demographics for the children undergoing ROP examinations included a mean birth weight (BW) of 1099g and a mean gestational age (GA) of 28 weeks. The authors reported that 3224 (43.1%) infants developed ROP, 459 (6.1%) developed type 1 ROP and 472 (6.3%) developed type 2 ROP. Regarding treatment, 514 (6.9%) infants underwent ROP treatment in 1 or both eyes and 147 (2.0%) had zone 1 disease. The authors report that secondary analysis shows that more than 40% of at-risk premature infants develop some stage of ROP and most ROP regresses without treatment. Of note, severe ROP was noted in 12.5% infants, especially with BW of less than 1251g. The authors suggest, similar to their earlier manuscript, that these stratified ROP results provide ROP risk profiles across BW and GA categories. Finally, the authors suggest that more specific guidelines are needed for low-risk infants with older GA and larger BW regarding the current criteria for ROP screening.

ROP - Other Topics

Evaluation of a deep learning image assessment system for detecting severe retinopathy of prematurity

Redd T, Campbell J, Brown J, Kim S, et al. *Br J* Ophthalmol. May 2019;103:580-584.

Previous studies have shown that inter-examiner diagnostic variability is high when examining for ROP, even among “expert” clinicians. Therefore there is high interest in artificial intelligence technologies for ROP to improve screening and standardization of diagnosis. The artificial intelligence technique known as deep learning (DL) has already been used for certain eye conditions including diabetic retinopathy. These systems use computer-based imaging analysis to automatically evaluate images and detect disease. The DeepROP algorithm, developed by the Imaging and Informatics in ROP (i-ROP) research consortium has been used to detect plus disease with high accuracy. This system is used in this study to identify broader diagnostic categories of ROP from posterior pole images. A total of 4861 eye examinations from 870 infants were analyzed. Mean BW and GA were 901g and 27+/-2 weeks. A reference standard diagnosis of type 1 ROP was identified in 155 exams (3%). The deep learning system was found to have a 94% sensitivity for type 1 ROP. The negative predictive value was 99.7% - and high value for a screening test where underdiagnoses can have severe implications. The system’s vascular severity score was strongly correlated with expert ranking of overall disease severity. The system was able to detect severe ROP based only on the posterior pole vascular morphology. This suggests that severe ROP rarely occurs in the absence of detectable changers in the posterior vasculature. Overall the results suggest this screening device could be used to improve the objectivity of ROP diagnosis as well as improve access to screening.

9. STRABISMUS

Strabismus – double vision, binocular vision and visual perception

Anatomy

Strabismus – Cranial Nerve palsy

Strabismus – Childhood XT and ET

Strabismus – Convergence / Divergence insufficiency

Inconsistent diagnostic criteria for convergence insufficiency.

Lavrich JB, Warner NJK, Hauschild AJ, Thau A et al. *JAAPOS* 2019 Feb;23(1):32. e1-32. e4.

Convergence insufficiency (CI) is a common entity but seems to be an ill-defined diagnosis that incorporates many near-vision symptoms. The current literature often varies in its criteria for diagnosis. Without a clear definition and standardization of the clinical examination, there is the potential for misdiagnosis and/or the inclusion of other diagnoses as CI. The purpose of this retrospective study was to assess the uniformity of diagnostic criteria in a well-defined practice environment. The medical records of 387 individuals diagnosed with CI between June 2007 and November 2014 who were patients of 6 fellowship-trained strabismologists in private practices and at Wills Eye Hospital clinics were reviewed retrospectively. The following data were collected: age, sex, race, age at diagnosis, past medical and family history, relevant symptoms, visual acuity, near point of convergence (NPC), strabismus measurements, and fusional amplitudes at distance with base-out and base-in prisms. Half of the patients were diagnosed with CI with normal NPCs. Only 246 of patients (29.7%) diagnosed with CI had documented fusional amplitudes. This study has demonstrated the variable range of criteria within one group of practitioners to diagnose CI. The authors conclude that no uniformity exists across clinicians in the clinical evaluation and diagnosis of patients with CI. They advocate the need for an evidence-based definition of the disease and its diagnosis. Interestingly, this study describes a group of the patients with CI that have NPCs at 1 cm but are symptomatic. These patients had poor fusional vergence amplitudes. The authors suggest that they may represent a separate subset within this disease or a separate diagnosis.

Strabismus – Acquired

Strabismus – Misc

Identification and Correction of Restrictive Strabismus After Pterygium Excision Surgery

Baxter SL, Nguyen BJ, Kinori M, et al. *Am J Ophthalmol.* 2019 June; 202: 6-14.

The authors of this study aimed to describe the clinical characteristics of patients who had restrictive strabismus and double vision after pterygium excision and to describe a successful approach to treat these patients. This was a retrospective interventional case series of fifteen patients at a single academic institution. The authors found a mean time to double vision was 6 months after pterygium surgery, and that all patients had abduction limitation causing a mean esotropia of 18 prism diopters. More than half of the patients this cohort had multiple previous pterygium surgeries, and more than half had amniotic membrane with fibrin glue used at the time of the initial surgery. Surgery to remove the scar tissue was multidisciplinary with a strabismus surgeon and oculoplastic or corneal surgeon. Forced duction testing intraoperatively was used pre and post to make sure that the restriction was relieved. The medial rectus was isolated in all cases using a medial limbal approach and the pseudotendons were excised. All patients received either an amniotic membrane graft (with sutures) or conjunctival autograft. Additionally, the authors used provisc around the muscles, 5-FU, MMC, steroids, and symblepharon rings in some combination depending on the patient's specific situation and surgeon preference but no strict protocol was used. After intervention (follow up average of 24 months), all patients were diplopia free in primary gaze, though 73% still had a small angle esotropia in the abductive, restricted field. Two patients had additional surgery for scar tissue but none had medial rectus recessions. The authors concluded that double vison caused by restrictive strabismus after pterygium surgery is more likely in patients with recurrent pterygium and for those treated with amniotic membrane with glue, but that this is treatable with scar tissue lysis and not eye muscle surgery. The authors point out the main limitation, which was that there was no standard protocol in how these patents were treated, but nonetheless this is an important article sine it demonstrates how removal of scar tissue, and not eye muscle surgery, can be curative in cases of restrictive strabismus after pterygium surgery.

Does successful surgical correction of childhood large angle exotropia in adults make any difference to binocularity and quality of life?

Yao J, Qu X, Lin J, Liu H. *Strabismus*. 2019 Jul 23:1-7.

Prior studies have shown that strabismus surgery can have positive effects in adults with large angle exotropia. The authors sought to examine if successful postoperative alignment could significantly improve HRQOL and investigate the relationship between stereopsis and HRQOL in these patients. In this prospective, non-interventional study, the authors enrolled 34 patients (mean age 29.38 ± 8.78 years) with large angle exotropia of either the constant (15) or intermittent (19) subtype who underwent strabismus surgery. Success was achieved in 94.74% of the intermittent group and 73.33% of the constant group. Stereopsis

improved in 19 patients and remained unchanged in 10 patients, without any statistically significant difference between the groups. Earlier age of surgery (p=0.05) and smaller preoperative angle of deviation at near (p=0.6) were found to be associated with normal stereopsis. All quality of life scores improved after surgery. The postoperative functional scores had no statistically significant association with the normal stereopsis (AS-20: p=0.07; A&SQ: p=0.16).
The angle of deviation at distance was significantly associated with the functional score of the AS-20 (p=0.02). The results of this study suggest that successful surgical correction of childhood large angle exotropia in adults improves both stereopsis and health related QOL, therefore is not solely for cosmetic purposes.

Global and regional prevalence of strabismus: a comprehensive systematic review and meta-analysis.

Hashemi H, Pakzad R, Heydarian S, Yekta A, et al. *Strabismus.* 2019 Apr 23:1-12.

The authors sought to define the prevalence of strabismus and investigate the affect of patient characteristics on the prevalence. Of the 7980 articles considered, they reviewed 56 articles with a sample size of 229396 patients. They found the pooled prevalence of any strabismus to be 1.93%, exotropia to be 1.23% and esotropia to be 0.77%. Age had a direct effect on the prevalence heterogeneity, as did the WHO region. ET had a higher prevalence in AMRO and EURO while XT was the dominant subtype in Asia, especially WPRO. The authors attribute this to a lower prevalence of hyperopia in these locations. The study is limited by the exclusion criteria which limited the number articles reviewed as well as the limited data sets from some populations. Overall it was helpful in that this study revealed that 1 in every 50 people had strabismus, which is useful in estimating the impact of strabismus.

Anomalous Vertical Deviations in Attempted Abduction Occur in the Majority of Patients with Esotropic Duane Syndrome

Rhiu S, Michalak S, Phanphruk W, and Hunter D. *Am J Ophthalmol.* 2018 November; 195: 171-175

This is a retrospective, observational case series of patient diagnosed with esotropic Duane syndrome over 13 years. The authors used clinical photographs of the patient's motility to describe the vertical eye position in attempted abduction; they grouped the patients into midline, depression or elevation based on these photos. Three separate ophthalmologists evaluated the photos. Of patients with unilateral esotropic duane syndrome 74/133 patients (66%) had depression in attempted abduction. 18/42 (43%) of the eyes with bilateral esotropic Duane syndrome were also found to have depression on attempted abduction. In the midline group, the limitation in abduction was found to be less severe. In the elevation group, the vertical deviation was more severe. The authors concluded that

depression in attempted abduction is present in the majority of patients with esotropic Duane syndrome, yet the description of this is lacking. They speculate that this is likely another form of dysinnervation and that looking for this is important in surgical planning. This paper nicely describes a clinical finding we see often in pediatric ophthalmology practice, but one that has not been described in detail in the literature.

10. STRABISMUS SURGERY

Horizontal muscle surgeries

A Randomized Trial Comparing Bilateral Lateral Rectus Recession versus Unilateral Recess and Resect for Basic-Type Intermittent Exotropia

Sean P. Donahue, Danielle L. Chandler, Jonathan M. Holmes, Brian W. Arthur, et al for the Pediatric Eye Disease Investigator Group *Ophthalmology*. February 2019;126:305-317

Intermittent exotropia is the most common childhood exotropia. This prospective study randomized children with basic intermittent exotropia to receive either recess-resect unilateral surgery or bilateral lateral rectus recession surgery. The sample size was only powered to detect a 25% difference in effect between treatments. Although the enrollment criteria included manifest plus latent deviations, the success criterion was limited to only manifest deviations. Strengths included masked observations and relatively long follow up, while weaknesses included flexibility to allow surgeons to augment recession amounts for non-standardized reasons, variable preoperative treatment with patching and/or orthoptic exercises, and overlapping failure criteria. All treatment outcomes favored unilateral recess/resect surgery except for a slightly higher rate of esotropia, but the probabilities were only strong enough to exclude bilateral recessions as the superior treatment option. Given prior randomized control trials favoring unilateral recess/resect surgery for this condition, this study provides additional evidence that bilateral lateral rectus recessions are not equivalent, as the authors concluded, but rather the inferior treatment option, with a stronger conclusion limited by the power of the study.

Vertical muscle surgeries

Superior oblique tuck: evaluation of surgical outcomes.

Dwivedi R, Marsh IB. *Strabismus*. 2019 Mar;27(1):11-15.

A variety of techniques exist to surgically manage superior oblique palsy. The authors performed a retrospective chart review of 162 patients who underwent a superior oblique tuck from 1992-2016 to compare surgical success. Of the cases of superior oblique palsy, 110 patients had a congenital palsy. Pre-operatively the mean angle of deviation was 15.88 PD (range 4-35 PD) and the mean post-operative angle was 5.09 PD (range 0-20 PD). The mean overall reduction was 10.79 PD (range 0-34 PD). A significant difference was observed between those patients who had pre-operative angles of deviation >15 PD and those with <15 PD (14.85 PD vs. 6.83 PD; $p < 0.0001$). 54 patients (33.33%) required additional extraocular muscle surgery. 24 patients (14.82%) experienced post-operative iatrogenic Brown's syndrome but only two of these required further corrective surgery. Patients with acquired superior oblique palsy tended to have worse clinical outcomes with a greater incidence of post-operative diplopia and the requirement for further surgery. There was no linear relationship between the amount of the tuck and surgical outcomes. Overall, a superior oblique tuck seems to be an effective manner of surgically managing superior oblique palsy, although there appears to be a somewhat unpredictable amount of correction.

Superior Oblique Palsy: Efficacy of Isolated Inferior Oblique recession in Cases with Ipsilateral Hypertropia in Abduction

Torrado, Laura A. and Brodsky, Michael C. *Journal of Binocular Vision and Ocular Motility*, 2019; 69:1, 8-12

The purpose of this retrospective review is to evaluate the effects of single inferior oblique (IO) recession in superior oblique palsy (SOP) patients with persistent hypertropia in abduction. Numerous studies have illustrated the effect of isolated IO weakening in patients with SOP with a hypertropia in primary position of 15Δ or less. Secondary superior rectus (SR) contraction can lead to spread of comitance and persistent hypertropia of the paretic eye in abduction, and due to frequent overcorrections SR recessions are inadvisable in these patients. Patients with a SOP and hypertropia of < 20Δ in primary position with persistent hypertropia of > 3Δ in abduction were included. Seven patients were identified and they underwent a 14mm IO recession. All patients had a decrease in hypertropia in primary position, contralateral hypertropia, ipsilateral hypertropia, lateral incomitance, and subjective intorsion. The authors conclude that an isolated maximal IO recession is effective in the treatment of unilateral SOP that is accompanied by a modest hypertropia of the paretic eye in abduction.

Dose Effect and Stability of Postoperative Cyclodeviation After Adjustable Harada-Ito Surgery

Liebermann L, Leske DA, Holmes JM, et al. *Am J Ophthalmol.* 2018 December; 196: 91-95.

A retrospective cohort study of one surgeon's patients over a 20-year period was performed with the goal of reporting the dose-response relationship of the adjustable Harada-Ito surgery. The secondary goals of this study were to report the changes in the cyclodeviation over time and to recommend a target angle in the immediate postoperative period (adjustment target). There were 20 patients who underwent a unilateral adjustable advancement of the anterior fibers of the superior oblique tendon. Double Maddox rod was use to measure the cyclodeviation. The pre op measurements were compared to the 1 day and 6-week post op measurements in all patients and to the in 1- and 5- year measurements when available. The authors found that there was a dose effect of 1.3 degrees per mm of advancement (+ resection). There was a regression towards excyclodeviation between adjustment and the 6 week post op of 6.5 + 2.6 degrees, and to a lesser extent after that. The authors recommend an initial overcorrection target of 7 degrees of incyclotorsion after adjustment. The authors point out the limitations, which include lack of complete follow up data in all patients and continued debate about the need for an adjustable procedure for torsion. This paper's most important contributions are the reminder of the cyclodeviation regression with time and the dose effect calculations.

Transposition surgeries

Sutures / Adjustables

Strabismus surgery - Misc

The incidence and clinical outcome of complications in 4,000 consecutive strabismus operations.

Ritchie AE and Ali N *JAAPOS* 2019 June; 23 (3): 140.e1-140.e6

The British Ophthalmic Surveillance Unit (BOSU) estimated in 2013 the incidence of severe complications in strabismus surgery at 1 in 400 operations, with a poor or very

poor outcome in 1 in 2,400 cases. This landmark study provided a benchmark for audit and an evidence-base for discussing the risks of strabismus surgery with patients. The study, however, relied on anonymous surgeons volunteering to take part and remembering to return questionnaires; thus, complications may have been underreported. The purpose of this prospective audit was to test the validity of the British Ophthalmic Surveillance Unit (BOSU) study's incidence figure of severe complications following strabismus surgery and to determine the incidence, type, risk factors, and outcome of all strabismus surgery complications at a single institution. Patient diagnosis, age, sex, surgical details, complications, and outcome were recorded from hospital records. Complications were classified as minor, moderate, or severe. The outcome was graded using the Bradbury and Taylor grading system (I to IV), with a poor or very poor outcome meaning loss of corrected visual acuity or unexpected primary position diplopia. A total of 4,076 consecutive strabismus operations were performed during the study period. There were 46 (1.13%) complications, of which 28 (0.69%) were minor, 7 (0.17%) were moderate, and 9 (0.22%) were severe. The incidence rate of 0.07% (3 patients) for globe perforations in this study is comparable with the BOSU study rate of 0.08%. Two patients had pulled-in-two syndrome (PITS) intraoperatively (0.05%). Only 1 patient (0.02%) had a poor visual outcome. Optical coherence tomography (OCT) imaging was in keeping with paracentral acute middle maculopathy. It is most likely that cilioretinal artery territory infarction occurred during the perioperative period. Two patients had non-ocular postoperative complications (0.05%). Interestingly, of the patients who underwent surgery during the study period, 84% were adults (>16 years of age); 16% were children. The rate of severe complications was 0.23% for adults and 0.16% for children, a difference that was not statistically significant.
The authors conclude that in this large, prospective series, the rate of severe complications of strabismus surgery was found to be 1 in 455 cases. Their results validate the findings of the BOSU study. This seminal study might be the largest prospective series of consecutive cases reporting on the full range of complications of strabismus surgery and can be used as an evidence-base for discussing the risks of strabismus surgery with patients.

The management of large-angle esotropia in Graves ophthalmopathy with combined medial rectus recession and lateral rectus resection.

Garrity JA, Greninger DA, Ekdawi NS, Steele EA. *JAAPOS* 2019 Feb;23(1):15. e1-15. e5.

There are a multitude of surgical approaches to strabismus in Graves ophthalmopathy, including adjustable sutures, matching the restriction of ductions, and intraoperative relaxed muscle positioning. The purpose of this retrospective study was to describe surgical management and outcomes for large-angle esotropia of ≥50$^{\Delta}$ secondary to Graves ophthalmopathy using combined initial nonadjustable medial rectus recessions and lateral rectus resections. The medical records of 38 consecutive patients undergoing strabismus surgery for large-angle esotropia

secondary to Graves ophthalmopathy from 1995 to 2012 by a single surgeon were reviewed. The technique and surgical dosing are further described in the article. Of the 38 eligible patients, 36 had bilateral nonadjustable medial rectus recessions and lateral rectus resections as initial treatment for esotropia, and 6 patients underwent simultaneous vertical muscle surgery. Mean preoperative horizontal deviation was 60^{Δ} (range 50^{Δ} -95^{Δ}) and mean preoperative vertical deviation was 10^{Δ} (range 0 -65^{Δ}). A modified Gorman diplopia scale was used to assess outcome. Satisfactory outcome was defined as absence of constant diplopia in primary or reading position within the central 30^{o}, and unsatisfactory outcome was defined as presence of constant diplopia in primary and/or reading position. A total of 19 patients (50%) reached the primary outcome after one surgery, including 5 of 6 (85%) who had no preoperative vertical strabismus. A total of 21 patients (55%) required repeated surgery. The indications for reoperation were vertical strabismus in 13 of 21 patients (62%), residual esotropia in 7 of 21 (33%), and consecutive exotropia in 1 of 21 (5%). With a median follow-up of 13.2 months, 32 of 38 patients (84%) reached the satisfactory results after consecutive surgery.The authors conclude that combined nonadjustable medial rectus recessions with lateral rectus resections can be beneficial as a primary treatment for large-angle esotropia in patients with Graves ophthalmopathy. The study is limited by its retrospective nature and relatively short follow-up, nonetheless it offers yet another alternative for these difficult cases with comparable success rate to other techniques.

11. ANTERIOR SEGMENT

Monotherapy of topical tacrolimus 0.03% in the treatment of vernal keratoconjunctivitis in the pediatric population.

Samyukta SK, Pawar N, Ravindran M, et al *JAAPOS* 2019 Feb;23(1):36. e1-36. e5.
The successful off-label use of tacrolimus in VKC has been previously reported, however some conflicting results have been shown. The aim of this prospective, nonrandomized observational study was to report the results of treating children with vernal keratoconjunctivitis (VKC) using a monotherapy of topical tacrolimus 0.03%. The severity of the disease was graded on a 4-point scale of symptoms and signs. Patients were treated with tacrolimus 0.03% ointment and were followed for 8 months according to a schedule based on the severity of the disease. The primary measure of treatment efficacy was the change in the score of objective signs. The incidence and severity of adverse events, if any, were recorded. A total of 60 children aged 5-15 years were enrolled, only 45 (37 males [82%]) were available for analysis. The mean composite *symptom* score was 6.84 ± 2.26 at baseline and 0.71 ± 1.62 at 8 months, a statistically significant reduction ($P < 0.001$). The mean composite *sign* score was 9.6 ± 3.14 at baseline and 1.16 ± 1.28 at 8 months, also a statistically significant reduction ($P < 0.001$). Four patients had to be

started on steroids within the first month of treatment and were considered treatment failures. Thus, 89% of patients showed significant improvement. No participant experienced adverse effects, although some reported a transient stinging sensation. In this cohort topical tacrolimus ointment 0.03% as a monotherapy for VKC was successful in the majority of subjects, and there was no adverse effect. The study was limited by its small sample size and its short follow-up. It is also biased by high rate of loss to follow-up. Nevertheless, the results indicate that early inclusion of low-strength tacrolimus (0.03%) in the management of pediatric patients with VKC can prevent the development of blinding sequelae of the disease.

Keratoconus Natural Progression *A Systematic Review a Meta-analysis of 11529 Eyes*

Alex C Ferdi, Vuong Nguyen, Daniel M Gore, Bruce D Allan, et al
Ophthalmology. July 2019;126(7): 935-945.

The purpose of this study was to describe the natural history of keratoconus through systematic review and meta-analysis. Interventions including corneal cross-linking, intracorneal ring segments, refractive laser, and grafting are utilized to stabilize disease or improve vision but they carry risks. Detailed knowledge of the natural history keratoconus is fundamental in make informed decisions. Their search yielded 3950 publication titles, of which 41 were included in their systematic review and 23 were incorporated into the meta-analysis. The meta-analysis of 12-month outcomes found that younger patients progress more aggressively: patients younger than 17 years old are likely to have more than 1.5 diopters (D) of maximum keratometry (Kmax) progression. Patients with steeper Kmax demonstrated more severe progression: patients is greater than 55 D K max are likely to progress by at least 1.5 D Kmax. Middle eastern patient also experienced more progression. They conclude that closer follow-up and a lower threshold for cross-linking should be adopted in patients less than 17 years with steeper than 55 D Kmax.

A Randomized, Controlled Trial of Cyclosporine A Cationic Emulsion in Pediatric Vernal Keratoconjunctivitis

Andrea Leonardi, Serge Doan, Mourad Amrane, Dahlia Ismail, et al
Ophthalmology. May 2019;126(5): 671-681.

The purpose of the VErnal KeratoconjunctivTIs Study (VEKTIS) was to evaluate the safety and efficacy of an investigational therapy, cyclosporine A (CsA) cationic emulsion (CE) for severe vernal keratoconjunctivitis (VKC). CsA is practically insoluble in water and must be delivered topically in a lipid-based system.

With CsA CE, there is increased residence time at the ocular surface due to attraction between positively charged nanodroplets and the negatively charged cell membranes thereby providing improved ocular bioavailability. VEKTIS is a phase 3, multicenter, double-masked, vehicle-controlled trial. Participants included pediatric patients ages 4 to 18 years with active severe VKC (Grade 3 or 4 on Bonini severity scale) and severe keratitis (corneal fluorescein staining [CFS] score of 4 or 5 on modified Oxford scale). One hundred sixty-nine patients were randomized to CsA CE 0.1% (1mg/ml) eyedrops 4 times per day (high-dose), CsA CE twice daily (low dose) plus vehicle twice daily, or vehicle 4 times daily for 4 months. Dexamethasone 0.1% 4 times daily for up to 5 days served as the rescue medication. Study visits occurred every four weeks, and efficacy was evaluated utilizing 3 primary criteria: (1) keratitis assessed by CFS, (2) need for rescue medication, and (3) occurrence of corneal ulceration. Results showed statistically significant improvement for both the high-dose (0.76; P=0.007) and low-dose (0.67; P=0.010) groups versus the vehicle group with treatment effect driven largely by CFS score. Significant differences were found between both active treatment groups and vehicle for use of rescue medication. VKC symptoms and patient quality-of-life improved in all three groups with significant improvement for high-dose CsA CE versus vehicle. The greatest improvement in the composite efficacy score was achieved from baseline to month one, indicating that treatment benefits occurred rapidly. The safety data were consistent with the known safety profile of topically applied CsA and no unexpected safety findings were identified. Instillation site pain was noted in all three groups, but it was slightly more in the high-dose group. One limitation of the study was lack of a true placebo but any topical products including eyewash will potentially have an effect due to dilution of allergens and mediators. In addition, the authors note it is not ethically acceptable to have children with severe VKC receiving placebo and a clinical trial. The other limitation was a four-month comparative period. The effects of continued treatment with CsA CE at an eight-month safety follow-up will be reported in a subsequent publication.

12. CATARACT

13.CATARACT SURGERY

Pediatric cataract surgery outcomes

Outcomes of Unilateral Cataracts in Infants and Toddlers 7 to 24 Months of Age: Toddler Aphakia and Pseudophakia Study (TAPS)

Erick D. Bothun, M. Edward Wilson, Elias I. Traboulsi, Nancy N. Diehl, et al for the Toddler Aphakia and Pseudophakia Study Group (TAPS)
Ophthalmology. August 2019;126:1189-1195

Intraocular lens implantation after lensectomy in children younger than 2 years of age is becoming more commonplace. This study retrospectively reports long-term visual outcomes in children ages 7 to 24 months originally enrolled in the Toddler Aphakia and Pseudophakia Treatment Study between 2004-2010. The primary treatment outcomes were determined at the eye examination closest to age 5. The average age at surgery was 14 months and average treatment follow up was 4 years. The average final vision in the operated eye was 20/125; only 11% of subjects demonstrating 20/40 or better vision, all older than 13 months at time of surgery. Visual axis opacification occurred in 14% of children, resulting in unplanned surgeries. Only one child was considered a glaucoma suspect. Only 32% of subjects did not manifest strabismus; stereopsis was only detectable in 3 children. Compared with intraocular lens implantation in children less than 7 months, this older study cohort had dramatically fewer adverse events and unplanned surgeries. In addition, the range of refractive outcomes at age 5 was much narrower, implying that the expected myopic postoperative shift in refraction is much more predictable in the older patients. The data provides strong support to lower the standard of care age for intraocular lens implantation after lensectomy to 13 months or less.

Long-term outcomes for pediatric patients having transscleral fixation of the capsular bag with intraocular lens for ectopia lentis

Julia M. Byrd, Marielle P. Young, Wei Liu, Yue Zhang, et al. *Journal of Cataract and Refractive Surgery*; 2018;44(5):603-609.

This study from the Moran Eye Center in Utah of 37 patients (67 eyes) with atraumatic ectopia lentis having transscleral fixation of the capsular bag using a capsular tension ring fixated with 9-0 or 10-0 polypropylene, 8-0 polytetrafluoroethylene, or 9-0 nylon found a 78.5% improvement in corrected distance visual acuity at a mean follow up time of 35.3 months (0.25-120 months). The mean age at time of surgery was 7.25 years (2-18 years). The range of resulting refractive error was similar to that seen with traditional IOL placement. Short-term complications included hyphema in 1 eye and IOL repositioning at 3 months in 1 eye and long-term complications included posterior capsule opacification in 35 eyes (52%), uveitis-glaucoma-hyphema syndrome in 1 eye (1.5%), and spontaneous IOL dislocation in 3 eyes (4.4%) requiring IOL repositioning. As 7 patients who were initially considered for transscleral CTR suturing were unable to receive the procedure for various reasons determined intraoperatively, the authors note that the technique presented may not be appropriate for all cases. Nevertheless, this is an important article for pediatric ophthalmologists given the paucity of data regarding long-term outcomes in pediatric patients having surgical intervention for visually significant ectopia lentis.

14.GLAUCOMA

Pediatric glaucoma - surgical management

15.REFRACTIVE SURGERY

Corneal indices following photorefractive keratectomy in children at least 5 years after surgery.

Ram R, Kang T, Weikert MP, Kong L, et al. *JAAPOS* 2019 June; 23 (3): 149.e1-149.e3

The literature regarding haze and keratectasia after refractive surgery in children is scarce. The aim of this prospective interventional case series was to evaluate long-term corneal outcomes in pediatric patients who underwent photorefractive keratotomy (PRK) for the treatment of refractive amblyopia. Children with refractive amblyopia underwent PRK between January 1, 2007, and December 31, 2011, at Texas Children's Hospital's Department of Ophthalmology, a single tertiary eye center, and were followed for at least 5 years after surgery. Main outcome measures were 5+ years postoperative indices of corneal thickness, keratometry, degree of corneal haze, and presence or absence of keratectasia. A total of 12 eyes of 8 subjects (aged 3-9 years) who underwent PRK and were followed for at least 5 years were included. The mean PRK treatment dose was 8.46 D for the myopic cohort and 4.49 D for the hyperopic cohort, which removed an average of 72 µm of corneal stromal tissue in addition to the 50 µm of corneal epithelium that was removed prior to laser ablation. The mean corneal thickness was 563 µm preoperatively, which decreased to 441 µm immediately following the PRK. The mean corneal thickness 5+ years after PRK was stable, at 498 µm, because of epithelial regrowth. None of the subjects developed visually significant corneal haze or topographic evidence of keratectasia. The authors conclude that in this study cohort, there were no topographic signs of keratectasia or corneal haze in children treated with PRK for high refractive error 5 years or more after surgery. The study main limitation is its small sample size.

16. GENETICS

Iris anomalies and the incidence of ACTA2 mutation

Kenneth J Taubenslag, Hannah L Scanga, Jennifer Huey, Jennifer Lee, et al

Br J Ophthalmol 2019;103:499–503. doi:10.1136/bjophthalmol-2018-312306

Iris flocculi, are central iris pigment epithelial cysts, that are reported in the literature to be associated with thoracic aortic aneurysm and dissection due to smooth muscle alpha-actin 2 (ACTA2) mutations. Children with the ACTA2 mutation may also present with congenital mydriasis. The authors retrospectively reviewed all children who presented over a 4 year period at their institution with iris floccule or congenital mydriasis. None of the 10 children presenting with iris flocculi had ACTA2 mutation. All children with congenital mydriasis had multisystem smooth muscle dysfunction while 2 had R179 ACTA2 mutations. The child who was negative had no cardiac disease and may have had a different unknown genetic mutation. This is a limitation of this study as well as small sample size. The authors suggest that all patients with congenital mydriasis should have genetic testing for ACTA2 mutation and cardiac workup while patients with iris flocculi should have workup guided by history and physical in order to identify those patients who should have genetic and cardiac workup. This paper is important as it challenges the theory that iris flocculi are associated with with thoracic aortic aneurysm and dissection challenging previous literature.

IMI - Myopia Genetics Report.

Tedja MS, Haarman AEG, Meester-Smoor MA, Kaprio J, et al. *Invest Ophthalmol Vis Sci.* 2019 Feb 28;60(3):M89-M105.

The knowledge on the genetic background of refractive error and myopia has expanded dramatically in the past few years. This white paper aims to provide a concise summary of current genetic findings and defines the direction where development is needed. An extensive literature search was performed and the authors conducted informal discussions with key stakeholders. Specific topics reviewed included common refractive error, any and high myopia, and myopia related to syndromes. To date, almost 200 genetic loci have been identified for refractive error and myopia, and risk variants mostly carry low risk but are highly prevalent in the general population. Several genes for secondary syndromic myopia overlap with those for common myopia. Polygenic risk scores show overrepresentation of high myopia in the higher deciles of risk. Annotated genes have a wide variety of functions, and all retinal layers appear to be sites of expression. The current genetic findings offer a world of new molecules involved in myopiagenesis. As the missing heritability is still large, further genetic advances are needed. The paper recommends expanding large-scale, in-depth genetic studies using complementary big data analytics, consideration of gene-environment effects by thorough measurement of environmental exposures, and focus on subgroups with extreme phenotypes and high familial occurrence. Functional characterization of associated variants is simultaneously needed to bridge the knowledge gap between sequence variance and consequence for eye growth.

Potential lifetime quality of life benefits of choroideremia gene therapy: projections from a clinically informed decision model.

Halioua-Haubold CL, Jolly JK, Smith JA, Pinedo-Villanueva R, et al. *Eye* (Lond). 2019 Aug;33(8):1215-1223.

The first gene therapy for an inherited retinal dystrophy recently received market approval in the United States; multiple other gene therapies are in the clinical pipeline. Thus far, gene therapy has commanded prices in the range of $500,000 to over $1,000,000 for the one-time doses and have been indicated for highly orphan diseases where there is no other viable treatment option. To be adopted by healthcare systems, gene therapy will need to show clinical benefit in line with its increased costs. Before longitudinal patient studies are available, model-based estimations will be necessary to project the full clinical benefit of gene therapy. This study aims to investigate the lifetime benefit of gene therapy for the retinal dystrophy choroideremia, based on a Markov model of disease progression informed by clinical data of AAV.REP1 and voretigene neparvovec (Luxturna, Spark Therapeutics). Gene therapy patient benefit was estimated by quality-adjusted life years (QALYs) in three hypothetical disease severity patient groups. The severity of disease was defined by the combined effect of remaining retinal area and visual acuity and assigned corresponding health utility values.
Early-stage patients treated with gene therapy were estimated to gain, in average, 14.30 QALYs over standard-of-care, mid-stage patients 6.22 QALYs, and late-stage patients 1.48 QALYs over untreated patients during their lifetime owing to treatment. Cost-effectiveness was not assessed as AAV.REP1 is still in clinical trials. In young adults in the earlier stages of choroideremia, successful gene therapy is expected to provide a significant increase in health-related quality of life.

Clinical and molecular characterization of familial exudative vitreoretinopathy associated with microcephaly.

Hull S, Arno G, Ostergaard P, Pontikos N, et al. *Am J Ophthalmol.* 2019 May 8.

Familial exudative vitreoretinopathy (FEVR) is a rare finding in patients with genetic forms of microcephaly. This study documents the detailed phenotype and expands the range of genetic heterogeneity. The design is a retrospective case-series including twelve patients (ten families) with a diagnosis of FEVR and microcephaly who were ascertained from pediatric genetic eye clinics and underwent full clinical assessment including retinal imaging. Molecular investigations included candidate gene Sanger sequencing, whole-exome sequencing (WES) and whole-genome sequencing (WGS).
All patients had reduced vision and nystagmus. Six were legally blind. Two probands carried bi-allelic *LRP5* variants, both presenting with bilateral retinal folds.

A novel homozygous splice variant, and two missense variants were identified. Subsequent bone density measurement identified osteoporosis in one proband. Four families had heterozygous *KIF11* variants. Two probands had a retinal fold in one eye and chorioretinal atrophy in the other; the other two had bilateral retinal folds. Four heterozygous variants were found, including two large deletions not identified on Sanger sequencing or WES. A family of two children with learning difficulties, abnormal peripheral retinal vasculogenesis and rod-cone dystrophy were investigated. They were found to have bi-allelic splicing variants in *TUBGCP6*.Three families remained unsolved following WES and WGS. WGS enabled molecular diagnosis in three families after prior negative Sanger sequencing of the causative gene. This has enabled patient-specific care with targeted investigations and accurate family counseling.

The Natural History of Inherited Retinal Dystrophy Due to Biallelic Mutations in the *RPE65* Gene.

Chung DC, Bertelsen M, Lorenz B, Pennesi ME, et al. *Am J Ophthalmol*. 2019 Mar;199:58-70.

This study delineates the natural history of visual parameters over time in individuals with biallelic *RPE65* mutation-associated inherited retinal dystrophy (IRD); describes the range of causative mutations; determines potential genotype/phenotype relationships; and describes the variety of clinical diagnoses. The design is a global, multicenter, retrospective chart review. Seventy individuals with biallelic *RPE65* mutation-associated IRD were identified and relevant data was extracted from patient charts. This included measurements of visual acuity (VA), Goldmann visual field (GVF), optical coherence tomography, color vision testing, light sensitivity testing, and electroretinograms (retinal imaging and fundus photography were collected and analyzed when available).
VA decreased with age in a nonlinear, positive-acceleration relationship ($P < .001$). GVF decreased with age ($P < .0001$ for both V4e and III4e), with faster GVF decrease for III4e stimulus vs V4e ($P = .0114$, left eye; $P = .0076$, right eye). On average, a 1-year increase in age decreased III4e GVF by ~25 sum total degrees in each eye while V4e GVF decreased by ~37 sum total degrees in each eye, although individual variability was observed. A total of 78 clinical diagnoses and 56 unique *RPE65* mutations were recorded, without discernible *RPE65* mutation genotype/phenotype relationships.
The number of clinical diagnoses and lack of a consistent *RPE65* mutation-to-phenotype correlation underscore the need for genetic testing. The data may have implications for optimal timing of treatment for IRD attributable to biallelic *RPE65*
mutations.

Efficacy Outcome Measures for Clinical Trials of USH2A Caused by the Common c.2299delG Mutation.

Calzetti G, Levy RA, Cideciyan AV, et al. *Am J Ophthalmol.* 2018 Sep;193:114-129.

Usher syndrome (USH), an autosomal recessive disorder with 3 clinical types and multiple molecular subtypes, leads to retinal degeneration with accompanying hearing and vestibular impairment. There are no therapies at this time for the progressive retinal degeneration of any form of USH. One of the common forms of USH is owing to mutations in the *USH2A* gene, and the most common *USH2A* mutation is the c.2299delG variant in exon 13, which causes a frameshift at codon 767 resulting in a premature termination or a splicing defect. The goal of this paper was to determine the change in vision and retinal structure in patients with the common c.2299delG mutation in the *USH2A* gene in anticipation of clinical trials of therapy. Eighteen patients, homozygotes or compound heterozygotes with the c.2299delG mutation in *USH2A*, were studied with regard to visual acuity, kinetic perimetry, dark- and light-adapted static perimetry, optical coherence tomography (OCT), and autofluorescence (AF) imaging. Serial data were available for at least half of the patients, depending on the parameter analyzed. The kinetics of disease progression in this specific molecular form of USH2A differed between the measured parameters. Visual acuity could remain normal for decades. Kinetic and light-adapted static perimetry across the entire visual field had similar rates of decline that were slower than those of rod-based perimetry. Horizontal OCT scans through the macula showed that inner segment/outer segment line width had a similar rate of constriction as co-localized AF imaging and cone-based light-adapted sensitivity extent. The rate of constriction of rod-based sensitivity extent across this same region was twice as rapid as that of cones. In conclusion, in patients with the c.299delG mutation in *USH2A*, rod photoreceptors are the cells that express disease early and more aggressively than cones. Rod-based vision measurements in central or extracentral-peripheral retinal regions warrant monitoring in order to complete a clinical trial in a timely manner.

17. TRAUMA

NON-ACCIDENTAL HEAD TRAUMA

MISCELLANEOUS

18. RETINA

Prevalence and Onset of Pediatric Sickle Cell Retinopathy

Jonathan Li, Lloyd Bender, James Shaffer, Daniel Cohen, et al
Ophthalmology. July 2019;126(7): 1000-1006.

This retrospective cohort study sought to determine the prevalence, age of onset, and risk factors associated with sickle cell retinopathy (SCR) to inform development screening guidelines for asymptomatic children. Risk factors evaluated included markers of sickle cell hemoglobinopathy (SCH) severity (number of emergency room or hospital admissions for crises, number of transfusions, hydroxyurea therapy, and transcranial Doppler-confirm cerebral vasculopathy), genotype, gender, and race. Of 398 children (mean age, 9.6+ +/- 4.6 years; age 0–18 years), 208 (52%) showed sickle cell homozygote (SS) genotype, 113 (28%) showed sickle cell hemoglobin C (SC) genotype, and 77 (19%) showed trait genotype. Forty-eight children (12.1%) demonstrated SCR, 44 of 398 children (11.1%; 95% confidence interval, 8.3%-14.5%) demonstrated NPR, and 9 of 398 children (2.3%; 95% confidence interval, 1.2%-4.2%) demonstrated PR. Prevalence was higher for SC than SS genotype for NPR (21% vs 9%) and PR (5% vs 1%); onset for SC genotype was earlier than that for SS genotype for NPR (youngest diagnosis 4.8 vs 6.1 years) and PR (12.2 vs 15.4 years). No other risk factors were associated significantly with SCR. This is the largest study of children with SCH to date in North America even if children with sickle cell trait are excluded from the cohort. The study period is also the most recent permitting and analysis of new potential risk factors that have emerged as standard of care for children with SCH and have not been analyzed previously. The authors identify potential referral bias relating to referral of sicker children which makes their recommendations more conservative in terms of not missing any treatable SCR. They suggest screening to identify PR in children without ophthalmologic symptoms begin by nine years of age for children with SC disease and by 13 years of age for children with SS disease. Clinical markers SCH severity evaluated in the study do not seem to have value in determining screening guidelines

Choroidal neovascular membrane in paediatric patients: clinical characteristics and outcomes

Padhi T, Anderson B, Abbey A, Yonekawa Y, et al. *Br J* Ophthalmol. September 2018;102:1232-1237.

The incidence of choroidal neovascular membrane (CNVM) is relatively small compared to adults, but when present can have a profound impact on children. The authors of this study performed a retrospective review of patients 18 years old or less with CNVM. They analyzed demographics, vision, pathology, and other parameters. 35 subjects (43 eyes) were identified with mean age of 11.2 years. The CNVMs were mostly type 2, classical, and subfoveal. The most common association was with Best vitelliform macular dystrophy (32.5%). The CNVM was active in 36 of 43 eyes. 30 of these underwent treatment, of which anti-VEGF injection was the initial therapy choice in all. Responsive eyes required a mean of 2.11 injection. 50% of recurrent CNVM stabilized with repeat injection, with the remaining requiring photodynamic therapy, laser or surgery. Mean visual acuity gain for peripapillary and subfoveal groups was 0.7752 and 0.4361 log-

MAR. However, mean gain in visual acuity on comparison for all CNVM subgroups was not statistically significant. The authos note that overall recurrent rate and number of recurrences were lower in children compared to adult patients, with a lower average number of injections needed for resolution.

Traumatic macular retinoschisis in infants and children

Shouldice M, Al-Khattabi F, Thau V, McIntyre S, et al. *JAAPOS*. Dec 2018;22(6):433-437.e2.

The purpose of this paper is to provide detailed description of pediatric traumatic retinoschisis. The medical records of children with either abusive head trauma and traumatic macular retinoschisis seen at a single center from 1993 to 2006 were reviewed retrospectively. Clinical details were extracted from the record and photographic documentation. Evaluation regarding abuse excluded ophthalmology findings to avoid circular reasoning. Of 134 patients with suspected abusive head trauma, 31 (23/1%) had retinoschisis; no other patients were identified who had retinoschisis during this time period. Mean age of these patients was 9 months. Of the 31 patients, 22 (71%) offered a history of injury, and 9 (29%) were found unresponsive without history of injury; 6 were reportedly shaken. All patients had seizures, vomiting, and/or altered responsiveness. All had subdural hemorrhage, with cerebral edema in 17 (55%). In 10 (32%), there were findings of blunt force head injuries; in 4 of these there was no impact history. Retinal hemorrhages were present in all cases. Agreement between sidedness of retinoschisis and subdural hemorrhage was poor. Two thirds of the patients had associated physical injury. One third of the patients had associated vitreous hemorrhage. Eleven patients had retinal folds, 3 of which had a hemorrhagic edge to the schisis; nine of these patients suffered from future neurological conditions or cortical visual impairment, reinforcing the fact that retinal folds are associated with worse visual and neurological outcomes. Nine patients had extracranial manifestations of abuse. Multidisciplinary team adjudications were as follows: of the 31 cases, 18 were suspicious for abuse, 11 were indeterminate, and 2 were possibly accounted for by accidental severe crush injury. Three children died, and 11 suffered neurological sequelae. The authors conclude that traumatic retinoschisis in children is highly associated with subdural hemorrhage, neurologic symptoms, and poor outcomes. Even with a conservative approach to opinion formulation, traumatic retinoschisis was associated with likely abuse.

OCT IMAGING IN DISEASE

19.RETINOBLASTOMA / INTRAOCULAR TUMORS

RETINOBLASTOMA

Vision and visual potential for perifoveal retinoblastoma after optical coherence tomographic-guided sequential laser photocoagulation

Soliman S, VandenHoven C, Mackeen L, Gallie B. *Br J* Ophthalmol. June 2019;103:753-760.

The authors of this study hypothesized that avoiding direct laser treatment to the foveal edge of perifoval RB tumors might enhance visual potential while still adequately achieving tumor control. Therefore they performed this retrospective interventional case series of children with perifoveal RB treated with laser after chemotherapy monitored at each session by optical coherence tomography (OCT). 22 eyes (20 patients) were analyzed, including 14 juxtafoveal (fovea <3000 µm from tumor edge) and 8 foveolar (tumor underlying fovea) tumors. After tumor chemoreduction, laser was performed under general anesthesia with OCT guidance. The OCT was used to identify and document the fovea to design the foveal sparing laser crescent. In later sessions OCT was also used to dermine residual tumor areas and height. Post-laser OCT ensured accuracy of laser treatments. With juxtafoveal tumors, foveal pit preservation was observed in 13/14 eyes (with >= 500 µm of perifoveal retina tumor free). In 1 eye the fovea was flattened by an epiretinal membrane. 12 eyes had normal central fovealor thickness. Foveolar tumors had worse anatomical outcomes: 5/8 had tumor recurrences and none had restored foveal pit or perifoveal retina. Acceptable (>= 1.0 logMAR or good (>= 0.5 logMAR) visual acuity was found in 12/14 and 8/14 eyes with juxtafoveal tumors, and 5/6 and 0/6 eyes with foveolar tumors respectively. This study did not include data on children who underwent amblyopia therapy. The authors summarize that visual potential and anatomical results were better in juxtafoveal RB compared to foveolar RB in children treated with foveal-sparing laser photocoagulation guided by OCT.

The predictive value of magnetic resonance imaging of retinoblastoma for the likelihood of high-risk pathologic features

Hiasat J, Saleh A, Al-Hussaini M, Al Nawaiseh I, et al. *EJO,* March 2019, 29(2) 262–268

The goal was to evaluate the predictive value of magnetic resonance imaging in retinoblastoma for the likelihood of high risk pathologic features. A retrospective study of 64 eyes enucleated from 60 retinoblastoma patients. Contrast-enhanced magnetic resonance imaging was performed before enucleation. Main outcome measures included demographics, laterality, accuracy, sensitivity, and specificity of magnetic resonance imaging in detecting high-risk pathologic features. Optic nerve invasion and choroidal invasion were seen microscopically in 34 (53%) and 28 (44%) eyes, respectively, while they were detected in magnetic resonance imaging in 22 (34%) and 15 (23%) eyes, respectively. The accuracy of magnetic

resonance imaging in detecting prelaminar invasion was 77% (sensitivity 89%, specificity 98%), 56% for laminar invasion (sensitivity 27%, specificity 94%), 84% for postlaminar invasion (sensitivity 42%, specificity 98%), and 100% for optic cut edge invasion (sensitivity100%, specificity 100%). The accuracy of magnetic resonance imaging in detecting focal choroidal invasion was 48% (sensitivity 33%, specificity 97%), and 84% for massive choroidal invasion (sensitivity 53%, specificity 98%), and the accuracy in detecting extrascleral extension was 96% (sensitivity 67%, specificity 98%). Magnetic resonance imaging should not be the only method to stratify patients at high risk from those who are not, even though it can predict with high accuracy extensive postlaminar optic nerve invasion, massive choroidal invasion, and extrascleral tumor extension.

Ophthalmic Vascular Events after Primary Unilateral Intra-arterial Chemotherapy for Retinoblastoma in Early and Recent Eras

Dalvin LA, Ancona-Lezama DA, Lucio-Alvarez JA, Masoomian B, et al. *Ophthalmology* 125;11 Nov 2018: 1803-1811.

The purpose of this study was to assess risk factors for ophthalmic vascular events after intra-arterial chemotherapy (IAC) for retinoblastoma. Although IAC is efficacious in achieving tumor control, it can lead to thromboembolic or hemorrhagic events due to the technique itself or secondary to chemotherapy-induced toxicity. Ophthalmic vascular events include choroidal ischemia, branch or central retinal artery occlusion, ophthalmic artery spasm or occlusion, vitreous hemorrhage and others. Although early series reported ophthalmic vascular event rates as high as 35%, more recent series have described a lower rate of 1%. In this study, the authors conduct a retrospective, consecutive, comparative analysis to describe ophthalmic vascular events at a single center during two time periods: early IAC era (2009–2011) compared with the recent era (2012–2017). The study population included patients who received unilateral IAC as primary treatment for retinoblastoma from January 1, 2009, to November 30, 2017, at Wills Eye Hospital. All patients underwent complete eye exam under anesthesia prior to administration of IAC and then monthly exams were performed, which included anterior and posterior indirect ophthalmoscopy, B-scan ultrasonography, RetCam fundus photography, Fluorescein angiography, and OCTS as needed. After tumor control was achieved, the interval between examinations under anesthesia was extended. Records were reviewed for patient demographics, tumor features, IAC parameters, and treatment-related vascular events. Change in event rates over time were assessed using Poisson regression analysis, with Spearman's rho used to test correlation. There were 243 chemotherapy infusions in 76 eyes of 76 patients, divided into early (22 eyes, 57 infusions) and recent (54 eyes, 186 infusions) eras. Intra-arterial chemotherapy consisted of melphalan (243 infusions), topotecan (124 infusions), and carboplatin (9 infusions). A comparison (early vs. recent era) revealed fewer mean number of infusions (2.6 vs. 3.4, $P = 0.02$) with similar mean patient age and presenting tumor features. Event rates decreased over time ($P < 0.01$), with fewer ophthalmic vascular events (early era vs. recent era) in the recent era (59% vs. 9% per eye, 23% vs.

3% per infusion, $P < 0.01$), including peripheral retinal nonperfusion (5% vs. 2% per eye, $P = 0.50$), vitreous hemorrhage (9% vs. 2%, $P = 0.20$), subretinal hemorrhage (0% vs. 2%, $P = 0.99$), branch retinal vein occlusion (5% vs. 0%, $P = 0.29$), choroidal ischemia (14% vs. 4%, $P = 0.14$), and ophthalmic artery spasm/occlusion (27% vs. 0%, $P < 0.01$). Event rates did not correlate with patient age ($P = 0.75$), tumor diameter ($P = 0.32$), tumor thickness ($P = 0.59$), or cumulative dosage of melphalan ($P = 0.13$) or topotecan ($P = 0.59$). There were no IAC-induced vascular events in 72 infusions of 21 consecutively treated eyes in 2016 to 2017. This study shows that the ophthalmic vascular events after IAC have decreased from the early era (2009–2011) through the current era (2012–2017) at this center. Experience performing this highly specialized procedure could be an important factor predicting IAC-related vascular events. There were technical changes made between the two time periods. This includes pulsatile delivery of the infusion, eliminating the guide wire and advancing the catheter only to the ostium of the ophthalmic artery. This alone does not explain the observed change. The later time period also eliminated the use of carboplatin but it does not show more toxicity compared to melphalan in non-human primate studies. The authors surmise that the technique and experience is what accounts for the reduced rate of the ophthalmic vascular events.

NON-RETINOBLASTOMA

20.ORBIT

Computed tomography-based 3D modelling to provide custom 3D-printed glasses for children with craniofacial abnormalities.

Brodie FL, Nattagh K, Shah V, Swarnakar V, et al. *JAAPOS* 2019 June; 23(3): 165-167.e1.

Children with craniofacial malformations frequently require spectacles but have difficulty finding an acceptable fit with current offerings of pediatric spectacle frames. The authors describe a novel method for creating custom 3D-printed spectacle frames based on a 3D reconstruction of a prior computed tomography scan. This method offers the ability to create better-fitting spectacles to children who are not served by "off the rack" frames. The authors suggest that some improvements are still warranted with the current design. They are working to automate the design process and have also begun exploring other methods for digitizing patient anatomy, such as photogrammetry (measurement of relative distances using multiple photographs from varying perspectives), which will decrease our reliance on existing and potentially outdated imaging.

Long-term Methimazole Therapy in Juvenile Graves' Disease: A Randomized Trial

Fereidoun Azizi, Miralireza Takyar, Elham Madreseh, and Atieh Amouzegar

Pediatrics May 2019; 143 (5) e:20183034

Hyperthyroidism is not a common disease in children and adolescence. For a majority of these patients, it is caused by a toxic goiter. The three standard treatment modalities have been suboptimal because of significant side effects and a high relapse rate. There have been a few studies that report long-term therapy of antithyroid drugs as effective and safe in curing hyperthyroidism. The study aimed to compare short and long term usage of methimazole treatment in juvenile Graves' as well as variables associated with remission of hyperthyroidism. In a randomized, parallel group trial, 66 consecutive patients with untreated Graves' were enrolled. After a medial of 22 months of methimazole treatment, the group was randomized to either receive low-dose methimazole treatment or to discontinue the treatment. The long-term group completed 96-120 months of methimazole treatment. At baseline, the short and long term treatment groups had similar profiles (age, sex, goiter degree, ophthalmopathy. fT4, T3, and thyrotopin levels). After 48 months, 16 patients in the short-term group (67%) and 3 patients in the long-term group (12.5%) relapsed ($p< 0.001$). Side effects only occurred in the first stage of methimazole treatment when all patients were being treatment and these were cutaneous reactions (3 patients). No serious complications occurred in the long-term group on low-dose treatment. In this study, the researchers demonstrate that long-term low-dose methimazole treatment is both effective and safe in treating the hyperthyroidism and preventing relapse. The other benefit of using methimazole is that the other choices of therapy (surgical resection and radioiodine) can lead to other medical issues and life-long hypothyroidism. The limitations of the study include small number of patients, the subjects were only of west Asian descent potentially limiting its applicability to other populations, and that the study was not double-blinded possibly creating selection bias. In summary, this study suggests that long-term methimazole is safe and effective treatment for juvenile Graves' hyperthyroidism with higher recovery rates than the short term treatment.

the most affected extraocular muscle, and also to compare OCT findings with MRI findings. Further limitations of our study were the relatively small number of patients with active Graves' ophthalmopathy, and the fact that the posterior portion of the lateral rectus could be measured only in a few cases. Accordingly, studies including larger patient populations are needed to confirm the results of the current study.

Orbital fractures in children: clinical features and management outcomes

Barh A, Swaminathan M, Mukherjee B. *J AAPOS*. Dec 2018;28(6)415.e1-415.e7

This paper's purpose was to report the clinical characteristics and management outcomes of orbital fractures in children. The medical records of pediatric patients (<18 years of age) who presented with orbital fractures over a 15-year period (January 2001-December 2015) were reviewed retrospectively. The cause of injury, imaging findings, clinical features, management, and outcomes were noted. A total of 52 patients (39 males) were included in this study. Mean age at presentation was 10.9 years (range, 2-18). Road traffic accidents (18/52 [35%]) were the most common cause of the fractures with sports being the second most common cause, with the orbital floor (42/52 [81%]) being the most common fracture site with frequency occurring then in the medial, lateral, and roof in that order. The most common complaint in the patients was double vision (52%). Most patients were managed conservatively, however thirty-eight patients underwent surgical intervention, and extraocular muscle entrapment (56%) was the most common indication for surgery. Early surgical intervention within 15 days of injury resulted in complete resolution of diplopia in all the patients underwent surgery in this time frame. The authors conclude that orbital floor fracture was most common. The trapdoor type of fracture was seen in almost half of the patients, with diplopia being the most common presenting complaint. Early surgical intervention (within 15 days) was associated with complete resolution of ocular motility limitation and diplopia.

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

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

J of Ped Ophth & Strabismus.2018;55(1);37-42

The purpose of this randomized, controlled comparison trial is to evaluate the safety and efficacy of combined oral and topical beta blockers for the treatment of superficial periocular infantile hemangioma at the early proliferative stage. Patients were randomly enrolled into two groups: the topical and systemic treatment and systemic treatment only groups. The topical and systemic treatment group was treated with oral propranolol (1 mg/kg per day initially, increased to 2 mg/kg per day gradually in 2 weeks) and timolol maleate 0.5% gel. The systemic treatment only group received oral propranolol (1 mg/kg per day initially, increased to 2 mg/kg per day gradually in 2 weeks) and simple eye ointment to be applied to the lesion. The Hemangioma Activity Score was used to record the proliferative activity of the hemangioma. The main outcomes of the study were the change in the hemangioma size, the proliferative activity, and the treatment side effects. At the end of the treatment period, the Hemangioma Activity Score was significantly

improved in both groups from their values before treatment. However, the score obtained after treatment was significantly better in the topical and systemic treatment group ($P < .05$). Regarding the response to treatment, 10 and 3 cases in the topical and systemic treatment and systemic treatment only groups, respectively, showed a good response, with a significant difference between the two groups ($P < .50$). There were no recorded serious local or systemic complications during treatment in either group. The results from combining topical with oral beta blockers showed that topical beta blockers are of additive value in treating superficial periocular infantile hemangioma in the early proliferative stage. The limitations of this study included the small number of patients and the short follow-up period.

21.OCULOPLASTICS

Conservative management of congenital dacryocystocele: resolution and complications

Lee M, Park J, Kim N, Choung H, et al. *Can J Ophthalmol.* August 2019;54(4):421-425

Incidence of congenital dacryocystocele varies from 0.02% to 0.1% of newborns. The best treatment approach is controversial. Some people recommend early surgical intervention to reduce risks of infection and avoid further complex surgery. Others recommend monitoring due to high rates of spontaneous resolution. The authors of this study looked at a population of Asian children to evaluate the outcomes of conservative management for congenital dacryocystocele. 30 dacryocystoceles (28 infants) were retrospectively reviewed. Conservative treatment included digital massage four times daily and antibiotic eye drops if needed. 27 cases did not develop infection. Of these, 20/27 (74%) resolved spontaneously after conservative treatment. The mean duration of this treatment was 27.5 days. In 5 cases probing was needed due to persistent dacryocystoceles after 1 month of massage. 5 total cases developed infection including 3 at presentation. 2 cases became infected during the period of conservative management. These all received systemic antibiotic treatment, and 3 cases required external incision and drainage. All of these resolved without needing additional procedures. The authors conclude that uninfected cases of congenital dacryocystocele could be managed conservatively in a majority of cases. Vigilance is still needed to detect infection, but after infection is controlled conservative management is still an option.

Surgical Timing for Congenital Ptosis Should Not Be Determined Solely by the Presence of Anisometropia

Chisholm SAM, Costakos DM, and Harris GJ *Ophthalmic Plast Reconstr Surg* July-Aug 2019;35:374–377

Timing of surgery in children with congenital ptosis is a critical component of care, and anisometropia is frequently cited as an indication for early intervention. The purpose of this study is to evaluate the change in refractive error following surgery for congenital ptosis to better inform decisions regarding the timing of surgery. A retrospective review of clinical records was performed on patients who underwent surgical correction of congenital ptosis in an academic oculoplastic surgery practice from 2002 to 2017. Patients with complete preoperative and postoperative refractive data were included in the study. Changes in refractive error following surgery were analyzed. Among 184 pediatric patients who underwent ptosis surgery during the study period, 56 patients (71 eyes) met inclusion criteria. The mean age at surgery was 5.1 years. Mean refractive error change in all the operated eyes was a 0.82D decrease in spherical equivalent ($p = 0.1920$) and a 0.40 D increase in cylinder ($p = 0.0255$). There were no statistically significant changes in spherical equivalent or cylinder in the control eyes. The authors data did not show movement toward normalization of refractive error following ptosis surgery. In fact, it showed a statistically significant worsening of astigmatism following surgery. Because refractive error does not improve following surgery, anisometropia should not be the sole indication for early surgery in congenital ptosis.

Ophthalmic Pyogenic Granulomas Treated With Topical Timolol—Clinical Features of 17 Cases

Lauren N. DeMaria, Nora K. Silverman, Roman Shinder *Ophthal Plast Reconstr Surg* Nov/ Dec 2018;34:579–582

Topical timolol has been increasingly demonstrated to be an effective treatment for pyogenic granulomas (PG). The authors review the treatment outcomes of 17 patients with ocular PG treated with topical timolol. Retrospective interventional study of 17 patients with ocular PGs treated with timolol 0.5% solution. Patient demographics, clinical features, treatment response, and recurrence were noted. Nine females and 8 males with a mean age of 23 years (range, 3–67 years) were included. Mean duration of disease prior to treatment was 3.81 months (range, 0.25–11 months). Etiologies included chalazia (12 cases, 71%), postsurgical (4, 24%) and trauma (1, 6%). Five patients (29%) had treatment with topical steroids prior to presentation. Fifteen patients (88%) had PG located on the palpebral conjunctiva and 2 (12%) involving the bulbar conjunctiva. Mean lesion size was 5.06 × 6.06 mm (range, 3–8 × 3–18 mm). Fifteen patients (88%) had complete lesion resolution with a mean treatment duration of 3.07 weeks (range, 2–5 weeks) and no adverse events or recurrences with a mean follow up of 9.47 months (range, 6–27 months). Two patients (12%) underwent lesion excision after 6 weeks of timolol failed to yield resolution. Topical timolol appears to be a

well-tolerated nonsurgical treatment of ocular PG in both children and adults. Clinicians may wish to consider topical timolol to treat PG as opposed to topical steroids, given the inherent risk of steroid response ocular hypertension and the difficulty to measure intraocular pressure in younger children who require general anesthesia for excision.

22.INFECTIONS

23.PEDIATRICS/ INFANTILE DISEASE/ SYNDROMES

Adrenal Suppression in Infants Treated with Topical Ocular Glucocorticoids

Bangsgaard R, Main KM, Boberg-Ans G, Monten La Cour et al. *Ophthalmology* 125; 10 Oct 2018: 1638-1643.

Increasingly, clinical evidence suggests that the any treatment with glucocorticoids (GC) may suppress adrenal function and cause Cushing's syndrome irrespective of administration route. Adrenal suppression after topical ocular GCs is not well documented. The main objective of the study was to analyze the incidence of adrenal suppression and the glucocorticoid (GC) dose per kilogram body weight in infants treated with standard protocol for topical ophthalmic GCs after congenital cataract surgery. The authors analyzed retrospectively collected data from patients younger than 2 years of age who underwent operation for congenital cataract between January 2011 and May 2015 in a single center. Standard regimen after cataract surgery was subconjunctival injection at the time of surgery 0.5 to 1.0 mL methylprednisolone acetate 40 mg/ml (Depo-Medrol, Pfizer, Belgium). This was followed by topical administration of dexamethasone 1 mg/ml (Maxidex, Alcon, UK) eye drops 6-8 x/day for the first week, then 4 to 6 drops for the second week then tapering by one drop per week, hence up to 6 weeks of administration of drops. A standard ACTH provocation test was scheduled approximately 1 month post-operatively whenever possible. Among 26 consecutive infants, 15 (58%) were tested while they were still on GC treatment. Ten of these 15 infants (67%) had adrenal suppression, 2 of whom had obvious clinical signs of Cushing's syndrome and 1 of whom had signs of Addisonian crises during general anesthesia. Eleven of the 26 infants (42%) were tested at a median time of 21 days (range, 6–89) after treatment cessation, and they all had

normal test results. Infants with suppressed adrenal function had received cumulative GC doses per body weight that were significantly higher the last 5 days before testing compared with children with normal test results. Infants with adrenal suppression were treated with hydrocortisone replacement therapy. Adrenal function recovered after a median of 3.1 months (range, 2.3 months to 2.3 years). In conclusion two thirds of the infants tested during treatment with a standard GC protocol after congenital cataract surgery showed adrenal suppression. There was a significant association between the cumulative daily dose of GCs and the test result. Because adrenal suppression is a serious but treatable condition, the authors recommend a systematic assessment of adrenal function in infants treated with doses of topical ocular GCs comparable to our regimen and careful evaluations of other treatment regimens.

24.UVEITIS/ SYSTEMIC

Post-streptococcal uveitis syndrome in a Caucasian population: a case series.

Curragh DS, McAvoy CE, Rooney M, McLoone E. *Eye* (Lond). 2019 Mar;33(3):380-384.

Uveitis is an uncommon manifestation of post-streptococcal syndrome (PSUS). Despite reports, the condition is often not well recognized. This retrospective study reports a case series of children with post-streptococcal uveitis.
All cases of PSUS were identified from all new pediatric patients diagnosed with uveitis over a 6-year period. Diagnosis of PSUS was based on the following diagnostic criteria:
unilateral or bilateral uveitis with positive anti-streptolysin O titres (ASOT) or anti-deoxyribonuclease (anti-DNase) titers, and negative routine investigations for other causes of uveitis.
Eleven Caucasian pediatric patients were diagnosed with PSUS. One had a novel finding of peripheral corneal endotheliopathy, 73% of patients presented in Spring or Winter months and 88% of eyes had a final VA of better than or equal to 6/12 at a mean follow-up of 22 months. Systemic immunosuppressant treatment was used in 36% of patients. Adalimumab was used in 18% of patient's refractory to other treatment.
This is the largest consecutive series of Caucasian patients under 16 years of age with PSUS. The study demonstrates a seasonal preponderance with presentation typically in Winter or Spring. A novel finding of corneal endotheliopathy in one PSUS patient is reported. The authors also report on the benefit of adalimumab in the management of severe cases of PSUS; use of biologics in this particular cohort of uveitis patients has not previously been reported.

Symptoms in noninfectious uveitis in a pediatric cohort: initial presentation versus recurrences.

Marino A, Weiss PF, Davidson SL, Lerman MA. *J AAPOS*. 2019 Jun 26.

This study aims to describe the prevalence of symptoms with noninfectious uveitis (NIU) in a pediatric cohort and to assess the association between the presence of symptoms with first episode of uveitis (first-U) compared to symptoms at uveitis recurrence. The medical records of patients with NIU treated at a tertiary referral hospital from March 2008 to November 2107 were reviewed retrospectively. Symptomaticity (eye pain, eye redness, photosensitivity) was captured at initial uveitis activation and subsequent episodes. Univariate logistic regression modeling was used to identify clinical features associated with symptomatic first-U. Ordinal regression identified patient characteristics associated with symptomatic recurrence.

A total of 118 cases were reviewed; of these, 92 were followed for at least 6 months and had at least 1 reactivation. Juvenile idiopathic arthritis-related uveitis (JIAU) was the most common diagnosis (67/118 [57%]), followed by idiopathic uveitis (33%). In the majority, uveitis was restricted to the anterior chamber (82%). Of the 118 cases, 58 patients (49%) had symptomatic first-U, 34% JIA versus 69% non-JIA. Non-JIAU, age ≥7 years, and negative antinuclear antibody (ANA) test were significantly associated with symptomatic first-U; spondyloarthritis was not. With recurrence, half had symptoms: 41% JIA versus 66% non-JIA. Of those who had symptomatic first-U, 35% were asymptomatic at recurrence. Those with JIA had 50% or less odds of symptomaticity at reactivation. Complications did not vary based on having had symptoms at first-U.

The authors conclude that non-JIA diagnosis, older age, and ANA-negativity were associated with symptomatic first-U in our study cohort, but no patient characteristics were significantly associated with symptomatic recurrence. Clinical patterns may change during disease course, with uveitis switching from symptomatic to
asymptomatic, which has implications for uveitis monitoring recommendations.

Visual and Clinical Outcome of Macular Edema Complicating Pediatric Noninfectious Uveitis

Eiger-Moscovich M, Tomkins-Netzer O, Amer R, et al. *Am J Ophthalmol.* 2019 June; 202: 72-78.

A retrospective case series of 25 children (33 eyes) was performed with the purpose of better understanding the clinical course and visual outcomes of pediatric patients with chronic noninfectious uveitis and macular edema (ME). The patients from this study were from four academic institutions in Israel and the UK over a 10-year period. The mean follow up was 48 months. They authors found that the most common diagnosis was intermediate uveitis, that most patients had active uveitis at the time of ME diagnosis, that it took a median of 6 months for

the ME to resolve, and that baseline visual acuity was worse than 20/40 in 75% of patients but that decreased to 50% of patients by 3 months after diagnosis. ME resolved in 75% of patients during the 24 month follow up. They could not find any correlation between treatment strategy or structural characteristics on the ME and the visual outcomes. The conclusion was that despite the chronic course of ME in pediatric patients, the prognosis is favorable, which is in contrast to adult studies. This is the largest study of pediatric macular edema and is an important contribution to the pediatric uveitis literature.

Therapeutic Advances in juvenile idiopathic arthritis- associated uveitis.

Julie Gueudry, Sara Touhami, Pierre Quartier et al. *Curr Opin Ophthalmol* May 2019, 30 179-186

The authors undertake a review of JIA associated uveitis and current treatment modalities. The prevalence of uveitis is between 11.6-30% and its incidence is 2.8% per year. Usually presents as asymptomatic chronic anterior uveitis. Risk factors include young age at onset, female sex, ANA+, oligoarticular disease, however a large multivariate analysis found that independent predictive risk is young age at diagnosis and ANA+ only. Screening is recommended at diagnosis and then in 3-12 month intervals based on different risk factors (table 1 in the paper). The authors then go through different therapeutic agents including, corticosteroids, methotrexate, and biologics with emphasis on the fact that adalimumab is now approved as a second line treatment and is being used earlier in the disease process. A new class of agents known as JAK inhibitors are being investigated. The SHARE network has attempted to put together a treatment algorithm which is provided in the article. The authors then conclude with a discussion of the difficulties with tapering medications and the complications associated with uveitis such as glaucoma and cataract. Of note is the change in attitude towards the absolute contraindication to IOL implantation in those patients and more dependent on the specific case and the level of disease activity.

25.PRACTICE MANAGEMENT/ HEALTH CARE SYSTEM

Outbreak of Adenovirus in a Neonatal Intensive Care Unit: Critical Importance of Equipment Cleaning During Inpatient Ophthalmologic Examinations.

Sammons JS, Graf EH, Townsend S, Hoegg CL, et al. *Ophthalmlogy* 2019. Jan;126(1):137-143.

Adenovirus is a common cause of respiratory infections and conjunctivitis in children and adults. Although these infections are often benign and self-limited, they can have severe complications and even death in vulnerable populations. In this

report, the authors describe an outbreak of adenovirus in neonatal intensive care units (NICUs) due to contaminated handheld ophthalmologic equipment used during retinopathy of prematurity (ROP) screening and describe the investigation, response, and successful containment of an adenovirus outbreak in a NICU. A total of 23 hospitalized neonates, as well as NICU staff and parents of affected infants were included in this epidemiologic investigation. In August 2016, a routine surveillance identified an adenovirus outbreak in a level IV NICU. Epidemiologic investigation followed, including chart review, staff interviews, and observations. Cases were defined as hospital-acquired adenovirus identified from any clinical specimen (NICU patient or employee) or compatible illness in a family member. Real-time polymerase chain reaction (PCR) and partial- and whole-genome sequencing assays were used for testing of clinical and environmental specimens. A total of 23 primary neonatal cases and 9 secondary cases (6 employees and 3 parents) were identified. All neonatal case-patients had respiratory symptoms. Of these, 5 developed pneumonia and 12 required increased respiratory support. Less than half (48%) had ocular symptoms. All neonatal case-patients (100%) had undergone a recent ophthalmologic examination, and 54% of neonates undergoing examinations developed adenovirus infection. All affected employees and parents had direct contact with infected neonates. Observations revealed inconsistent disinfection of bedside ophthalmologic equipment and limited glove use. Sampling of 2 handheld lenses and 2 indirect ophthalmoscopes revealed adenovirus serotype-3 DNA on each device. Sequence analysis of 16 neonatal cases, 2 employees, and 2 lenses showed that cases and equipment shared 100% identity across the entire adenovirus genome. Infection control interventions included strict hand hygiene, including glove use; isolation precautions; enhanced cleaning of lenses and ophthalmoscopes between all examinations; and staff furlough. The authors recommended that ophthalmologists performing inpatient examinations take measures to avoid adenoviral spread from contaminated handheld equipment.

Guidelines for the cleaning and sterilization of intraocular surgical instruments (Review/ Update)

David F. Chang, MD, Nick Mamalis, MD, Ophthalmic Instrument Cleaning and Sterilization Task Force *Journal of Cataract and Refractive Surgery*;2018;44(6):765-773.

Postoperative infectious endophthalmitis and toxic anterior segment syndrome are rare but potentially sight-threatening complications of intraocular surgery. The small volume of the eye and its sensitivity to minute amounts of chemical or microbial contaminants means that improper instrument cleaning or sterilization practices might pose a significant risk to patients. A 3-year collaborative effort by the Ophthalmic Instrument Cleaning and Sterilization (OICS) Task Force recently produced evidence-based, specialty-specific guidelines for the cleaning and steri-

lization of intraocular instruments. A large outbreak of toxic anterior segment syndrome (TASS) in 2006 was the impetus for these updated guidelines as was subsequent regulatory pressure on high-volume cataract surgeons in adult ambulatory surgery centers. The OICS designed a study that established the safety and acceptability of short-cycle ophthalmic instrument processing for sequential same-day surgery, even when the dry cycle is interrupted, if allowed by the instructions for use for the sterilizer. The use of enzymatic detergents to clean intraocular instruments was also studied as enzymatic detergents have been associated with TASS outbreaks. Thorough rinsing reduced but did not eliminate enzymatic residue on phaco tips in one study. Therefore, the new guidelines state that if intraocular surgical instruments are thoroughly rinsed with critical water promptly after each use, the routine use of enzymatic detergents is unnecessary and should not be required for the routine decontamination of intraocular instruments. The findings of these studies and resulting OICS guidelines are relevant for instruments used in other intraocular surgical procedures and may be useful to pediatric ophthalmologists in educating and assisting surgical staff in implementing appropriate practices for the cleaning and sterilization of intraocular surgical instruments.