What's New and Important in Pediatric Ophthalmology and Strabismus in 2021

Complete Unabridged Handout

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Presented by the

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1. AMBLYOPIA

Self-perception in Preschool Children With Deprivation Amblyopia and Its Association With Deficits in Vision and Fine Motor Skills.
Birch EE, Castaneda YS, Cheng-Patel CS, Morale SE, Kelly KR, Wang SX.
JAMA Ophthalmol. 2020 Dec; 138(12): 1307-1310.

This is a cross-sectional study from 2016 to 2019 at a pediatric vision research laboratory in Dallas, Texas. The authors enrolled children ages 3 to 6 years old, 15 with deprivational amblyopia and 20 controls. Self-perception was assessed using the Pictorial Scale of Competence and Acceptance for Young Children, including: cognitive competence, peer acceptance, physical competence, and maternal acceptance. Fine motor skills were evaluate with Manual Dexterity and Aiming & Catching Scales of the Movement ABC-2 test. Demographics of the study included 37% girls and 80% non-Hispanic White children. Results showed that children with deprivational amblyopia had significantly lower peer acceptance and physical competence scores when compared with control children (mean difference 0.45, P=0.002 and mean difference 0.47, P=0.002, respectively). Regarding the 15 children with amblyopia, the authors noted an associate between self-perception domain scores and motor skills, including peer acceptance and manual dexterity (r+0.68, P=0.005), peer acceptance and aiming (r+0.54, P=0.03) and physical competence and aiming (r=0.55, P=0.03). Conclusions revealed lower self-perception of peer acceptance and physical competence were associated with early visual deprivation in children. Limitations of the study include small sample size of less than 50 children, the lack of racial diversity, and single-center study. Strengths of this study include the evaluation of self-perception from the children directly, rather than from a proxy. In summary, this small study is helpful reminder that self-perception and fine motor skills in young children with deprivational amblyopia have an impact on their visual development and learning. In the future, larger studies, with more racial and ethnic diversity, will be important to do.

Interocular Suppression as Revealed by Dichoptic Masking Is Orientation-Dependent and Imbalanced in Amblyopia
Ling Gong, Alexandre Reynaud, Zili Wang, et al
Invest Ophthalmol Vis Sci. 2020 Dec;61, 28

This small study looked at suppression in amblyopic subjects in both monocular and binocular testing. They compared these individuals to age appropriate controls. They firstly noted similar measurable amounts of suppression under monocular conditions of amblyopic eyes when compared to prior studies. When testing under binocular conditions, masking of the amblyopic eye was noted to have less of an effect on the fellow eye than masking of the fellow eye. This is yet another study that shows that best corrected vision is far from the only end goal of amblyopia treatment and that amblyopia does not only affect high contrast vision.

Understanding the Impact of Residual Amblyopia on Functional Vision and Eye-related Quality of Life Using the PedEyeQ
Sarah R. Hatt, David A. Leske, Yolanda S. Castañeda, Suzanne M. Wernimont, Laura Liebermann, Christina S. Cheng-Patel, Eileen E. Birch and Jonathan M. Holmes
American Journal of Ophthalmology 2020 October; 218: 173-181.

This prospective cross-sectional study was designed with the purpose of understanding the effects of residual amblyopia and functional vision and vision related quality of life. The authors used a specific questionnaire (PedEyeQ) in children aged 8-11 and compared 17 children with residual amblyopia, 48 visually normal controls without glasses and 19 controls without amblyopia who wear glasses. The median acuity in the patients with amblyopia was 20/50. The authors found that residual amblyopia does affect both functional vision and eye related quality of life. Additionally, the parents of the amblyopic children also had lower QOL scores. This paper is important not only because it validates the work that we do but it emphasizes the importance of amblyopia treatment for the entire family.

Amblyopia Outcomes Through Clinical Trials and Practice Measurement: Room for Improvement: The LXXVII Edward Jackson Memorial Lecture.
Michael X. Repka
American Journal of Ophthalmology 2020 November; 219: A1-A26.

This literature review and analysis of data from the intelligent research in sight (IRIS) registry is a personal perspective from one respected pediatric ophthalmologist on the topic of amblyopia prevalence and outcomes. The author provides a very comprehensive review of amblyopia studies. I would recommend this as a great read for residents before they start their pediatric ophthalmology rotation and a staple before starting fellowship.

The use of atropine for treatment of amblyopia using the OptumLabs Data Warehouse
Pineles SL, Repka MX, Yu F, Velez FG, Perez C, Sim D, Coleman AL,
Journal of AAPOS (2021), doi: https://doi.org/10.1016/j.jaapos.2020.11.003.

Both occlusive patching and atropine penalization are accepted methods to treat amblyopia and have been determined to have similar outcomes when studied by Pediatric Eye Disease Group (PEDIG) and other investigators. The frequency of use of atropine penalization has not been determined. The authors used a “big data” study to determine the frequency of the use of atropine penalization for the treatment of amblyopia. The OptumLabs Data Warehouse claims data was mined to identify the use of atropine in children with a diagnosis of amblyopia. Amblyopic patients were divided into 2 groups: those who had been prescribed atropine on at least 2 claims and those who had not been prescribed atropine or were prescribed only once. The authors found 55.2% of children with a diagnosis of amblyopia were prescribed atropine on 2 or more occasions. Children who lived in families with the highest familial net worth and household income had the highest rate of atropine use, 81.5% and 83.8%. Use of atropine was higher in the South (59.4%) compared to the Northeast (47.1%). This study is important for helping to understand the frequency of use of atropine penalization for the treatment of amblyopia in the United States. The geographic and socioeconomic data findings suggest more study is necessary to ensure that equity exists in treatment of children with amblyopia.

Prevalence of amblyopia and its determinants in a rural population: a population-based cross-sectional study.
Hashemi H, Nabovati P, Pakzad R, Yekta A, Aghamirsalim M, Sardari S, Rafati S, Ostadimoghaddam H, Khabazkhoob M.
Strabismus. 2021 Jan 16:1-9.

The authors performed a cross-sectional population-based study of 3314 participants from 3-93 years old from two different underserved areas of Iran to determine the prevalence and causes of amblyopia. They found the prevalence to be 2.23% of unilateral and 0.50% of bilateral amblyopia, which overall which similar to prior reports from Iran and reports from other countries such as China. Amblyopia was most common in children 6-20 years old (1.36%) and adults over 70 years old (5.97%). There was also an inverse relationship between amblyopia prevalence and education, with lower prevalence in patients with higher education. Amblyopia was most often due to anisometropia (53%), followed by strabismus (29.5%) and mixed (17.5%) types. The authors note that amblyopia screening began in 1996, which likely played a role in the overall decrease in prevalence by age. Although helpful in determining the characteristics of amblyopia, the design of the study does not allow for analysis of eye care access or conclusions regarding causality.

Clinical Aniseikonia in Anisometropia and Amblyopia.
South J, Gao T, Collins A, Lee A, Turuwhenua J, Black J.
British and Irish Orthoptic Journal. 2020;16(1), 44–54.

The authors state that, clinically, aniseikonia is often neglected in anisometropic amblyopia due to assumed measurement difficulties and that lack evidence on whether correction of aniseikonia is beneficial. This study aimed to determine whether subjective aniseikonia is measurable in anisometropia with or without amblyopia. The study included participants (15–52 years) with Anisometropic Amblyopia (n = 7), Anisometropia without amblyopia (n = 6) and Isometropic Controls (n = 6). Subjective aniseikonia was measured using three clinical techniques: Robertson Technique (RT) (penlight and Maddox rod), Aniseikonia Inspector Version 3 (AI3), and the New Aniseikonia Test booklet (NAT), and a psychophysical adaptive method, the Contrast-balanced Aniseikonia Test (CAT), where dichoptic contrast adjustments compensate for any suppression. The authors found that eighteen participants completed all tests, one Anisometropic Amblyopia participant could only complete the CAT and NAT due to fusion loss. The Anisometropic Amblyopia group exhibited the most aniseikonia (range –1.50–+10.50%) followed by Anisometropic Controls (range –3.30–+4.50%) and Isometropic Controls (range –1.50–+3.28%). There was a significant trend of more subjective aniseikonia with increasing amounts of anisometropia across all four tests (AI3 r = 0.630, p = 0.005; NAT r = 0.542, p = 0.017; RT r = 0.499, p = 0.035; CAT r = 0.440, p = 0.059. Bland Altman analysis demonstrated clinically significant levels of variability between the tests. The authors concluded that aniseikonia can be reliably measured in patients with anisometropia and suppression. Subjective aniseikonia measurement is recommended as four of the most commonly used clinical tests did not support the 1% per diopter rule of thumb.

Impact of Amblyopia on the Central Nervous System
Miller NP, Aldred B, Schmitt MA, Rokers B.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):182-192.

Amblyopia is a common perceptual disorder resulting from abnormal visual input during development. The clinical presentation and visual deficits associated with amblyopia are well characterized. Less is known however, about amblyopia's impact on the central nervous system (CNS). While early insights into the neuropathophysiology of amblyopia have been based on findings from animal models and postmortem human studies, recent advances in noninvasive magnetic resonance imaging (MRI) techniques have enabled the study of amblyopia's effects *in vivo*. We review recent retinal and neuroimaging research documenting amblyopia's structural and functional impact on the CNS. Clinical imaging provides some evidence for retinal and optic nerve abnormalities in amblyopic eyes, although the overall picture remains inconclusive. Neuroimaging studies report clearer changes in both structure and function of the visual pathways. In the optic nerves, optic tracts, and optic radiations of individuals with amblyopia, white-matter integrity is decreased. In the lateral geniculate nuclei, gray matter volume is decreased and neural activity is reduced. Reduced responses are also seen in the amblyopic primary visual cortex and extrastriate areas. Overall, amblyopia impacts structure and function at multiple sites along the visual processing hierarchy. Moreover, there is some evidence that amblyopia's impact on the CNS depends on its etiology, with different patterns of results for strabismic and anisometropic amblyopia. To clarify the impact of amblyopia on the CNS, simultaneous collection of retinal, neural, and perceptual measures should be employed. Such an approach will help (1) distinguish cause and effect of amblyopic impairments, (2) separate the impact of amblyopia from other superimposed conditions, and (3) identify the importance of amblyopic etiology to specific neural and perceptual deficits.

A randomized clinical trial of contrast increment protocols for binocular amblyopia treatment.
Jost RM, Kelly KR, Hunter JS, Stager DR Jr, Luu B, Leffler JN, Dao L, Beauchamp CL, Birch EE.
J AAPOS. 2020 Oct;24(5):282.e1-282.e7.

This is a prospective s a randomized clinical trial of 63 amblyopic children (age 4-10 with amblyopic visual acuity 20/40 – 125) randomly assigned to one of four daily contrast increment protocols for 4 weeks, all starting with 20% fellow eye contrast: : 10%, 5%, 0%, or 10% for first 4 weeks then reset to 20% and repeat 10% increment for the final 4 weeks. Children played contrast-rebalanced games for 1 hour/day, 5 days/week. Best-corrected visual acuity, stereoacuity, and suppression were assessed at baseline and every 2 weeks until the 8-week outcome visit. At baseline, mean amblyopic eye best-corrected visual

acuity was 0.47 0.14 logMAR (20/ 60), improving overall 0.14 0.08 logMAR (1.4 lines; P\0.0001) at 8 weeks. All four protocols resulted in similar improvement in visual acuity (0.13-0.16 logMAR; all Ps \ 0.0002). Stereoacuity and suppression also improved (all Ps \ 0.05). One limitation of the current study was the absence of long-term follow-up. Although 92% of children had improved visual acuity at 8 weeks, 60% remained amblyopic and returned to patching. Thus, we were unable to determine the lasting effects of binocular treatment. This study suggests that none of the new protocols resulted in less improvement than the original 10% contrast increment protocol. Contrast-rebalanced binocular games yielded significant improvements in visual acuity, stereoacuity, and suppression with or without daily contrast increments.

Retinal Sensitivity and Fixation Analysis Using Microperimetry in Children With Anisometropic Amblyopia
Funda Dikkaya, MD; Sevil Karaman Erdur, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):246-250.

The purpose of the study was to determine retinal sensitivity and fixation in children with anisometropic amblyopia. Amblyopic and non-amblyopic eyes of 39 children with the diagnosis of anisometropic amblyopia were compared using macular microperimetry. Anisometropic amblyopia was defined as >1D of anisometropia and 2 lines or greater difference in visual acuity between eyes. The authors found that certain parameters evaluated by macular microperimetry differed between amblyopia and fellow eyes. Retinal sensitivity was significantly higher in non-amblyopic eyes compared to amblyopic eyes. In fixation analysis, P1 fixation index (how often the eye fixated within 1 degree of target) was also significantly higher in the non-amblyopic eyes and it was significantly correlated with visual acuity. Because measuring visual acuity does not represent all functions of the visual system, microperimetric evaluation may give extra information about total visual function of amblyopic eyes.

Short-term Perceptual Learning Game Does Not Improve Patching-Resistant Amblyopia in Older Children
Lee, Yoon H; Maniglia, Marcello; Velez, Federico; Demer, Joseph L; Seitz, Aaron R; et al.
J Pediatr Ophthalmol Strabismus 2020 May 1;57(3):176-184.

Limitations of patching and atropine to treat amblyopia include resistance to therapy, recurrence and reduced stereoacuity. Binocular dichoptic therapy for amblyopia involves presenting balanced contrast to each eye by decreasing stimulus intensity to the non-amblyopic eye. Perceptual learning uses specific stimuli and tasks to purposefully stimulate specific areas of the visual cortex. In this study an at home self-administered perceptual learning game was administered to amblyopic patients who did not respond to two hours of patching for 6 weeks. The game was both tested monocularly and binocularly. A third group of enrolled patients were assigned to continue patching for two hours daily. Enrolled patients played the game 20/minutes per day. Twenty five patients completed the study, with baseline vision between 20/40 and 20/200. Low contrast increased in the amblyopic eye in all three groups and there was no difference between them. The other visual parameters remained unchanged between the groups including reading speed and visual acuity. The largely negative results of this study are important to guide further work in developing alternative amblyopia therapies. The authors suggest that evaluating perceptual learning games on untreated amblyopes, and larger studies that identify responsive subgroups could be useful.

Improved monitoring of adherence with patching treatment using a microsensor and Eye Patch Assistant.
Wang J, Xu H, De La Cruz B, Morale SE, Jost RM, Leske DA, Holmes JM, Birch E.
J AAPOS. 2020 Mar;24(2):96e1-6.

To monitor patching adherence as well as the ease and comfort of use, the authors designed an Eye Patch Assistant (EPA) to decrease the likelihood of the microsensors being lost or swallowed and to facilitate consistent placement of the microsensor on an adhesive patch. 13 adults and 30 children were enrolled; each group was randomized to wearing an adhesive patch alone or a patch + EPA for 2 hours each and then completed the questionnaire about the ease of use and comfort of use.
Of note, the sensory sampling intervals were every 5 minutes or every 1 minute. Results of the patch + EPA group show that with the 5-minute sampling, there was excellent accuracy for both adult and child

groups. In the adult group, the ease of use scores were lower for patch + EPA versus patch alone (P< 0.01) but the comfort score for the patch + EPA was higher compared to patch alone (P < 0.01). For the child group, the patch + EPA versus patch alone scores did not different significantly for ease of use or comfort. Moreover, the authors report that the patch + EPA functioned well in adults and children between 45 degrees F and 82 degrees F. Limitations include that the authors do not report the specifics of this cohort of 30 children regarding the sub-set of ages, as this is often associated with previous research with patching adherence as well as research with the occlusion dose monitor (ODM). Another limitation is that the ages of the 10 children with the sampling interval of 1 minute versus the ages of the 20 children with the sampling interval of 5 minute is not revealed. In summary, the patch + EPA technology was well tolerated by both adults and children. Improved patching adherence with this microsensor technology is valuable to accurately and precisely monitor the patching regimen of our amblyopic patients.

Prevalence and pattern of amblyopia in a rural hospital in Ghana.
Asare AK, Akuffo KO, Kumah DB, Agyei-Manu E, Darko CK, Addo EK.
Strabismus. 2020 Jul 5:1-9.

This study identified the prevalence and characteristics in a rural hospital in Ghana. In this retrospective chart review, 258 cases of amblyopia were identified in 12602 records. The most prevalent form of amblyopia was refractive with a prevalence of 1.42%. Strabismic and stimulus deprivation amblyopia accounted for 0.36% and 0.21% of all amblyopic cases, respectively. Of note, the presenting age of amblyopic patients was 24.3 ± 16.1 years. This study highlights the importance of vision screening for early detection of amblyopia in childhood.

Association of Optical Coherence Tomography Angiography Metrics With Detection of Impaired Macular Microvasculature and Decreased Vision in Amblyopic Eyes. The Hong Kong Children Eye Study.
Wong ES, Zhang XJ, Yuan N, Li J et al.
JAMA Ophthalmol. 2020;138(8):858-865.

The microvascular abnormalities in amblyopic eyes were documented with the high resolution imaging of OCT-A in this population-based nested case-control study in children 6-8 years old. The patients were recruited from January 2016 to July 2017 from the population-based Hong Kong Children Eye Study (HKCES). The non-invasive and quantification of the OCT-A imaging system make this technology helpful to further understand amblyopia and its association with visual acuity. The authors describe that the macular microvasculature of the superficial capillary plexus analyzed and quantified by an fully automated image analysis program (MathWorks). The analysis for the OCT-A metrics included: foveal avascular zone (FAZ) area, FAZ circularity, vessel density, vessel diameter index, and fractal dimension between amblyopic and non-amblyopic eyes. Amblyopia was defined as BCVA between 20/40 and 20/200 OD/OS or OU, without an identifiable organic cause of decreased vision. Only children with strabismic or anisometropic amblyopia were included and in cases with bilateral amblyopia, the eye with poorer vision was selected for OCT-A analysis. Of note, in patients with unilateral amblyopia, the fellow eye without amblyopia was not included in the control group, even if the BCVA of fellow eye was 20/20. Participants included 30 children with amblyopia (with mean age 7.57 years with SD 1.2 years) and 1045 controls (with mean age 7.65 years with SD 1.0 year). Analysis of 1075 eyes was reported from 1075 participants. In both amblyopic and control groups, a majority of girl participants were reported, 53.3% and 55.5%, respectively. All children were reported as ethnically Chinese. BCVA (Snellen equivalent) in the amblyopic group was 20/40 (logMAR 0.31) as compared to control group 20/20 (logMAR 0.02). Results from OCT-A metrics showed amblyopic eyes had decreased FAZ circularity (P=0.002), decreased fractal dimension (P=0.01), increased vessel diameter index (P<0.001). No statistical difference was noted in FAZ area and vessel density. LogMAR VA was associated with FAZ circularity (P< 0.001) and vessel diameter index but not with vessel density or FAZ area. Limitations of the study is that because the study design being cross-sectional, the authors could only report an association, not a causal relationship, between OCT-A metrics and amblyopia. Another study limitation is because only 1 eye was studied per participant, the interocular difference between eyes, could not be commented upon. In summary, this study of high resolution OCT-A findings of macular microvasculature abnormalities in

amblyopic eyes and its association with VA is a helpful reminder about the complexities of amblyopia diagnosis.

Global prevalence of amblyopia and disease burden projections through 2040: a systematic review and meta-analysis
Fu Z, Hong H, Su Z, Lou B, Pan C, Liu H
Br J Ophthalmol 2020 Aug;104:1164–1170.

The authors of this study performed a systematic review of the literature to estimate the global prevalence of amblyopia and to project the prevalence of disease in the future. They looked at 60 studies (for a total of 1,859,327 subjects) to calculate the prevalence of amblyopia at 1.44% (CI 1.17% to 1.78%). Prevalence rates in Europe (2.90%) and North America (2.41%) were higher than Asia (1.09%) and Africa (0.72%). They also found higher rates in Hispanics. There was no difference between genders. Their estimates using a hierarchical linear model predict 99.2 million people (95% CI 71.7 to 146.1 million) with amblyopia in 2019 which will increase to 175.2 million (95% CI 81.3 to 307.8 million) by 2030 and 221.9 million (95% CI 83.7 to 429.2 million) by 2040. The authors note that there was a limited amount of information from population-based studies from Africa and Latina America. However their studies highlights the global disease burden of amblyopia and the need for screening, treatment, and public health strategies to reduce its burden in the future.

Objective Assessment of the Effect of Optical Treatment on Magnocellular and Parvocellular-biased Visual Response in Anisometropic Amblyopia
Zitian Liu, Zidong Chen, Yunzhi Xu, Lei Feng, Junpeng Yuan, et al
Invest Ophthalmol Vis Sci. Feb 2020;61,21

This small study looked to show a change in the magnocellular, and parvocellular response using visual-evoked potentials in patients with and without anisometropic amblyopia before and after treatment with optical correction. Compared to the controls, patients with previously corrected anisometropic amblyopia, as well as those with previously uncorrected anisometropic amblyopia had both a decrease in magnocellular, and parvocellular response. Upon correction, there was a noted improvement in magnocellular response, though no significant change in parvocellular response. This study shows that not only is there a neural change in the cells in the retina, but that with optical correction, some of these changes can be reversed. This study will lead to further studies understanding how to potentially reverse all of the neural changes of different types of amblyopia.

Effect of Stimulus Orientation on Visual Function in Children with Refractive Amblyopia
Tiong Peng Yap, Chi D. Luu, Catherine Suttle, Audrey Chia, Mei Ying Boon
Invest Ophthalmol Vis Sci. May 2020;61,5

In this small study, pattern onset–offset visual evoked potentials were presented to patients with meridional anisometropic amblyopia. The stimuli were presented at 45, 90, 135, and 180 degrees. Patients had their astigmatism either horizontally or vertically. The authors found that low and moderate astigmats did not have a decrease in pattern onset–offset visual evoked potentials, but those with high levels of astigmatism showed a decrease in pattern onset–offset visual evoked potentials, though not relative to their meridional astigmatism. This study shows the deleterious effect of higher levels of refractive amblyopia, though not necessary meridional amblyopia. Future studies should show a comparison to patients without meridional, but still anisometropic amblyopia, as well as other types of amblyopia.

Binocular Imbalance in Amblyopia Depends on Spatial Frequency in Binocular Combination
Yu Mao, Seung H Min, Shijia Chen, Ling Gong, et al
Invest Ophthalmol Vis Sci. Jul 2020;61,7

This small study of adult patients with different types of amblyopia the authors sought to determine if there was an effect on the binocular imbalance of these patients in regards to level of spatial frequency. The authors noted that the binocular balance in amblyopic patients was more greatly disrupted with higher spatial frequencies. They postulate that this may be caused by the difference in contrast sensitivity between the two eyes. This study had a wide variety of types of amblyopia with highly variable refractive errors, visual acuities, and stereopsis. In order to better understand the role of binocular imbalance in relationship to spatial frequency, a much larger study needs to be performed with better stratification of disease states.

Two Patterns of Interocular Delay Revealed by Spontaneous Motion-in-Depth Pulfrich Phenomenon in Amblyopes with Stereopsis
Yidong Wu, Alexandre Reynaud, Chunwen Tao, Yu Mao, et al
Invest Ophthalmol Vis Sci. Mar 2020;61:22.

This stud investigated 20 amblyopic and 20 control patients with an induced Pulfrich Effect to determine the relationship in delayed response between eyes. The amblyopic children were not stratified based on type of or density of amblyopia, or degree of stereopsis. There was noted a clinically significant difference in response time between the amblyopic and non-amblyopic eyes, though it was not always the amblyopic eye that had a slower response time. These results lead to potentially interesting further studies to determine whether there is an increase in neural response from treated amblyopic eyes or if this difference was noted due to a small sample size.

Rather Than Visual Acuity Loss Limits Stereoacuity in Amblyopia
Ann L Webber, Katrina L Schmid, Alex S Baldwin Robert F Hess
Invest Ophthalmol Vis Sci. June 2020;61(6):50.

The authors of this small study compared amblyopic adults to age controlled participants and measured a number of visual functions in order to determine which aspects of visual function have the strongest relationship to stereoacuity. The authors found that suppression of the amblyopic eye, rather than visual acuity is the limiting factor in those patients' stereoacuity. This study reminds us that visual acuity is not the only measurement that we should be assessing. This study will lead to future larger studies that can determine levels of visual acuity and level of suppression that may limit stereoacuity as well as other measurements of both monocular and binocular visual function.

Factors Associated with Impaired Motor Skills in Strabismic and Anisometropic Children
Krista R Kelly, Sarah E Morale, Cynthia L Beauchamp, Lori M Dao, et al
Invest Ophthalmol Vis Sci. Aug 2020;61(10):43.

This study evaluated motor skills of children with strabismic and anisometropic amblyopic children. The children were further stratified into age groups. Once completing age appropriate visual function testing including BCVA, stereoacuity, Worth 4 Dot, and depth of perception, the children were tasked to perform a number of age appropriate movement assessments including manual dexterity, aiming, catching, and balancing. As expected, the worse that the child performed on any of the visual function tests, the worse they performed on the motor skills tests. The importance of this study is in the fact that not only are these children at a disadvantage in terms of reading, but their motor skills are also affected and this needs to be understood by their parents and teachers. The only aspect of this study that needs to be enhanced is the age grouping as at the younger ages, the disparity in manual dexterity is quite different and grouping a 3 year old together with six year olds may lead to confounding biases.

Binocular game versus part-time patching for treatment of anisometropic amblyopia in Chinese children: a randomized clinical trial
Yao J, Moon H, Qu X
Br J Ophthalmol 2020 Mar;104:369-375.

Binocular treatment for amblyopia is thought to overcome interocular suppression, and a number of initial studies have shown promising results for using binocular treatment for amblyopia in children. However there has been inconsistent results in visual acuity improvement in several randomized trials. This study was a randomized clinical trial evaluating children age 3-13 with anisometropic amblyopia who were randomly assigned to binocular treatment, patching, and combined groups. Primary outcome was amblyopic-eye visual acuity at 3 months. The binocular game was played on a computer with the subject wearing polarized anaglyphic glasses over refractive correction if needed. They utilized “push-pull” model training system in which the attention cue was presented to the amblyopic eye preceding the binocular competitive stimulation. The binocular stimulation was then presented in a virtual reality background with high contrast elements to the amblyopic eye and low contrast elements to the fellow eye. 85 children were recruited with mean age of 5.99 years. At 3 months VA improved in all 3 groups. Mean amblyopic VA improved 0.18 logMAR in the binocular group, 0.28 logMAR in the patching group, and 0.30 logMAR in the combined group. Overall, the binocular game improved visual acuity, but was less effective than patching and was not superior to combined treatment. The authors note that adherence to game play was not accurately recorded and there was a high percentage of loss to follow-up. Therefore they state that it remains unclear if low treatment response to the binocular game was due to limitations of the study or low treatment effect.

Effect of Primary Occlusion Therapy in Asymmetric, Bilateral Amblyopia
Shoshany TN, Michalak S, Staffa SJ, et al.
Am J Ophthalmol. Mar 2020; 211:87-93.

This retrospective interventional comparative case series aimed to compare acuity outcomes in patients with bilateral amblyopia who began patching right away versus those who were treated with spectacles alone. The authors included patients who had acuity > 0.3 LogMAR bilaterally and an inter ocular difference (IOD) > 0.18logMAR. They excluded patients with poor follow up, surgical management, and deprivation amblyopia. The comparison was those who had primary occlusion (defined as initiated with vision > 0.3logMar bilaterally) and secondary – initiated to correct IOD when acuity improved to 0.18 logMar in the better eye). In sum, the question is if the pediatric ophthalmologist should wait to see if the acuity in each eye improves with spectacle correction alone as a primary treatment or if patching of the dominant eye should begin right away. The authors found that of the 98 patients who met inclusion criteria, half had primary and half had secondary occlusion. They found no differences in the final acuity, intraocular differences, or stereopsis improvement between the two groups and they concluded that primary occlusion does not provide further benefit over glasses alone. Importantly the authors also found that primary occlusion therapy did not cause any decrease in the final acuity of the stronger eye. The main limitations of the paper include the limitations that are inherent from being retrospective, the inter-provider variability in acuity testing, and the lack of data on compliance with therapy. However this is an important paper for the pediatric ophthalmologist as it reminds the physician that patching treatment in these cases does not need to be started at the initial visit.

Binocular Treatment of Amblyopia: A Report by the American Academy of Ophthalmology
Stacy L. Pineles, Vinay K. Aakalu, Amy K. Hutchinson, Jennifer A. Galvin, Gena Heidary, Gil Binenbaum, Deborah K. VanderVeen, Scott R. Lambert
Ophthalmology. 2020 Feb(2);127:261-72.

This technology assessment for the American Academy of Ophthalmology reviewed the literature comparing various binocular treatments for amblyopia compared with standard penalization treatment. Binocular treatment involved either presenting different visual stimuli to each eye or dichotic interventions where the contrast sensitivity of the dominant eye is reduced to the level of the amblyopic eye. The outcome measures were the increase in visual acuity in the amblyopic eye and improvement in binocular sensory measures. A total of 30 studies were identified and stratified based on strength of evidence: six Level 1, one Level 2, and 13 Level 3. Although the smaller studies reported improved outcomes with binocular amblyopia treatment compared with and especially combined with patching, the larger,

randomized trials showed patching was superior in improving vision. There was also no convincing evidence of improved binocular sensory outcomes. The main limitation was compliance with the binocular treatment, especially the lack of engaging content for the hours of treatment required. The conclusion was that traditional penalization therapy was superior, especially if the increased cost of binocular treatment is considered.

Comparison of Pre-Treatment vs. Post-Treatment Retinal Vessel Density in Children with Amblyopia
Gunzhauser RC, Tsui I, Velez FG, Fung SSM, Demer JL, Suh SY.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3): 79-85.

Prior studies have reported a lower retinal vessel density (RVD) in amblyopic vs. non-amblyopic eyes. No studies have shown if amblyopic eye RVD changes following patching therapy. This pilot study assessed RVD differences between pre-treatment vs. post-treatment amblyopic eyes of 12 patients <10 years old with unilateral amblyopia. Patients were excluded if they had deprivation amblyopia, bilateral amblyopia, nystagmus, media opacity, intraocular inflammation, or any retinal disease. All participants underwent optical coherence tomography angiography (OCTA) using a spectral domain device before and after refraction and patching treatment. Outcomes included superficial (SCP) and deep (DCP) capillary plexus RVD.12 patients with 12 amblyopic eyes) were included in this study. Mean (SD) age, gestational age (GA), birth weight (BW), and follow-up time were: 6.5 (1.7) years, 39.4 weeks (1.4 w), 3271 g (262 g), and 114 days (46d), respectively. There was a significant increase in the RVD of the DCP in 3 × 3-mm scans after treatment, specifically in the whole image (52.6 ± 5.75 vs 56.5 ± 2.48%, p = .046) and superior hemisphere regions (52.47 ± 6.17 vs 56.73 ± 2.27%, p = .048). The authors propose that amblyopic eye RVD potentially increases after amblyopia treatment in specific regions of the retina, however do state that the study was limited by the number of patients included. Further research is required to refine this clinical parameter and to determine if this change in RVD is a cause or an effect of changes in visual acuity.

Evaluating Amblyopia Treatment Success Using the American Academy of Ophthalmology IRIS50 Measures
Talia N. Shoshany, Suzanne M. Michalak, Ryan N. Chinn, Steven J. Staffa, David G. Hunter
Ophthalmology. 2020 Jun(6);127:836-8.

This retrospective study attempted to quantify amblyopia outcome measures using defined standards set by the American Academy of Ophthalmology; reduction in interocular visual acuity difference from > 0.29 logMAR to < 0.23 logMAR, final visual acuity ≤ 0.18 logMAR, or visual improvement of 2 lines or more. Unfortunately, out of 1226 patients with amblyopia between the ages of 3 and 7, only about 20% met all inclusion criteria and only 70% of those patients had a follow up visit between 3 to 6 months after their initial visit. Successful treatment of amblyopia occurred in 71% of patients, but only 50% when accounting for non-returning patients. Going forward, implementing standard criteria for treatment success within large aggregate computerized medical records should facilitate better analysis of real-world outcome measures for amblyopia.

2. VISION SCREENING

Prevalence of Amblyopia After Photoscreening.
Laiginhas R, Ferreira CC, Leitão R, Geraldes R, Chibante-Pedro J, Monteiro M, de Matos C.
J Pediatr Ophthalmol Strabismus. 2020 Nov 1;57(6):372-377.

This cross-sectional study evaluated the prevalence of amblyopia in an adolescent population who had previously undergone photoscreening (MTI or PlusoptiX) while preschool aged. Patients born in the authors' hospital underwent two screenings, at age one and age four. Patients born at another hospital who moved to the area under went one screening, at age four. Included subjects had their near acuity, distance acuity, and stereopsis measured. Three of 299 subjects had unilateral amblyopia. This rate, 1%, is lower than prevalence of amblyopia in Europe, the study's location. Of the three amblyopes identified, two had been previously identified during the initial preschool screening but were lost to follow up. The remaining amblyopic subject had micro strabismus and was missed during the preschool aged screening. A robust amblyopia prevention program using photoscreening can reduce amblyopia prevalence to very low levels. The authors note that by adding a "borderline" outcome for the screening done at age one, over-referral for full eye exams was reduced. Patients who fell into the borderline category had screening repeated one year later.

Diagnostic Test Accuracy of the Red Reflex Test for Ocular Pathology in Infants. A Meta-analysis.
Subni Y, Chabane-Schmidt D, Al-Bakri M, Bach-Holm D, Kessel L.
JAMA Ophthalmol. 2020; 139(1):33-40.

This is a meta-analysis review of the literature until April 2020 on the diagnostic accuracy of the red reflex test in infant screening for ocular pathologies. The data was extracted independently by 2 authors. Results showed that 8713 infants from 5 unique studies were eligible for qualitative and quantitative review. Of note, all the included studies used the red reflex test without pupillary dilation and were compared with a reference test performed with pupillary dilation. The sensitivity of 7.5% and specificity of 97.5% was found in infants with any ocular pathology. The authors noted that for ocular pathology needing medical and/or surgical intervention, the sensitivity of 17.5% and specificity of 97.6%. Result from the meta-analysis indicate that an abnormal red reflex most likely reflects an underlying ocular pathology but a normal red reflex finding during screening does not exclude ocular disease. Limitations of the study include the meta-analysis itself and the selection bias; of note, four studies were excluded due to not meeting the study criteria. In summary, this meta-analysis is helpful, especially reporting the high specificity of the red reflex test in infant screening ocular pathology. Moreover, the authors remind us that not performing the red reflex screening has serious effects on ocular health and visual potential and overall health of the child.

Teleophthalmology: Evaluation of Phone-based Visual Acuity in a Pediatric Population.
Evan Silverstein, Jonathan S. Williams, Jeffrey R. Brown, Enjana Bylykbashi and Sandra S. Stinnett.
American Journal of Ophthalmology, 2021 Jan; 221:199-206.

The purpose of this prospective, comparison study was to determine if the visual acuity measured by a telemedicine platform (GoCheck Kids) compared to the acuity measured with the Amblyopia Treatment Study protocol (ATS) in the clinic. The transition to telemedicine sparked by the COVID-19 pandemic put the pediatric ophthalmologist in an interesting situation since without accurate visual acuity testing, guiding parents to the appropriate treatment is obviously quite difficult. The authors studied 53 established patients who were ages 3-18. The visual acuity of these children were checked by the GoCheck Kids mobile app by a family member and then by HOTV-ATS by study personnel, and lastly by regular clinic protocol with an ophthalmic technician. The authors then compared the results and found that GoCheck Kids app had a moderate correlation compared to the chart screen in the clinic and a fair correlation to HOTV-Amblyopia protocol, though most patients had acuity of one line of difference or less.

The major weakness of the study was that the patients were not patched when the acuity was checked at home. Overall, this paper is quite relevant since we are rushing to find better ways to remotely check visual acuity of our patients. This information will be helpful both during the pandemic and as patients (especially those who live far from a pediatric ophthalmologist) and physicians become more comfortable with telemedicine. The authors point out that for many patients being treated for amblyopia, the exact acuity measurement is less important than the difference in acuity between the eyes.

Referral outcomes from a vision screening program for school-aged children.
Silverstein M, Scharf K, Mayro E, Hark L, et al.
Can J Ophthalmol. 2021 Feb;56(1):43-48.

This study reported outcomes from the Wills Eye Vision Screening Program for Children (WEVSPC), which screened students in grades K-5 in public schools between January 2014 and June 2015. The screening program included visual acuity, color vision, stereopsis, and manifest refraction if acuity was suboptimal. If acuity remained below normal or other pathology suspected the subject was referred for further pediatric ophthalmology consultation. A total of 10,726 children were screened. 509 (5%) were referred for further evaluation. Of these only 35% returned consent forms for further consultation. Ultimately 127 children ended up completing a consultation. Of these 76% had a refractive error, 43% with amblyopia, 16% strabismus and 13% had anisometropia. 17% had no ocular conditions found (false positives). Treatment included eyeglasses (79%), patching (21%), and surgery (6%). The authors believe that the low consent form for further consultation resulted in an overall low amblyopia detection rate. Extrapolation indicated an additional 118 children who failed screening but did not have follow-up might have had amblyopia. Incentives provided for families did not seem to increase participation. They speculate that future initiatives should focus on connecting with families in advance of screening to help decrease children lost to follow-up as well as to help decrease false-positive referrals.

Successes and shortfalls of community Plusoptix photoscreening: results from the iSee study in Southwestern Ontario
Kiatos E, Armstrong J, Makar I.
Can J Ophthalmol. 2020 Oct;55(5):49-55.

This paper reports a prospective, multicenter photoscreening program in Ontario for children. Photoscreening was performed with the Plusoptix S12 photoscreening. This photoscreener has 5 levels of referral criteria, and this study used a setting for 80% sensitivity and 95% specificity. 5959 children (18-72 months) were screening over 210 locations over 3 years. The positive referral rate was 6.8% (403 children) and results were unreadable in 2.9% (170 children). The unreadable results were highest for children less than 36 months. The estimated risk factor prevalence was 4.0% for anisometropia, 3.1% for astigmatism, 1.1% for hyperopia, 0.4% for myopia, and 0.4% for strabismus. 99 out of the 403 children (24.5%) completed a formal eye exam. Of these 78/99 received treatment for refractive errors. The authors found that this photoscreening program was an effective tool for identifying amblyopic risk factors for children. However, there was no mandatory follow-up for these children to receive proper treatment, therefore the overall efficacy of the screening program was reduced. The authors suggest that future work should be geared toward ensuring compliance with proper exams and care after photoscreening referral.

Comparison of refractive value and pupil size under monocular and binocular conditions between the Spot Vision Screener and binocular open-field autorefractor.
Satou T, Takahashi Y, Niida T.
Strabismus. 2020 Oct 16:1-8. doi: 10.1080/09273972.2020.1832542.

In this cross-sectional study, the authors evaluated the reproducibility of the Spot Vision Screener and binocular open-field autorefractor to determine refraction and pupil size. They enrolled 22 right eyes of 22 adults (14 females, mean age 22.0 years, range 20.0-29.2 years) who were emmetropic or myopic and did not have strabismus, intraocular surgery, or eye pathology. The authors found that the spherical

equivalent values obtained with the Spot Vision Screener were significantly less myopic than the Grand Seiko autorefractor (−2.98 D in monocular condition and −2.93 D in binocular condition) (P = .037 and P = .018, respectively), however the spherical equivalent values did not significantly differ from the binocular values for either instrument (P = .417 in the Spot Vision Screener and P = .601 in the Grand Seiko autorefractor). Similarly, pupil size did not differ significantly between the two device, but the pupils in monocular conditions were larger than binocular conditions (P<0.001). The authors conclude that both devices have high repeatability and reproducibility in monocular and binocular conditions with a high correlation between devices.

Association of state vision screening requirements with parent-reported vision testing in young children.
Lillvis JH, Lillvis DF, Towle-Miller LM, Wilding GE, Kuo DZ.
J AAPOS. 2020 Oct;24(5):291.e1-291.e6.

This is a retrospective review of data obtained nationally from the 2016 National Survey of Children's Health on children ages 3-5 (n=7,567) and available sources to compile state policies that mandate childhood vision testing. The rates of parent-reported vision testing for each state and fit logistic regression model were calculated using survey-based estimation methods with nationally representative weights. The model controlled for factors such as age, sex, race/ethnicity, and insurance coverage. Additional analyses added comorbidities that may lead to an eye care provider referral. Parent-reported vision testing rates by state ranged from 41% to 84%. A significant association was found between the presence of state-level vision screening requirements and parent-reported vision testing, which remained after controlling for comorbidities (OR = 1.374; P = 0.016). Of these comorbidities, arthritis, blindness, and very low birth weight were associated with a higher rate of vision screening (all P < 0.05). This study suggests that the presence of a state-level school vision screening requirement is associated with increased parent-reported and the survey also relies on parent reported information. vision testing in children 3-5 years of age. The study is limited by publicly available survey data. This suggests that state policy may ensure timely screening for amblyopia and other sight-threatening complications.

Vision screening outcomes in children less than 3 years of age compared with children 3 years and older.
Stiff H, Dimenstein N, Larson SA.
J AAPOS. 2020 Oct;24(5):293.e1-293.e4.

This is a retrospective review of medical records of children who failed vision photoscreening over a 13-year period at University of Iowa. The rates of amblyopia and treatment outcomes in children 0-2 years and 3-5 years of age were compared. 319 subjects, 67 (21%) were 0-2 years of age and 252 (79%) were at least 3 years of age at screening. Amblyopia was found in 19% of the younger group and 30% of the older group (*P* = 0.12). Follow-up time was similar between groups. At final follow-up, 8% of children in the younger group did not attain normal vision, compared with 40% in the older group (OR = 8.92; 95% CI, 1.65-92.95; *P* = 0.009). Normal vision was attained on average at 35 months of age in the younger group and 69 months in the older group (P < 0.0001). In this study cohort, children <3 years of age were found to have an equivalent rate of amblyopia compared with children ≥3 of age. Those screened between ages 0-2 years of age attained normal vision at a significantly younger age and were more likely to attain normal vision.

Comparison of photoscreening and autorefractive screening for the detection of amblyopia risk factors in children under 3 years of age.
Kara C, Petriçli İS.
J AAPOS. 2020 Feb;24(1):20.e1-20.e8.

This study is a cross-sectional study comparing the effectiveness of Spot Vision photoscreener and the SureSight autorefractor in detecting amblyopia risk factors (ARFs) in preterm and term-born children less than 3 years of age. The instruments were operated by one performer. Retinoscopy was performed by both authors randomly in the same room. 368 patients (44.8% preterm and 55.2% term-born) were

included. 25% had ARF according to the 2013 AAPOS criteria. The diagnostic and predictive values of the devices in detecting ARFs were calculated by applying the manufacturer criteria, as well as the Vision in Preschool (VIP) study VIP90 and VIP 94 criteria, and the criteria recommended by Rowatt and colleagues. Results were evaluated using receiver operating characteristics (ROC) curves. The highest specificity and positive predictive value (PPV) were obtained with Spot Vision manufacturer criteria (specificity, 0.91; PPV 0.69) and SureSight manufacturer criteria showed low specificity (0.43) and PPV of 0.35 and a high false positive rate (57%). The highest specificity (0.86) and PPV (0.62) for Suresight was obtained with the Rowatt criteria. In this study's cohort photoscreening with Spot Vision manufacturer criteria was sufficient for vision screening ages 0 to 3 years with high specificity values. The Rowatt criteria may increase the performance of SureSight results. Limitations of the study is children were evaluated in the ophthalmology clinic and not in a primary care setting and the examiners were not masked to the screening results.

Evaluation of the Spot Vision Screener in School-Aged Children
Mae Millicent W. Peterseim; Trivedi, Rupal H; Feldman, Samuel; Husain, Mahvash; Walker, Mollianna; et al.
J Pediatr Ophthalmol Strabismus. 2020 May;57(3):146-153.

In this prospective study patients who presented to pediatric ophthalmology aged 6-16 were screened using the Spot Vision Screener (Welch Allyn, Skaneateles Falls, NY). The eye examination following the screening identified the patients' refractive error. The sensitivity and specificity of the Spot screening was calculated using three progressively more restrictive "Gold Standards". The first and least restrictive "Gold Standard" being the AAPOS amblyopia risk factors and the second and third with progressively less Differences of megalopapilla refractive error. The underlying idea behind this is that in young children detection and prevention of amblyopia and identification of relatively large refractive error is paramount, whereas in older school aged children smaller refractive errors should be identified and corrected to promote optimal vision. The Spot screener's sensitivity of detecting AAPOS amblyopia risk factors was 90% and the specificity was 77%. In this population, patients referred to pediatric ophthalmology, the prevalence of amblyopia risk factors was 42%, which is higher than the general population. To estimate the PPV and NPV in the general population, 24% was used as the disease prevalence making the PPV 55% and NPV 96%. As the "Gold Standard" was made more restrictive to include smaller refractive errors, the sensitivity moderately decreased to 75.3% and the specificity increased. For older patients Spot screening is a quick process that can be performed by lay persons with similar results as traditional visual acuity screening. Even with restrictive targets that could be more appropriate for older children the Spot screener maintains good sensitivity and excellent specificity and could be useful in this population.

Traditional and instrument-based vision screening in third-grade students.
Silverstein E, McElhinny ER.
J AAPOS. 2020 Aug;24(4):232.e1-232.e6.

AAPOS recommends optotype screening for children >5 years, though younger children may benefit from instrument-based screening due to difficulty cooperating with optotype screening. For this reason, this observational study screened 1,593 third grade children with both optotype screening and an instrument-based screening (Plusoptix S12) with the goal of determining which screening tool is most effective. Of those screened, 516 (32%) were referred for an ophthalmologic examination: 118 uniquely from optotype, 229 uniquely from Plusoptix, and 169 by both. Optotype screening took 120 seconds on average compared to 30 for Plusoptix. Positive predictive value for identifying children with visual acuity <20/30 by optotype screening was 75% and 71% for Plusoptix. A limitation of this paper is that only 48% of those that were referred underwent a cycloplegic refraction. The authors conclude that due to similar positive predictive values and decreased time required for instrument screening, instrument screening may be preferred in this age range.

Normative data for the redesigned Kay Pictures visual acuity test.

O'Connor AR, Milling A.
J AAPOS. J AAPOS 2020 Aug;24(4):242-244.

The Kay picture test is a validated optotype test of visual acuity used internationally since its introduction in the 1980's. Since its introduction, it has undergone multiple small iterations including the ability to use isolate or linear optotypes. The purpose of this short report of 283 children was to provide normative data for the most recent iteration of the Kay pictures. The report includes data by age regarding intraocular difference, testability rates, and normative monocular visual acuity data. Generally, compared to the older version, children performed better with the redesigned optotypes. As expected, ability to resolve optotypes increased with increasing age. This report provides a useful reference for those testing children with Kay pictures if there is a concern about deviation from normal by age.

A community-based effort to increase the rate of follow-up eye examinations of school-age children who fail vision screening: a randomized clinical trial.
Musch DC, Andrews C, Schumann R, Baker J.
J AAPOS. 2020 Mar;24(2):98e1-6.

This was a randomized clinical trial for children who failed vision screening at 11 selected schools in Wayne County, Michigan from January to April 2017. Children were in grades 1 and grade 3 and were randomly assigned to receive the standard follow-up protocol provided by the state's screening program or an enhanced follow-up protocol. Results included 162 children participants from both grade 1 and grade 3. Mean age was 7.9 years, SD 1.1years and 84 (52%) participants were male. In the standard protocol, a letter is sent to the child's parent within 1 week of the failed vision screening, informing them of the need for an eye exam with a licensed eye care provider (ECP) for their child. A form is enclosed for the parent to give a form to the ECP and in turn, the parent will submit to the vision screening program. If no ECP form is received within 6 weeks, a reminder letter is sent to the parent. In the enhanced protocol, there were 3 more steps: (1) follow-up telephone call by a study coordinator within 3 weeks of the initial letter mailing to parent to determine if the visit with ECP was completed or scheduled. If not scheduled or completed, the parent is given a list of ECP to schedule the visit; (2) another telephone call is made after 6 weeks if no ECP form is received with the same reminder; (3) if the examine was completed but the form documentation is missing, the study coordinator calls the ECP to prompt form submission. With the enhanced protocol with a study coordinator, the authors sought to evaluate the percentage of children who received an ECP follow-up exam within 16 weeks of the date of the child's failed vision screening. Results showed that 52 (65%) of 80 children had a documented eye examination within 16 weeks of the failed vision screening. In comparison, children receiving the standard follow-up was 48%. The intergroup difference in follow-up was 17.4% and the enhanced follow-up group's odds of obtaining a documented eye exam was twice that of the standard follow-up group (p=0.026). Limitations of the study include using the study coordinators who already had access to the contact information of the parents/participants. Another study limitation is that the follow-up eye exam does not indicate what was the value of the exam: amblyopia suspect, amblyopia diagnosis, normal eye exam. In summary, this randomized cohort shows that enhanced efforts to ensure stricter compliance with follow-up with an ECP after failed vision screening is effective and successful.

Effectiveness of the iPhone GoCheck Kids smartphone vision screener in detecting amblyopia risk factors
Walker M, Duvall A, Daniels M, Doan M, Edmondson L, Cheeseman EW, Wilson ME, Trivedi RH, Peterseim MMW.
JAAPOS. 2020 Feb;24(16):16.e1-5

GoCheck Kids iPhone photoscreening app was released in 2018 for vision screening children from 6 months to 6 years of age. This is a prospective study performed at Medical University of South Carolina that evaluates the accuracy of this app in detecting amblyopia risk factors as established in 2013 by the AAPOS vision screening committee. A total of 244 children age 6 to 83 months (average age 42 months) participants were screened and received a comprehensive eye examination on the same day or within 6 months by a pediatric ophthalmologist. The GoCheck Kids results were evaluated in 2 circumstances: 1)

in the first 90 days were all manually reviewed, 2) after the 90 days trial, only images with “not gradable” or with “risk factors identified” or if automatically reviewed as “no risk factors identified” were manually reviewed. The sensitivity of GoCheck Kids screening with remote review of all images was 90.5%, specificity was 68.1%, positive predictive value of 56.8% and a negative predictive value of 94% when “not-gradable” images were excluded. There were 7 false negatives, of these 4 had astigmatism (+1.75 to +2.25), one had anisometropia, and 2 had hypermetropia greater than +4.00 D in each eye. The sensitivity was 82.4%, and specificity was 82.6% when select images automatically graded as not gradable or risk factors identified” were manually reviewed. The limitation of the study is its small size and the disease prevalence (31.6%) is higher than the 20% estimated for the general population. Compared to other marketed photoscreeners and autorefractors the degree of sensitivity and specificity in detecting amblyopia risk factors is good in their enriched cohort of young children.

Positive predictive value and screening performance of GoCheck Kids in a primary care university clinic
Law M, Pimentel MF, Oldenburg CE, de Alba Campomanes AG
JAAPOS 2020 Feb; 24(17):e1-5.

GoCheck Kids, a smartphone-based photoscreening app has shown to detect Amblyopia risk factors. This is a retrospective study at UCSF evaluating the positive predictive value (PPV) in detecting refractive amblyopia risk factors (ARFs)in children age 3 to 48 months of age. The medical records of screened children who presented to the UCSF pediatric ophthalmology clinic after an abnormal GoCheck Kids photoscreening results between February 2017 to 2018 were reviewed. 2936 children were screened during the study period and a total of 172 (5.8%) had an abnormal result. 115 of them returned for a comprehensive eye exam. The mean age was 24.9 months. A total of 57 patients met criteria for amblyopia risk factors, a PPV of 50% (95% CI, 41-60%). The PPV was lowest for patients 3 to 12 months of age (26%). The PPV was higher in Latino/Hispanic ethnic patients (P<0.01). In this subset of patients, 10 of 12 “true positive” were due to asigmatic refractive errors. The PPV found in this study was lower than the PPV calculated in previous GoCheck Kids validation studies, and other photoscreeners: Plusoptix (51%), Spot (67%) and iScreen (87%). Children younger than 12 months of age were not included in their studies and may explain the difference between studies. The limitations of this study is the restrospective nature, limited follow up of patients who failed the GoCheck kids, and the pediatric ophthalmologists and optometrists in the study were not masked to the GoCheck kids results. This study suggests that GoCheck Kids have a limited utility in detecting ARFs in early screening of children ages 12 months and younger.

Comparison of photoscreening and autorefractive screening for the detection of amblyopia risk factors in children under 3 years of age
Kara C, Petricli IS.
JAAPOS 2020 Feb;24(20):e1-8

This study is a cross-sectional study comparing the effectiveness of Spot Vision photoscreener and the SureSight autorefractor in detecting amblyopia risk factors (ARFs) in preterm and term-born children less than 3 years of age. The instruments were operated by one performer. Retinoscopy was performed by both authors randomly in the same room. 368 patients (44.8% preterm and 55.2% term-born) were included. 25% had ARF according to the 2013 AAPOS criteria. The diagnostic and predictive values of the devices in detecting ARFs were calculated by applying the manufacturer criteria, as well as the Vision in Preschool (VIP) study VIP90 and VIP 94 criteria, and the criteria recommended by Rowatt and colleagues. Results were evaluated using receiver operating characteristics (ROC) curves. The highest specificity and positive predictive value (PPV) were obtained with Spot Vision manufacturer criteria (specificity, 0.91; PPV 0.69) and SureSight manufacturer criteria showed low specificity (0.43) and PPV of 0.35 and a high false positive rate (57%). The highest specificity (0.86) and PPV (0.62) for Suresight was obtained with the Rowatt criteria. In this study’s cohort photoscreening with Spot Vision manufacturer criteria was sufficient for vision screening ages 0 to 3 years with high specificity values. The Rowatt criteria may increase the performance of SureSight results. Limitations of the study is children were

evaluated in the ophthalmology clinic and not in a primary care setting and the examiners were not masked to the screening results.

Scottish Pre-School Vision Screening – First 3 Years of National Data
Pentland L, Patel S.
British and Irish Orthoptic Journal. Apr 2020;16(1):13-18.

Pre-school orthoptic vision screening (POVS) was implemented by the Scottish government and is a standardised assessment to promote early detection of visual problems in children. The target conditions are amblyopia, refractive errors and strabismus. This study presents the preliminary findings for the first three years of the screening program. The data from POVS was collected retrospectively. The data includes screening years 2013 to 2016 inclusive and was collected from each health board in Scotland. The authors report the coverage, referral rate, true positives and positive predictive values. A total of 167,962 children were due to have vision screening over the 3 screening years included in this paper. This figure did not include the children that opted out of the eye test (mean opt-out rate was 1.8%) and children that already attended the hospital eye service (mean already attended was rate 3.1%). The POVS program had a mean coverage of 85.5%, ranging from 63.7% to 94.8% between health boards. Over the 3 year screening period, the mean referral rate was found to be 17.9%. The mean true positive rate was 88.9%, and the mean positive predictive value was 86.9%. Overall, the authors point out that the Scottish data set on pre-school orthoptic vision screening showed excellent mean coverage, allowing better screening for children who are in more vulnerable backgrounds. A consistently high true positive rate over the three screening years demonstrates it is a sensitive screening program, which is essential for the detection of visual problems in children. The authors point out the importance of need to look at false negative data, which is likely low due to the orthoptic tests performed at time of screening.

How many Plusoptix S04 measures yield the most sensitive amblyopia screening.
Sandra Guimarães, MD, PhD; Andreia Soares, MD; Patrício Costa, PhD; Eduardo Silva, MD, PhD
J Pediatr Ophthalmol Strabismus. 2019 Sep 1;56(5):305-312.

The Plusoptix S04 (Plusoptix, Atlanta, GA) is one of the most common amblyopia screening devices used worldwide.It is a photoscreening technology used by many pediatricians, primary care physicians, and screeners . Although the Plusoptix's performance for amblyopia risk factors has been largely demonstrated, its sensitivity and specificity in predicting amblyopia has not been studied. The purpose of this study was to evaluate Plusoptix performance in amblyopia prediction. It also examined the best readings for that prediction, while answering the following questions: is it enough to have one Plusoptix measure or should we have more? And, if so, which is the best measure to use? A total of 1,547 children aged 3 to 4 years underwent a non-invasive eye examination in a whole population screening. The Plusoptix was measured binocularly three consecutive times. Seven models were developed: the first (P1), second (P2), and third (P3) measure of Plusoptix, the mean of P1, P2, and P3 (Pmean123), the maximal value of P1, P2, and P3 (Pmax123), the mean of P1 and P2 (Pmean12), and the maximal value of P1 and P2 (Pmax12).The results showed that internal consistency was excellent for sphere, cylinder (alpha = 0.92 vs 0.97), aniso-sphere, and anisocylinder (alpha = 0.87 vs 0.86). All models predicted amblyopia ($P < .001$); there was 2.3% new diagnosis and 5.1 events per variable. A bootstrap analysis with 1,000 samples confirmed the stability of the model. Astigmatism ($P < .001$; odds ratio [OR] = 2.1 to 3.6) and anisosphere ($P < .001$; OR = 3.6 to 9.0) predicted amblyopia. Although sphere, when measurable, did not predict amblyopia ($P > .19$; OR = 1.2 to 1.3), the likelihood of amblyopia presence was 100 times higher when the Plusoptix displayed "hyper." All receiver operating characteristic (ROC) curves were significant ($P < .001$), with no differences between them (all $P > .16$). Adjusting the cut-off from ROC curves for the highest sensitivity, Pmax12 referred 31.9% and 16.1% fewer patients than P1 and Pmean12, respectively. A third measure revealed accommodation-related false-negative results; therefore, adding measurements showed no benefit. In conclusion, this was the first study to assess the Plusoptix's prediction of amblyopia. When aiming for maximal sensitivity, the Plusoptix refers many children (> 20% children in all models). The first measure refers more children than two measures. Non-measurable results must be considered abnormal because the chance of amblyopia presence was high.

Refractive Errors and Amblyopia Among Children Screened by the UCLA Preschool Vision Program in Los Angeles County.
Margines JB, Huang, C, Young A, Mehravaran S, Yu F, Mondino BJ, Coleman AL.
Am J Ophthalmol. 2020 Feb; 210: 78-85.

This was a five year retrospective evaluation of a vision screening program at UCLA, called the UCLA Preschool Vision Program (UPVP). From 2012 to 2017, the visual acuity and undilated noncycloplegic refractive screening of 93, 097 children was performed. From the total number of children screened, 85.3% were between the ages of 3 to 5 years old. From the total number of children screened, 15.3% met the specific refractive criteria for a referral for a full cycloplegic examination. Data analysis only from the right eye was included in this manuscript. From this pediatric cohort, UPVP performed 6779 cycloplegic examinations. Results noted 4018 (61%) with hyperopia, 1336 (20%) with myopia, 6122 (93%) with astigmatism. Regarding the demographics of the cohort indicated that Latino children had higher rates of astigmatism and worse visual acuity when compared to all other races and ethnicities. The diagnosis of refractive amblyopia was noted in 780 children (1% of the screened population and 11.5% of the examined population) and 27% of these children had both eyes affected (ie bilateral refractive amblyopia). The authors of the UPVP retrospective 5-year evaluation report the largest published data sampling on pre-school children in the USA. This study has limitations in its retrospective nature; however, the common refractive errors in this pediatric cohort as well as the diverse demographics of the children provide a helpful perspective for the diagnosis and treatment of refractive amblyopia. Furthermore, the screening criteria used for UPVP is a helpful tool and model for other amblyopia programs at the metropolitan, state, and national level.

3. REFRACTIVE ERROR

Association of Age at Myopia Onset With Risk of High Myopia in Adulthood in a 12-Year Follow-up of a Chinese Cohort.
Hu Y, Ding X, Gua X, Chen Y, Zhang J, He M.
JAMA Ophthalmol. 2020 Sep 17; 138(11):1129-1134.

This is a population-based prospective cohort study of twins in Guangzhou, China from 2006 to 2018. The first-born twins completed follow-up until 17 years or older and the 443 participants who developed myopia were included in the analysis. Results from the 443 eligible participants, 55.8% 247 participants (55.8%) were female with a mean age of myopia at 11.7 years and 54 participants (12.2%) developed high myopia in adulthood. The analysis from the multivariate logistic regression results indicated that the risk of developing high myopia in adulthood decreased significantly with delay in the age at myopia onset (odds ratio, 0.44; P < 0.001), from greater than 50% for 7 or 8 years of age to approximately 30% for 9 years of age and 20% for 10 years of age. The authors suggest that the risk of high myopia is high in children with myopia onset during the early school ages. In particular, each year of delay in the age of onset significantly reduces the chance of developing high myopia in adulthood. Of note, the participants included in analysis were from the participants from the first-born twins in the Guangzhou Twin Eye Study. Limitations of the study include a relative smaller sample size, especially of the participants with age of myopic onset at 7 and 8 years old. Furthermore, limitations include the homogenous sample of ethnicity and race and the level of myopia in this Chinese region. In summary, this cohort study is very helpful because of the 12-year follow-up assessment from the school ages of 7 or 8 years old indicates that more than 50% of the study participants developed high myopia in adulthood. The findings from this Chinese study teaches us the importance of prevention and slowing the progression of myopic onset at early school ages.

Safety and Efficacy of Low-Dose Atropine Eyedrops for the Treatment of Myopia Progression in Chinese Children. A Randomized Clinical Trial.
Wei S, Li SM, An W, Du J, Liang X, Sun Y, Zhang D, Tian J, Wang N.
JAMA Ophthalmol. 2020 Oct 1; 138(11):1178-1184.

This is a randomized, placebo-controlled, double-masked study to evaluate the efficacy and safety of Atropine 0.01% eye drops on slowing myopic progression and axial elongation in Chinese children. A total of 220 children from ages 6 to 12 years old with myopia levels of -1.00 D to -6.00 D in both eyes were enrolled for 1 year at Beijing Tongren Hospital in Beijing, China.
Of 220 participants, 103 (46.8%) were girls with mean age of 9.64 years with mean baseline refractive error and axial length (AL) measuring -2.58 D and 24.59mm, respectively. Results at 1 year showed that from the randomized participants, follow-up of 76 (69%) in the Atropine 0.01% treatment group and 83 (75%) in the placebo group. At 1 year, the mean AL was 0.32mm in the Atropine 0.01% treatment group compared with 0.41mm in the placebo group (mean difference, 0.09mm; P=0.004) with a relative reduction of 22.0% in AL. At 1 year, the mean myopic progression was -0.49 D in the Atropine 0.01% treatment group and -0.75 D in the placebo group (mean difference, 0.26 D; P < 0.001) with a relative reduction of 34.2% in myopic progression. Limitations of the study is the approximate 70% follow-up in both groups at 1 year and a homogenous sample of ethnicity and race at this single hospital enrollment site in Beijing, China. In summary, this Chinese randomized study is an important contribution to the literature about the benefits of dilute Atropine as compared to placebo with regards to both AL and myopic progression measurements during amblyopic age range.

Effects of Atropine Treatment on Choroidal Thickness in Myopic Children
Luyao Ye, Ya Shi, Yao Yin, et al
Invest Ophthalmol Vis Sci. Dec 2020;61, 15

In this study, 207 children aged 6-12 years were monitored over the course of six months to look at the change in a variety of ocular measurements. The groups were divided into receiving 1% or 0.01% atropine daily for 6 months (the 1% group was dosed with 1 drop weekly after the first week). Choroidal thickness and axial length were the two parameters that were mostly focused on in this study, though pupilometry, intraocular pressure, accommodation, and a number of other measurements were obtained. For the 1% group, they were noted to have an increase in choroidal thickness, though not in axial length over the 6 months, while the 0.01% group were noted to have a decrease in choroidal thickness and an increase in axial length over 6 months. As these parameters are extremely important to the progression of myopia, we must consider the findings of the ATOM2, LAMP, and other trials to try to understand why this study seems to show that 0.01% atropine did not show as strong of an effect as the 1%, though this may be due to the short timeline of this study.This should hopefully lead to larger and longer studies looking at all of the currently accepted treatments for myopia control.

Associations Between Fetal Growth Trajectories and the Development of Myopia by 20 Years of Age
Kathleen IC Dyer, Paul G Sanfilippo, Scott W White, et al
Invest Ophthalmol Vis Sci. Dec 2020;61, 26

This study looked at patients' fetal measurements and growth trajectories and compared those numbers to refractive error, corneal curvature of radius, and axial length at age 20 years. Femur length was the only fetal characteristic shown to have a relationship with myopia development. Faster growth of head circumference, femur length, and estimated fetal weight were correlated with significantly flatter corneas. While this study showed some relationship between fetal measurements and ocular characteristics, it did not take into account environmental factors throughout the growth of these subjects. Further studies need to stratify the different fetal characteristics based on childhood environmental factors to see if there is any predictive model of myopia based on fetal characteristics.

Independent Influence of Parental Myopia on Childhood Myopia in a Dose-Related Manner in 2,055 Trios: The Hong Kong Children Eye Study
Shu Min Tang, Ka Wai Kam, Amenda N. French, Marco Yu, Li Jia Chen, Alvin L. Young, Kathryn A. Rose, Clement C. Tham, Chi Pui Pang and Jason C. Yam.
American Journal of Ophthalmology, 2020 October; 218: 199-207.

This population-based cross-sectional study was designed to determine the effects on childhood myopia of parental myopia, parental education, children's outdoor time, and children's near work. The authors evaluated 6,155 patients in 2055 families and looked at the cycloplegic autorefraction of children and dry autorefraction of their parents. The authors also collected data about parental education, outdoor time by the children, and near work. The children were categorized into 10 different levels based on the refraction of their parents. The authors found that the risk of myopia of the child was 11 times higher with two myopic parents. Additionally, higher parental education and more reading time were both risk factors and that increased outdoor time decreased the odds of myopia. Overall parental myopia status accounted for almost 12% of the myopia in children. The association of parental myopia and childhood myopia development was independent of other risk factors (environment). The authors concluded that children highest risk of myopia were those with parental myopia and these children are a potential target for early intervention of myopia. This study helps council our patients who come in with questions about why their children are myopic. It is fair from this data to explain to families that both genetics and environment play a role. Interestingly the patients in this study were ages 6-8 so this may underestimate the percentage of high myopia as these patients have plenty of growing left to do.

Effect of low-dose atropine on myopia progression, pupil diameter and accommodative amplitude: low-dose atropine and myopia progression
Fu A, Stapleton F, Wei L, Wang W, et al.
Br J Ophthalmol. 2020 Nov; 104:1535-1541.

Vision Screening and Refractive Error

Atropine has been shown to have a dose-related effect on myopia progression in children. Low doses atropine can help mitigate bothersome side effects such as photophobia, poor near vision, and possible rebound effects seen after cessation in higher doses. This study conducted in China randomized children to either 0.02% or 0.01% atropine eye drops (with single vision glasses) vs single vision glasses only (control). Measurements of refractive error, axial length, pupil diameter, and accommodative amplitude were performed at baseline, and 4, 8, and 12 months after treatment. 400 total children were enrolled: 138 in 0.02% group, 143 in 0.01% group, and 120 in control group. Baseline demographics and characteristics were similar in the 3 groups. After 12 months, the spherical equivalent refractive error change was -0.38D, -0.47D, and -0.70D for the 0.02%, 0.01%, and control groups respectively. The axial length change was 0.30mm, 0.37mm, and 0.46mm in the groups respectively. The differences in all three groups for axial length and refractive error were significant. Change in accommodative amplitude was 1.50D in 0.02% and 1.61 in 0.01%. Change in pupil diameter was 0.78mm in 0.02% and 0.69mm in 0.01%. Both of these measurements were significantly different compared to control, but there was no statistical difference between the two atropine groups. Therefore, the authors conclude that 0.02% had a better effect on myopia progression with a similar effect on pupil diameter and accommodative amplitude as 0.01%. Note that this study did not address rebound effects after cessation of atropine.

Objectively measured near work, outdoor exposure and myopia in children.
Wen L, Cao Y, Cheng Q, Li X, et al.
Br J Ophthalmol. 2020 Nov; 104:1542-1547.

Environmental factors are thought to play an important role in the development of myopia. Several studies have reported that increased amount of time spent outdoors has a lower risk for myopia development. However, studies looking at near work have varied in quality, perhaps due to the use of questionnaires which may be questionable in their accuracy. This study used a new wearable device called Clouclip that is able to measure working distance and eye-level illuminance to help obtain near work and outdoor exposure times. The device attaches to the frame of glasses and used infrared and light sensors to measure distance and light intensity. 86 children (average 10.13 years) wore the device for 1 week. Mean daily time worn was 11.72 hours. Refraction of the children was determined by autorefraction, and 33% (28/86) were myopic (≤-0.50D). They found that myopic children were exposed to light intensities for shorter durations on average than non-myopic children. The myopic children also spent more time on activities <20cm than non-myopic children. Logistic regression showed that time spent with light intensity of >3000 lux was protective again myopia, and time spent with working distance <20cm) was found to be a risk factor). This study helps confirm previous associations of these environmental factors and myopia. Further work on cause and dose-effect is needed.

Puberty could regulate the effects of outdoor time on refractive development in Chinese children and adolescents
Wang J, Cheng T, Zhang B, Xiong S, et al.
Br J Ophthalmol. 2021 Feb; 104:191-197.

Outdoor activities have been showed to help prevent myopia progression. Some studies suggest that outdoor light could influence hormones in the body and retina which contribute to myopia prevention. Ocular growth and maturity during puberty might be more sensitive to environmental influences (such as outdoor activities) during this time. Therefore this observational study aimed to explore the effect of puberty on myopia and its interaction with outdoor time. Children age 7-13 were included in this study from 2015-2017 in China. Cycloplegic refraction and axial length measurements were obtained, and levels of testosterone and estradiol were detected using saliva. 776 children were included with average baseline age of 9.64 years. There was no significant difference in baseline refraction or myopia rates between genders. 55.2% of subjects were myopes at baseline. Myopic parents, less outdoor time, and more changes in estradiol were found to be associated with greater changes in axial length and spherical equivalent. Children whose menarche/spermatorrhoea had not occurred had faster changes in axial length. Outdoor time had a delaying effect on axial length elongation that was stronger in early puberty or prepuberty than in middle or late puberty, suggesting that puberty may play a regulatory role in the

process. The authors did find that the overall outdoor time spent by children was inadequate, and efforts should be made to increase outdoor time in children and adolescents during early puberty.

Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine
Fen Fen Li, Ka Wai Kam, Yuzhou Zhang, Shu Min Tang, Alvin L. Young, Li Jia Chen, Clement C. Tham, Chi Pui Pang, Jason C. Yam
Ophthalmology; 2020 Dec;127(12):1603-11

This study focused on the biometrics of the Low-Concentration Atropine for Myopia Progression (LAMP) study, specifically the effect of atropine on axial length, corneal curvature, and anterior chamber depth as measured by the IOLMaster after one year of treatment. There were 383 children, ages of 4 to 12, randomized to receive atropine 0.05%, 0.025%, 0.01%, or placebo. Similar to the findings for myopic refractive error, there was a statistically significant ($p<0.01$) stepwise reduction in the change in axial length with increasing concentrations of atropine. There were no significant changes in corneal curvature, anterior chamber depth, or calculated lens power. The biometry demonstrated that more than 70% of the myopic progression was accounted for by increasing axial length. With no significant weaknesses, this study provides convincing evidence that low concentration atropine reduces axial elongation as its mechanism to reduce myopic progression and thus may protect against the adverse health outcomes associated with high myopia.

Evolution of the Prevalence of Myopia among Taiwanese Schoolchildren: A Review of Survey Data from 1983 through 2017
Tzu-Hsun Tsai, Yao-Lin Liu, I-Hsin Ma, Chien-Chia Su, Chao-Wen Lin, Luke Long-Kuang Lin, Chuhsing Kate Hsiao, I-Jong Wang
Ophthalmology; 2021 Feb;128(2):290-301

This study was a stratified cluster sampling designed to extend the population data collection on myopia prevalence in Taiwan in 2016 compared with similar studies every ~5 years from 1983 to 2010. The age ranges studied were 7-12 years, 13-15 years, and 16-18 years. Children using orthokeratology for myopia control were excluded. Of the 10,000 recruited students, 7,348 participated with an extensive data survey and complete ophthalmic examination, including cycloplegic refraction. Any myopia was defined as > -0.25 diopters and high myopia was defined as > -6 diopters. Between 1983 and 2016, the prevalence of myopia more than doubled in all age groups, with more than 75% of 13-15 year old students having myopia in 2016 compared with 31% in 1983. The prevalence of high myopia also more than tripled over that same time span from 4% to 15%. The strongest predictors were more than 180 minutes of near work and more than 60 minutes of smart device or computer work per day. Unlike prior surveys, the 2016 survey did not find any protective effect for more than 60 minutes of daily outdoor activities. Weaknesses of the study include the use of tropicamide instead of cyclopentolate for cycloplegia and the lack of survey data for electronic devices in prior years simply because such devices did not exist before the 2005 survey. Also, by excluding children undergoing active myopia control, the survey likely underestimated the actual rate of myopia because all of those children had myopia. The dramatic increase in myopia and high myopia, however, over the relatively short time span highlights the epidemic nature of the problem and the need for effective interventions to reduce disease prevalence and severity.

Increased Time Outdoors Is Followed by Reversal of the Long-Term Trend to Reduced Visual Acuity in Taiwan Primary School Students
Ophthalmology. 2020 Nov;127(11):1462-1469.
Pei-Chang Wu, Chueh-Tan Chen, Li-Chun Chang, Li-Ling Liao, Kathryn Rose, Ian G. Morgan

This population based prospective study conducted in Taiwan from 2001-2015 included school age children of 7-12 years. The purpose of the study was to compare the prevalence of reduced visual acuity since the intervention promoting increased time outdoors (120 minutes daily) was implemented in September 2010. Of note, this intervention was in addition to the interventions already in place between

2001-2010 (gaze into distance, orbital rim massage, classroom light intensity > 500 lux, table height adjusted to student's height, near work breaks of 10 minutes after every 30 minutes of near work). 1.2-1.9 million students from more than 2600 schools were enrolled in the annual visual assessment program. Just about half were female (48%). Visual acuities were assessed using the Taiwan School Student Visual Acuity Screen. Reduced visual acuity was defined as uncorrected visual acuity of < 20/25 in either eye. Those children using orthokeratology or contact lenses were defined as having reduced visual acuity. The study found that that the reduction rate after 2010 when the outdoor program was implemented was 20.5% over 5 years and 4.10% per year. Children who were 7-9 years old showed a larger decline in prevalence of reduced visual acuity than the older children (10-12 years old) (P=0.002). Limitations of the study include variability in school compliance, school size, use of atropine and inability to control for outdoor time outside of school or genetics (parent myopia status). One of the most significant limitations is that decreased visual acuity was attributed to myopia without a comprehensive eye exam which should include a cycloplegic refraction. Despite the limitations, this study highlights the need for further studies on what exactly is it about the outdoors that may play a role in potentially decreasing myopia progression (ie. distance vision, UV light, break from near work).

Evaluation of the Necessity for Cycloplegia During Refraction of Chinese Children Between 4 and 10 Years Old
Xinting Liu, MD, PhD; Liang Ye, MD; Chong Chen, MD; Minfeng Chen, MD; Shuyun Wen, MD; Xinjie Mao, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):257-263.

The purpose of the study was to compared atropine refractions to uncyclopleged autorefractions in children aged 4 to 10 years, and to evaluate the necessity of cycloplegia for different refractive states and ages. This retrospective study performed at Wenzhou Medical University in China included patients with low, moderate, and high myopia and hyperopia, who were divided into two groups by age: 4 to 6 years (n = 5,320) and 7 to 10 years (n = 6,475). Every patient underwent cycloplegia with atropine. Refractive errors were measured by retinoscopy. Within each group, the differences between cycloplegic and non-cycloplegic refractive errors (DIFFC-N) were significant. DIFFC-N was negatively correlated with age (r = -0.356, P < .001). The differences in refractive error between prescribed glasses and non-cycloplegic refraction (DIFFG-N) were largest in the groups with high myopia (0.83 ± 1.15 diopters [D] in the 4 to 6 years group and 0.60 ± 1.47 D in the 7 to 10 years group). After cycloplegia, 62.5% of the patients with mild myopia became emmetropic or hyperopic in the 4 to 6 years group, and 11.3% of the patients with mild myopia became emmetropic or hyperopic in the 7 to 10 years group. Without cycloplegia, autorefraction tends to overestimate refractive error in children with myopia and underestimate refractive error in hyperopia. For accurate glasses prescriptions, cycloplegia should be used for children between 4 and 10 years.
Strengths of this study are the large sample size, and the finding that cycloplegia makes the largest difference in refraction for high myopes. I learned that in this hospital in China, myopic children require three visits to obtain a glasses prescription: the initial visit noting abnormal autorefraction or abnormal visual acuity, a second visit to measure cycloplegic refraction after home administration of atropine, and a third visit after the atropine has worn off that is when the final refraction is obtained and given (which is usually more myopic than the atropine refraction). Determining whether cyloplegia is truly necessary is important in terms of the work effort required to prescribe glasses for the large numbers of Chinese children with refractive error.

Eye-related quality of life and functional vision in children wearing glasses.
Leske DA, Hatt SR, Castañeda YS, Wernimont SM, Liebermann L, Cheng-Patel CS, Birch EE, Holmes JM.
J AAPOS. 2020 Mar;24(2):91e1-6.

This was a prospective study completed at two institutions to evaluate the eye-related quality of life (ER-QoL) and functional vision in children wearing glasses using the pediatric eye questionnaire (PedEyeQ). Children were ages 5-17 years old without other ocular morbities with normal visual acuity who wore

glasses for correction of refractive error and control participants who did not wear glasses. One parent per child was identified for the questionnaire completion. 40 glasses-wearing participants and 99 non-glasses wearing controls were included in this study. Results found that glasses-wearing children of 5-11 years old and 12-17 years old had lower PedEyeQ scores across all domains compared with non-glasses wearing controls ($P < 0.04$ for each domain). Parent scores were lower for glasses-wearing children ($P < 0.001$ for each domain). Limitations of the study include non-equal evaluation of glasses-wearing participants versus non-glasses wearing controls. Another limitation is that the authors didn't address the impact of uncorrected refractive error on QoL and functional vision. In summary, parents as well as the children wearing glasses had a reduced ER-QoL and functional vision as compared to non-glasses wearing controls.

Two-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study: Phase 2 Report
Jason C Yam FCOphthHK, FRCS, Fen Fen Li MMed, Xiujuan Zhang PhD, Shu Min Tang PhD, Benjamin H K Yip PhD, Ka Wai Kam FCOphthHK, FHKAM, Simon T Ko FCOphthHK, Alvin L Young FRCSI, Clement C Tham FCOphthHK FRCOphth, Li Jia Chen FCOphthHK, Chi Pui Pang Dphil.
Ophthalmology. 2020 Jul; 127(7):910-919.

In this double-masked randomized clinical trial conducted in Hong Kong, children meeting the inclusion criteria ($\geq$-1.0D of myopia in both eyes, <2.5 D of astigmatism and $\geq$ 0.5D progression of myopia in previous year) between ages 4 to 12 years old were randomized to nightly 0.05%, 0.025%, 0.01% atropine or placebo. This paper reports the myopia progression (in spherical equivalence or SE) following phase 2 of the study during which the placebo group was then started on 0.05% atropine with all others continuing within the same initial treatment groups. A total of 350 children completed the study at 2 years, 93 of which were in the 0.05% atropine group, 86 in the 0.025% atropine group, 91 in the 0.01% atropine group and 80 in the switchover group (placebo to 0.05% atropine). The mean SE change was -0.55 $\pm$ 0.86 D, -0.85 $\pm$ 0.73 D and -1.12 $\pm$ 0.85 D in the 0.05%, 0.025%, and 0.01% atropine groups, respectively, at the end of the two years ($P=0.015$, $P<0.001$ and $P=0.02$). The mean axial length changes showed similar trends between the groups. The switchover group had less myopia progression than the projected change had they never been switched over to 0.05% atropine. Photosensitivity and compliance were comparable between the groups as were the vision-related quality of life. Though the switchover data is a limitation of this study, the longer period of follow up of 2 years is an advantage to observing how myopia progressed relatively to each group.

Ametropia prevalence of primary school students in Chinese multi-ethnic regions.
Zhang Y, Qiu K, Zhang Q.
Strabismus. 2020 Mar;28(1):13-16.

The authors sought to determine the prevalence of visual impairment from refractive error in five regions in South China. They screened students between 7-12 years old and assessed the effect of gender, age, and region. Of the nearly 25,000 children screen, 19% had visual impairment from refractive of which the majority was due to myopia (94%). Refractive error was more common in girls and older children, as well as several of the ethnic minorities. Of interest, approximately three-quarters (77.5%) of students with refractive error had not received an eye exam in the past, which identified a public issue of importance to the region. Otherwise, the applicability of this study to the global population is quite limited.

Long-term refractive outcomes in children with early diagnosis of moderate to high hyperopia.
Laiginhas R, Figueiredo L, Rothwell R, Geraldes R, Chibante J, Ferreira CC.
Strabismus. 2020 Apr 22:1-6.

The authors sought to examine the long-term refractive outcomes in children with moderate to high hyperopia (≥3D). In total, 78 eyes from 39 children with a mean age at first evaluation of 1.8 ± 0.9 years and last evaluation of 10.6 ± 2.7 years were enrolled. The median follow up with 130 months (range 72-

193 months). At baseline evaluation, the mean SE was 4.5 ± 1.4 diopters and 49% has esotropia (23% partially accommodative, 26% accommodative). Interestingly, the mean refractive error in children with partially accommodative esotropia (4.53 ± 1.38 diopters), accommodative esotropia (4.33 ± 1.26 diopters), and without strabismus (4.58 ± 1.26 diopters) did not differ (p = .80). At the last evaluation, the mean SE was 4.6 ± 1.7 diopters. Four children developed unilateral amblyopia (one - anisometropia, three -anisometropia and strabismus) which was successfully treated in 3 of 4 cases. The authors conclude that even though half of the children had strabismus, early intervention is important to optimize outcomes.

Axial length for 7-8 years pupils of in Southern China.
Qiu K, Zhang Y.
Strabismus. 2020 Mar;28(1):20-24.

This manuscript evaluated the axial length, refractive error and visual acuity in 7-8 year olds in one school in Southern China. The 291 enrolled children were divided into 4 groups – emmetropia, mild myopia, severe myopia and astigmatism. The average axial length was 22.88 ± 0.09 mm and the average spherical equivalent was −0.75 ± 0.13D. The very brief results section does not provide details, but rather refers the reader to the five included graphs. The authors concluded that axial length correlated with refraction but not with uncorrected visual acuity. The Discussion section does not elaborate significantly on the findings, only stating that the accuracy of the IOL Master was regarded as the accuracy limitation from refraction. The multiple limitations of this paper including small sample size and no cycloplegic refraction severely limit its applicability to the field.

Accuracy of Autorefraction in Children: A Report by the American Academy of Ophthalmology
Lorri B. Wilson MD, Michele Melia, ScM, Raymond T. Kraker, MSPH, Deborah K. VanderVeen MD, Amy K Hutchinson MD, Stacy L. Pineles MD, Jennifer A. Galvin MD, Scott R. Lambert MD
Ophthalmology.
2020 Sep; 127(9):1259-1267.

This report described what was found in 15 studies in regard to the accuracy of autorefractors compared to cycloplegic refraction in children. These 15 studies were identified using various strategies involving combination of search terms related to the question at hand. Each study was then evaluated for quality of evidence ranging from Level I (met specific criteria including appropriate study population, refraction under cycloplegia, randomization of order of autorefraction versus retinoscopy, and others) to Level III (does not meet 2 or more of the criteria in for level I). There were 13 autorefractors in total amongst the 15 studies. A mean difference of 0.5D was reported by the 13 studies which compared spherical data from cycloplegic autorefraction with spherical data from cycloplegic retinoscopy. A mean difference in astigmatism of 0.25 D or less was reported by the 12 out of the 13 studies that evaluated the cylinder by autorefraction with or without cycloplegia. Myopia was reported to be overestimated and hyperopia underestimated when autorefraction was conducted in the absence of cycloplegia. Amongst the various studies, the general consensus seemed to be that autorefraction was more accurate with cycloplegia than without. However, when cycloplegic autorefraction compared to cycloplegic retinoscopy, one cannot easily discern whether one is more superior than the other in accuracy. Cycloplegia likely increases the agreement between retinoscopy and autorefraction. The results of this study show that refractions, whether autorefraction or retinoscopy, should be done under cycloplegic conditions to optimize accuracy and that the two data points should both be considered in ultimately deciding on the final refractive error.

Evidence That Emmetropization Buffers Against Both Genetic and Environmental Risk Factors for Myopia
Alfred Pozarickij, Clair A Enthoven, Neema G Mojarrad, Denis Plotnikov, et al
Invest Ophthalmol Vis Sci. Feb 2020;61, 41

This large study looked at the effect of a number of variables related to myopia in children between ages 7 and 15. The goal was to see which variables are related to myopia, the strength of their relationship, and which children were more susceptible to myopia based on these factors. The authors found that all factors (genetic risk, parental myopia, high time spent reading, low time outdoors) lead to an increased risk of myopia in these children. They also found that the more myopic a patient is the greater effect all of the factors had on increasing myopia. Although there was no standard of refraction, some received a cycloplegic refraction while others did not, and different autorefractors were used in the two study populations, this study provides important information on educating patients of the importance of environmental factors in myopia control and leads to further research in genetic considerations in myopia.

Sleep Duration, Bedtime, and Myopia Progression in a 4-Year Follow-up of Chinese Children: The Anyang Childhood Eye Study
Shi-Fei Wei; Shi-Ming Li; Luoru Liu; He Li;
Invest Ophthalmol Vis Sci. Mar 2020;61, 37

This large study looked at the relationship between sleep duration and bedtime and myopic progression in children. It measured both cycloplegic refraction and biometry. This study divided children by gender as well as a number of other confounding risk factors for myopic progression. Once all confounding variables were taken into account, neither bedtime nor duration of sleep were noted to have a clinically significant effect on refractive error or axial elongation. As there are numerous environmental risk factors for the progression of myopia, it is important for us to understand which environmental factors are actual risk factors and those that have no causal relationship to disease progression. This study helps us to focus on those environmental factors that can help our patients.

Association of Parental Myopia With Higher Risk of Myopia Among Multiethnic Children Before School Age.
Jiang X, Tarczy-Hornoch K, Cotter SA, Matsumura S et al for the POPEYE Consortium.
JAMA Ophthalmol. 2020 May;138(5):501-509.

This study from the POPEYE (Population-Based Pediatric Eye Disease) Consortium investigated the association of parental myopia with early-onset risk of myopic refractive error and ocular biometry in multiethnic children ages 6-72 months old. This was a cohort study of pooled data collected from 2003 to 2011 in children at three population-based study locations from the US, Singapore, Australia. Analysis included 9793 children; participants including 4003 Asian, 2201 African American, 1998 Hispanic white, 1591 non-Hispanic white children with mean age of 40.0 months, SD 18.9 months. The cohort reported 52.1% boys. Compared to children without parental myopia, the mean odds ratio for early-onset myopia was 1.42 for children with 1 parent with myopia, 2.70 for children with 2 parents with myopia, 3.39 for children with 2 parents with childhood-onset myopia. Of note, for the children without myopia, having a parent with myopia was associated with a greater axial length to corneal curvature radius ratio ($P<0.001$). Results indicated an association of parental myopia as an early-onset risk factor for myopia in children in all four racial/ethnic groups and across all age groups except for children younger than 1 year old. The findings of an association of parental myopia in children as young as 1 year old suggest that genetics play an important role in early-onset myopia with baseline myopia noted in children before school age. In summary, this study is helpful in that it addresses multiethnic children's risk relationship to parental myopia and helps us put into context the failed vision screenings for children with childhood-onset myopic parents versus non-childhood-onset myopic parents.

Protective behaviours of near work and time outdoors in myopia prevalence and progression in myopic children: a 2-year prospective population study
Huang P, Hsiao Y, Tsai C, Tsai D, Chen C, et al
Br J Ophthalmol 2020 Jul;104:956-961.

This paper reports results of a longitudinal population-based study of elementary school students in Taipei. 10,743 students completed the study, where vision and refraction exams were provided every 6 months. Questionnaires were given to assess time spent on near work, distance from near work, breaks, outdoor time (during school recess). The children who performed “persistent protective behaviour” (which included longer near work distance, discontinuing near work, more time outdoors) had significantly lower prevalence of myopia. The behaviours had protective impacts on myopia progression over 6 to 24 months. Students with shorter near work distance revealed the most myopic shift in spherical equivalent after adjusting for other variables. The authors conclude that the longer near work distance of >30cm, discontinuing near work every 30 minutes, and more outdoor activity during recess could decrease myopia prevalence and progression in children.

Effect of Pupil Size and Binocular Viewing on Accommodative Gain in Emmetropia and Myopia
Huang CY, SAtou T, Nida T.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):103-108.

The purpose of this study was to evaluate the differences in accommodative gain in response to different accommodative stimuli and determine the effects of pupil size, binocular viewing, and inherent eye refraction on accommodative gain. This study enrolled 47 healthy young adults (emmetropia: 21 eyes, myopia: 26 eyes). Refractive value and pupil size during accommodative stimulus were measured using an open-viewing type auto-refractor (Grand Seiko WAM-5500). The subject was continuously presented with six stimuli (0D, 1D, 2D, 3D, 4D, and 5D) in front of the eye. Measurements were performed under three conditions. Condition 1 involved the patient having monocular status with complete occlusion of the non-viewing eye; condition 2 involved the patient having monocular status with occlusion of the non-viewing eye by translucent occluder; condition 3 involved the patient having binocular status. In the emmetropia group, there was no significant difference in accommodative gain between conditions 1 and 2 ($p > .05$), but conditions 2 and 3 were significantly different ($p < .05$). In the myopia group, accommodative gain was significantly different between conditions 1 and 2 with stimuli 3D, 4D, and 5D ($p < .05$), but conditions 2 and 3 were not significantly different ($p > .05$). The effects of pupil size and binocular viewing on accommodative gain differed between emmetropia and myopia. In conclusion, accommodative accuracy under binocular conditions was different from that under monocular conditions. The present study suggests that this difference is caused by a change in pupil size and binocular viewing. Additionally, effects differed between emmetropic and myopic eyes. Myopic eyes showed a decrease in accommodative accuracy due to pupil constriction with binocular viewing, whereas emmetropic eyes improved in accommodative accuracy due to binocular viewing.

Spasm of Near Reflex: Objective Assessment of the Near-Triad
Shrikant R Bharadwaj, Saujanwita Roy, PremNandhini Satgunam
Invest Ophthalmol Vis Sci. Jul 2020;61, 18

This study of patients aged 9 to 23 years of age measured the near triad, accommodation, convergence, and pupillary diameter, in patients with spasm of the near reflex and aged matched controls. They wanted to determine whether there was any correlation of the level of accommodation to the pupillary diameter and convergence when compared to the age matched controls. While they found the obviously increased and highly variable pre-cycloplegic refractive errors and level of accommodation, the pupillary diameter and convergence were similar between the patients with the spasm of the near reflex and the controls. This shows that the accommodation in those patients with spasm of the near reflex is not necessarily connected to levels of convergence or pupillary diameter.

The Adaptation and Acceptance of Defocus Incorporated Multiple Segment Lens for Chinese Children.
LU Y, Lin Z, Wen L, Gao W, Pan L, Li X, Yang Z, and Lan W
Am J Ophthalmol. March 2020;211: 207–216.

This prospective cross over study was performed on 20 children and 10 adults with the purpose of describing the acceptance of a new spectacle lens aimed at decreasing myopic progression. The lens studied in this paper is the Defocus Incorporated Multiple Segments (DIMS) lens. The lens works by having a midperipheral honeycomb area of defocus. The patients wore either the DIMS lens or a single vision lens for the first week and then were switched to the other lens for the second week. The patients recruited were 7-15 years old and had a refractive error of 0.5 to 6 diopters of myopia (spherical equivalent), less than 1.5D of astigmatism, and no eye pathology that would limit the best corrected acuity. The authors found that both types of lenses (DIMS and single vision) had equivalent acuities at distance in regular and dim light settings, and also with high and low contrast sensitivity. There was an expected decrease in acuity in the DIMS lens when the subjects looked in the mid peripheral defocused zone. Of note 90% of the children preferred the DIMS lens, but they were not blinded to the goal of decreasing myopia with this treatment. Overall this is a very interesting study since using spectacle correction for peripheral defocus is a safer and less invasive way to treat progressive myopia compared to multifocal contact lenses and atropine and has the potential to provide the pediatric ophthalmologist another tool to help decrease the progression of myopia.

Changes in Choroidal Thickness Varied by Age and Refraction in Children and Adolescents: A 1-Year Longitudinal Study.
Xiong S, He X, Zhang B, et al.
Am J Ophthalmol. May 2020; 213:46-56.

This prospective cohort study of 756 pediatric patients aged 6 to 18 aims to clarify the changes of choroidal characteristics over time in different ages and refractive statuses. The authors collected data on axial length, cycloplegic refraction, and choroidal thickness and baseline and 1 year follow up and looked at changes in age and refraction over time. The OCT was performed with a Topcon Atlantis OCT , the axial length with the IOL master, and the refraction was don with an Topcon auto-refractor. Younger patients and newly myopic patients had the largest attenuation in choroidal thickness over the year. And the association between changes in axial length and choroidal thickness were least strong in patients with persistent myopia. They concluded that the choroidal thickness measurements changed by age with a rapid thinning of the choroid among newly developed myopic patients. The authors speculate that the choroidal attenuation plays and important role in the onset of myopia. The strengths of this paper lie in it's prospective nature and large number of patients.

Prevalence and Time Trends of Myopia in Children and Adolescents in China: A Systemic Review and Meta-Analysis
Dong L, Kang Y, Li Y, Wei W, Jonas J
Retina. Mar 2020; 40:399–411.

The study aimed to estimate prevalence, associated factors, and time trends of myopia in Chinese children and adolescents. Authors searched PubMed, EMBASE, and Web of Science for studies examining the prevalence of myopia in children and adolescents aged 3 years to 19 years in China before October 2018. They pooled the prevalence and associated factors for myopia and estimated time trends. Results: In 22 eligible studies including 192,569 individuals, the pooled prevalence (95% confidence interval [CI]) of myopia and high myopia in the study period from 1998 to 2016 was 37.7% (95% CI: 23.5–52.0%) and 3.1% (95% CI: 1.2–5.0%), respectively, with higher odds for girls than boys (myopia: odds ratio: 1.29; 95% CI: 1.14–1.46; P , 0.001; high myopia: odds ratio: 1.37; 95% CI: 1.05–1.78; P = 0.02) and with higher prevalences for urban areas than rural regions (myopia: 48.8% [95% CI: 32.3–65.3] vs. 31.9% [95% CI: 20.4–43.3; P , 0.001]). The pooled prevalence of myopia and high myopia increased from 4.7% (95% CI: 2.5–6.9) and 0.2% (95% CI: 0.0–0.5), respectively, in ,7-years-olds to 56.2% (95% CI: 29.8–82.5) and 15.1% (95% CI: 6.4–23.8), respectively, in 16- to 18-year-olds. Myopic refractive error increased with older age (P , 0.001), female gender (P , 0.001), and study year (P = 0.003). Studies performed after 2013 showed a prevalence of myopia and high myopia in the 16- to 18-year-olds of 84.8% (95% CI: 84.4–85.2%) and 19.3% (95% CI: 18.6–20.2%), respectively. Assuming a further linear relationship with the study year, myopia prevalence in 2050 among children and adolescents aged 3

years to 19 years would be estimated to be about 84%. The marked rise in high myopia prevalence among adolescents in China may be of importance for high myopia as risk factor for irreversible vision loss in Chinese adults in the future.

Impact of eyeglasses on academic performance in primary school children
Hark LA, Thau A, Nutaitis A, Mayro E, Zhan T, et al.
Can J Ophthalmol. 2020 Feb;55(1):52-57

This large retrospective study aimed to determine whether children who participated in a vision screening program displayed academic improvement after receiving glasses. Children in kindergarten through 5th grade participated in the Wills Eye Vision Screening Program for Children (WEVSPC). Eyeglasses were provided free of charge when needed. A total of 4523 children participated in the program, of which 485 (11%) required glasses. Of these, 349 (72%) were able to get consent and actually given glasses. Based on eyeglass adherence questionnaires completed by classroom teachers, 67.4% of children wore their glasses most of the time (>75%). 18.6% of children rarely or never wore their glasses (<25%). Children in kindergarten through grade 3 were given the Developmental Reading Assessment (DRA) and children in grade 3 through 5 were given the Pennsylvania System of School Assessment (PSSA). DRA from 2226 children showed that when glasses were worn initial high reading performances were less likely to decline. PSSA results for 847 children showed Asian children were more likely to score higher reading levels when glasses were prescribed and worn. A similar trend was seen in black and Hispanic children, but this was not statistically significant. Overall the results suggest high adherence to eyeglasses wear is associated with maintenance in standardized reading scores, although low DRA scores did not improve with glasses wear.

Myopia and Childhood Migration: A Study of 607,862 Adolescents
Alon Peled, Arnon Afek, Gilad Twig, Eran Pras, Ygal Rotenstreich, Ifat Sher, Estela Derazne, Dorit Tzur, Barak Gordon
Ophthalmology. 2020 Jun(6);127:713-23.

This study correlated age of migration to Israel with levels of myopia to provide insight into the effects of environment on development of myopia. The study benefited from a uniform endpoint, a mandatory medical exam at age 17 prior to enrollment into the military. There were three study groups: immigrants from the USSR and Ethiopia, Israeli-born immigrants from those same regions, and Israeli-born natives with no immigrant status for at least two generations. Orthodox Jewish woman were excluded because they were exempt from military service. Refractions were determined by current spectacle correction if the corrected vision was 20/20 or by noncycloplegic autorefraction if the vision was 20/20- or worse. Uncorrected 20/20 vision was assumed to be associated with no myopia. Myopia was defined as at least -0.75 D and high myopia as -6.00 D. Age at immigration was divided into three groups: 0 to 5 years, 6 to 11 years, and 12 to 19 years. Years of education and the educational system (secular, Orthodox, and highly Orthodox) were also recorded. Recent immigrants had a significantly lower risk of myopia and high myopia than native Israelis with no immigrant or recent immigrant status. Ethiopian immigrants and recent immigrants had the lowest risk of myopia. In both immigrant groups, arriving after age 11 had a significantly reduced risk of myopia. Each year of older age resulted in a 2.7% lower odds ratio of myopia. In addition, there was a significant increase in the risk of myopia with more rigorous educational systems. This study highlights the importance of environmental factors, particularly in younger children, in increasing the risks of myopia and higher myopia in children. Study strengths are the very large and inclusive population, while the weakness is the lack of granular detail on the actual environmental exposures associated with increased risk of myopia, such as the length of time spent on various activities.

4. VISUAL IMPAIRMENT

Actual Visual Acuity Demands in the Classroom.
Adams C, Leach S, Kresch YS, Brooks SE.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):48-54.

This cross sectional observational study evaluated the visual demands of 14 classrooms in five schools in New York City across various grades. The mean and range logMAR values of text displayed on whiteboards from various seating positions was determined. Additionally contrast sensitivity was evaluated using Pelli-Robson contrast sensitivity charts. Optotype contrast was high for black markers on whiteboards (Pelli-Robson chart optotype contrast sensitivity = 0.00), but varied from 0.15 to 0.60 on smartboards. The mean logMAR equivalent of lower case letters from seats in the center of the front row was 0.93 (Snellen equivalent = 20/170), whereas the mean value from the center of the back row was 0.46 (Snellen equivalent = 20/58). Current screening guidelines likely capture most children who would have difficulty seeing in school. Preferential seating in the front and use of high contrast optotypes can be helpful for some students.

Examining How Students with Visual Impairments Navigate Accessible Documents
Korey J. Singleton, Kristine S. Neuber
Journal of Visual Impairment & Blindness. 2020 Sep.114(5):393-405.

The use of information and communications technology resources such as leaning management systems and electronic documents is a critical part of the online education experience. This study examined how students with visual impairments navigate accessible documents (i.e., Word, PDF). The study's research design focused on how students with visual impairments at a 4-year research institution in the Commonwealth of Virginia navigate accessible documents and what structural elements (i.e., headings, lists, or alt-text) these individuals perceive to be most useful. The study utilized a combination of video observations and semi-structured interviews, and collected participants expressed and observed interactions with accessible Word and PDF documents. Four core themes emerged from these findings: useful navigation elements or features (i.e., alt text description of images), strategies for navigating accessible documents (i.e., basic keyboard shortcuts), barriers to access (i.e., image-only PDFs), and coping strategies (i.e., self-remediation, seeking third-party support). The findings suggest practical strategies for training participants to navigate accessible documents as well as the structural elements most useful to study participants. These findings may help universities implement targeted initiatives targeted towards basic document accessibility as well as assist students with visual impairments on how to access these elements to increase efficiency and reduce cognitive load.

Applying Video Modeling to Promote the Handwriting Accuracy of Students with Low Vision Mobile Technology
Chia-Jui Chang, C. Owen Lo, and Su-Chen Chuang
Journal of Visual Impairment & Blindness. 2020 Sep.114(5):406-420.

In Taiwan, although school-age students with low vision struggle with poor handwriting, there is a lack of evidence-based educational practices for handwriting enhancement. iPads have been identified as an effective tool to deliver video-based instruction designed to improve handwriting accuracy among students with low vision. The authors employed a multiple-baseline-across participants probe design to assess success of the intervention with three individuals in public school with low vision aged 9, 12, and 14 years of age. A baseline phase determined the handwriting accuracy for each of the participants was under 50%. The intervention phase included video modeling instruction using an iPad. After the intervention phase, the participants received three follow-up sessions identical to those in the baseline

phase. Handwriting accuracy increased during intervention and was maintained during follow-up sessions. This study demonstrated that iPads used with video modeling can lead to improved accuracy in handwriting for students with low vision.

Perceptions of Assistive Technology by Teachers of Students with Visual Impairments in Jordan
Eman Al-Zboon
Journal of Visual Impairment & Blindness. 2020 Dec.114(6):488-501.

This study examines the perceptions of assistive technology expressed by teachers of students with visual impairment (blindness, low vision) in Jordan. Data was collected using semi-structed interviews of 20 teachers and analysis was carried out using the constant-comparative method. The identified themes and illustrative quotes that best represented each interview were categorized and a consensus of central themes from all interviews was reached. Results highlighted the challenges that teachers perceive in using assistive technology with their students, particularly regarding computer use, willingness of a child to use a particular device, availability of technology in schools and at home, and a lack of training at home. The results also highlight perceived external barriers to the use of assistive technology, including financial, training, societal attitudes, and family support. The article also discusses that assistive technology can have negative effects which can be considered an ethical issue, since such technologies can expose students with visual impairment to negative community attitudes, addiction to an assistive technology device, bullying, abuse, and the possibility of developing political and religious extremism. The study recommends decision-makers in the field of visual impairment need to consider these issues by providing professional development, addressing financial barriers, and creating awareness programs for students regarding the effective use of assistive technology.

A Patient-reported Outcome Measure of Functional Vision for Children and Young People Aged 8 to 18 Years With Visual Impairment.
Alexandra O. Robertson, Valerija Tadić, Mario Cortina-Borja and Jugnoo S. Rahi.
American Journal of Ophthalmology, 2020 Nov; 219:141-153.

This is a questionnaire development and validation study with the purpose of developing an age-appropriate and patient-reported outcome measure for the functional impact of visual impairment in children. Current measures of functional vision in this group lumps all children 8-18 together. This author group previously reported a patient-reported outcome measure (PROM) for capturing functional vision in children ages 10-15years, and this is a more age-specific extension of their previous work. This tool will allow children to self-assess the functional impacts of their visual function and will be helpful in clinical practice, but mostly in research. The relevance to the pediatric ophthalmologist is mostly for those who are looking for tools to assess the functional vision for research purposes, though clinically may be useful to track a child over time.

Cerebral visual impairment captured with a structured history inventory in extremely preterm born children aged 6.5 years.
Hellgren K, Jacobson L, Frumento P, et al.
J AAPOS. 2020 Feb;24(1):28.e1-28.e8.

The authors administered a questionnaire to parents of extremely preterm children to determine whether the questionnaire could predict cerebral visual impairment (CVI). This was a prospective study performed in Sweden. 120 children born before 27 weeks' gestational age (66 males; mean, 25.4 +/- 1.0 weeks) and 97 full-term controls (56 males; mean, 39.9 +/- 1.1 weeks) were evaluated at the age of 6.5 years. Answers given by parents to a questionnaire designed for detection of CVI were compared with clinical asssessments of the children's vision, perception and cognition. Children born extremely preterm had worse questionnaire scores than control children: median sum score of 25 (95% CI, 18.1-31.9) compared to 11 (95% CI, 8.8- 13.2), P < 0.001). When parents reported few features of CVI on the questionnaire, those children had better results on direct assessments, and those children were more

similar to controls. The authors conclude that an easily used questionnaire was able to detect CVI nearly as well as time-consuming and resource-demanding examinations in a cohort of extremely preterm children. A critique of the study is the utility of giving a questionnaire to detect CVI at age 6.5 years; one would ideally identify CVI at a younger age.

High- and Low-Contrast Letter Acuity Perception Matures With Age in Normally Sighted Children.
Waldman AT, Lavery AM, Liu GW, Avery RA, Liu GT, Maguire MG, Ying GS, Banwell BL.
J Neuroophthalmol. 2020 Jun;40(2):148-156.

This study sought to establish normative data for low contrast letter acuity in children with healthy vision as low contrast acuity data are relevant to a number of conditions including neuro ophthalmic, retinal conditions and amblyopia. The authors evaluated 101 children with a mean age of 13 years and found that both high contrast and low contrast acuity continues to improve through the age of 14.9 years.

Causes of vision loss at China's largest blind school during a period of significant economic growth: 2008-2016.
Huang L, Silva ON, Wu Y, Zeng Y, Chen T, Yan Y, Chen X, Yu Y, Shi W, Ye W, Song L.
J AAPOS. 2020 Jun;24(3):153.e1-153.e5.

This was a cross-sectional study performed at the Quanzhou Blind School (QBS), China's largest blind school in 2008 (June to August) and in 2016 (September to October) to determine the different causes of vision loss and the different school-based treatment regimens at QBS. In 2008, there were 144 students and in 2016, 125 students who were analyzed. In 2008, the cohort average age was 15.2 years, SD 4.3 years and 86 (59.7%) were male. In 2016, the cohort average age was 14.5 years, SD 4.4 years and 84 (67.2%) were male. Results included a decrease in visual impairment reported at QBS: 105 (72.9%) of 144 students in 2008 compared to 60 (48%) of 125 students in 2016. However, results also indicated at QBS an increase in the number of blind students: 39 (27.1%) of 144 students in 2008 compared to 65 (52%) of 125 students in 2016. The main cause of visual impairment in 2008 was corneal scarring versus in 2016 was ROP (P =0.020). Of note, the authors describe that the percentage of students with corneal scarring decreased from 2008 to 2016 whereas the percentage of students with ROP increased from 2008 to 2016. The main cause of blindness in both 2008 and 2016 was congenital cataracts. The authors also noted with the increase in the number of blind students over the 8 year period from 2008 to 2016, there was a statistically significant increase in students using visual aides: 63.2% use in 2016 compared to 8.3% use in 2008 (P=0.0001). Limitations of this study is that it was conducted at one school for the blind as well as the type and use of visual aides in the students over this 8 year period of time. Also, it is uncertain why the time period of 2008 versus 2016 was chosen to analyze. In summary, this study reports the findings at the largest blind school in China (QBS) where ROP is the leading cause of visual impairment and congenital cataracts is the leading cause of blindness.

Reliability and validity of the PedsQL 4.0 Generic Core Scales in pediatric vision impairment.
DeCarlo DK, Forte E, Gao L, McGwin Jr G, Owsley C.
J AAPOS. 2020 Mar;24(2):94e1-6.

This was a case-cohort study in children and teenagers (8-18 years old) at one institution to assess if the health-related quality of life (HRQoL) instrument, PedsQL 4.0, could distinguish between visually impaired (20/40 to 20/800) versus non-visually impaired/normally sighted participants. The authors had two age groups for the completion of the PedsQL 4.0: ages 8-12 years old and ages 13-18 years old. Results included 70 study participants and 44 controls with similar age, gender, racial background. The PedsQL 4.0 total score in children with visual impairment differed significantly from normally sighted children for both age groups as well as the child/teen and parent questionnaires. Of note, HRQoL results showed a significant association with visual acuity, across all domains. The authors also reported a difference between parent and child questionnaires and poor correlation. Limitations of the study include the fact that only 1 parent per child/teen was included in the study and the bias that parents involved in a low

vision study may be more concerned with the HRQoL aspects of their child's vision. Another limitation is the age groupings of the two groups. In summary, the authors were successful in showing that PedsQL 4.0 can be used to assess HRQoL in children and teenagers with low vision and it has internal reliability and validity.

Investigating the efficacy of *Reading Adventure Time!* for improving reading skills in children with visual impairments.
Kamei-Hannan C, McCarthy T, D'Andrea FM, Holbrook MC.
J Vis Imp Blin 2020 Apr;114(2):88-100.

This article looks at the efficacy of *Reading Adventure Time!* (a pilot version of the *iBraille Challenge Mobile App*), an educational technology tool that supports braille reading and writing instrumentation for students in 1st – 12th grades. Designed for use on an Apple iPad with a refreshable braille display, the app uses gaming strategies to encourage students to improve literacy skills including fluency, comprehension, writing dictation and proofreading. Students' reading speed, comprehension, and miscues were measured by the app. The study also assessed the level of technology skills of teachers and caregivers before and after the study was completed. A total of 52 students completed the study. Teachers and students worked together using the app twice weekly for a minimum of 40 minutes per session for 16 weeks. Students completing the study demonstrated gains in reading and technology skills. Teachers also gained fluency in using technology designed for visual impairment (VoiceOver, braille display). The authors conclude the *reading Adventure Time!* app can be used as a supplemental intervention to address reading skills in children with visual impairments.

Comparisons of spatiotemporal and ground reaction force components of gait between individuals with congenital vision loss and sighted individuals.
Majlesi M, Farahpour N, Robertson G.
J Vis Imp Blin 2020 Aug;144(4):277-288.

The absence of visual cues about the physical pathway and obstacles in people who are visually impaired result in abnormal kinematic patterns due to fear of falling accidents. The kinetic aspects of the atypical waking pattern are not well understood. The goal of this study was to compare the spatiotemporal and ground reaction force variables of sighted individuals to those with vision loss. Ten adult males with congenital vision loss (experimental group) and 10 fully sighted adult males (control group) were selected. Between group differences on age, height and mass were not statistically significant. A Vicon motion analysis system with cameras and Kistler force plates was used to quantify spatiotemporal and ground reaction force components of both groups during walking without shoes. The study demonstrated vision loss is associated with decreased step and stride length, slower walking, and smaller propulsive reaction force. The authors conclude the decreased step and stride length, slower walking, and smaller propulsive reaction force may be an adaptation to a new neuromuscular response for dynamic postural control due to lack of vision, and a rehabilitation program to enhance mobility and strength is suggested for individuals with vision loss.

Visual Impairment in Retinitis Pigmentosa.
Vezinaw CM, Fishman GA, McAnany JJ.
Retina 2020 Aug;40(8):1630-1633.

The authors of this paper sought to evaluate the genetic subtypes by age range of patients with retinitis pigmentosa who have vision of 20/200 or worse in the better seeing eye. All patients were examined by one physician. The charts of 1095 RP patients were reviewed and 215 were included in the study (excluding systemic diseases and unconfirmed genotypes). The authors found that 0.46% patients had no light perception in each eye and 80.4% had vision better than 20/200. In the cohort of patients who had vision of 20/200 or worse in one eye had no significant differences in the mode of inheritance. They

ultimately found that 80% of the patients had better vision than 20/200 and thus not legally blind. This is helpful in counselling patients with a diagnosis of RP.

How Does Vertical Reading Affect Reading Speed?
Porter K, Arblaster G.
British and Irish Orthoptic Journal. Apr 2020;16(1):38-43

Vertical reading is an adaptive reading strategy sometimes used in homonymous hemianopia. This study aimed to measure horizontal and vertical reading speeds in visually normal volunteers using the Radner Reading Chart. Fifteen orthoptic students, mean age 19.7 years, took part in this repeated measures study. Participants read sentences aloud from the Radner Reading Chart horizontally and rotated vertically, to read up and down the line.
the Radner Reading Chart is a sentence based reading chart that has been developed as an alternative to reading charts composed of individual words presented in a random order. Text was rotated so the words were vertically up or down for the testing. Words read correctly and the time taken to read each sentence were recorded. Reading speeds were calculated (words read correctly per second) for horizontal text (2.95 words per second) and for vertical text, reading up the line (1.73 words per second) and reading down the line (1.57 words per second). Reading horizontal text was significantly faster than reading vertical text. Reading horizontal text was 1.22 words per second faster than reading text vertically up ($p < 0.0001$) and 1.38 words per second faster than text vertically down ($p < 0.0001$). There was no statistically significant difference between reading text vertically up the line and vertically down the line (0.16 words per second, $p = 0.42$). Horizontal reading speed, measured with the Radner Reading Chart, was significantly faster than both vertical reading speeds. There was no significant difference between reading vertically up the line and reading vertically down the line. The slower time taken to read the vertically orientated sentences had a greater effect on reading speed than the number of errors made. This study also attempted to validated the Radner Reading chart as a modality to measure horizontal and vertical reading speed. The use of vertical reading may be important in patients who have hemianopias but would need to be further studied.

An Age- and Stage-Appropriate Patient-Reported Outcome Measure of Vision-Related Quality of Life of Children and Young People with Visual Impairment
Valerija Tadi, Alexandra O. Robertson, Mario Cortina-Borja, Jugnoo S. Rahi for the Child Vision Patient-Reported Outcome Measures Group
Ophthalmology. 2020 Feb;127(2):249-260.

Patient-reported outcome measures are an increasingly prominent tool to determine the quality of medical interventions. Most quality of life measures are not specific for vision problems and/or younger patients. This study used multiple methods and phases to extend, refine, and validate a prior vision-related qualify of life survey. The first phase involved interviews to refine the original questionnaire. The second phase tested the questionnaire on a small group to refine legibility and improve comprehension. The third phase tested the revised instrument on a small group of children, followed by phase 4, testing the survey questions on a larger group of visually impaired subjects. The strength of the study is the rigorous and detailed psychometric refinements applied to the various stages of the questionnaire. Major weaknesses include the low response rate, less than 50% of those mailed the survey, and the small numbers of subjects in each phase of the study. Overall, the final survey instrument does appear to add a useful tool to quantify quality of life in children and young adults.

An Age- and Stage-Appropriate Patient-Reported Outcome Measure of Vision-Related Quality of Life of Children and Young People with Visual Impairment
Valerija Tadi, Alexandra O. Robertson, Mario Cortina-Borja, Jugnoo S. Rahi for the Child Vision Patient-Reported Outcome Measures Group
Ophthalmology. 2020 Feb;127:249-60.

Patient-reported outcome measures are an increasingly prominent tool to determine the quality of medical interventions. Most quality of life measures are not specific for vision problems and/or younger patients. This study used multiple methods and phases to extend, refine, and validate a prior vision-related qualify of life survey. The first phase involved interviews to refine the original questionnaire. The second phase tested the questionnaire on a small group to refine legibility and improve comprehension. The third phase tested the revised instrument on a small group of children, followed by phase 4, testing the survey questions on a larger group of visually impaired subjects. The strength of the study is the rigorous and detailed psychometric refinements applied to the various stages of the questionnaire. Major weaknesses include the low response rate, less than 50% of those mailed the survey, and the small numbers of subjects in each phase of the study. Overall, the final survey instrument does appear to add a useful tool to quantify quality of life in children and young adults.

5. NEURO-OPHTHALMOLOGY

Assessment of Pediatric Optic Neuritis Visual Acuity Outcomes at 6 Months.
Writing Committee for the Pediatric Eye Disease Investigator Group (PEDIG), Pineles SL, Repka MX, Liu GT, Waldman AT, Borchert MS, Khanna S, Heidary G, Graves JS, Shah VS, Kupersmith MJ, Kraker RT, Wallace DK, Cotter SA, Holmes JM. Assessment of Pediatric Optic Neuritis Visual Acuity Outcomes at 6 Months.
JAMA Ophthalmol. 2020 Oct 15;138(12):1253–61.

This is a non-randomized prospective cohort study of children with a first episode of optic neuritis (ON) and evaluation of visual acuity (VA) after 6 months. Study objectives were also to evaluate if enrollment was possible in the PEDIG network's ON prospective study, which had a target of 100 pediatric patients with ON to evaluate neuroimaging, antibodies for NMO and MOG. Findings included a total of 44 children, ages 3 to 15 years old, (mean age of 10.2 years) presented with their first episode of ON within 2 weeks of symptom onset. Of the 44 participants enrolled, 26 (59%) boys and 23 (52%) White. Sixteen (36%) participants had bilateral ON disease and neuroimaging revealed white matter lesions in 23 (52%) enrolled participants. Of the 23 participants with abnormal neuroimaging, 8 (18%) participants had MOG-associated demyelination, 7 (16%) participants had acute disseminated encephalomyelitis, 5 (11%) participants had multiple sclerosis, and 3 (7%) had neuromyelitis optica. Baseline mean high contrast visual acuity (HCVA) was 20/200 (0.95 logMAR), which improved by a mean 0.76 logMAR to 20/25 (0.12 logMAR) at 6 months. Baseline mean low contrast visual acuity was 20/640 (1.49 logMAR) and improved by a mean 0.72 logMAR to 20/100 (0.73 logMAR) at 6 months. The authors noted that the baseline HCVA was worse in younger participants, under age 10 years old, with associated neurologic autoimmune diagnoses, white matter lesions, and non-White and non-Hispanic ethnicity. Results from this cohort pediatric ON study indicate that although the authors didn't reach its target enrollment of 100 pediatric patients with ON over 2 years old, further treatment trials may need to plan a longer enrollment period due to the rarity of the disease. Furthermore, results indicate that despite poor visual acuity at presentation, for both high contrast and low contrast, most participants had a significant improvement in VA by 6 months. Limitations of the study, in addition to its small sample size and that only a few children with ON were enrolled for over 2 years. Moreover, since ON treatment and timing was at the discretion of the treating physician, the authors noted that nearly all enrolled participants were treated with corticosteroids. Although the authors cannot address the treatment impact of corticosteroids in this study, it will be helpful for further studies to include analysis of treatment versus no treatment regarding childhood ON. In summary, findings from this small cohort study is helpful foundation which shows most children with ON who present with poor VA will have an improvement in VA at 6-month follow-up. In turn, this study is useful tool for counseling parents and families of children with ON and visual impact from presentation to 6 months.

Early Onset and Severe Progression of Neuro-ophthalmological Manifestations in a Case with Parry-Romberg Syndrome
Imen Zone Abid, Sihem Ben Nsir, Emna Jarrar, Jamel Feki, Fatma Kamoun, Chahnez Triki
J Pediatr Neurol 18: 246-250 2020

Parry Romberg syndrome is a rare and sporadic disorder characterized by unilateral facial atrophy affecting the skin, subcutaneous tissue, muscle cartilage and bone. Periocular, ocular, and neuro-ophthalmological manifestations are described in less than one-third of cases. This case report describes numerous neuro-ophthalmological manifestations on the left side including enophthalmos, pseudoptosis, asymmetry of the eyebrows, diffuse chorioretinal atrophy, reduced visual acuity and amblyopia, reduced central retinal thickness with interruption of the ellipsoid zone, alteration of the outer nuclear layer, with

abnormal ERG findings (reduced photopic and scotopic amplitudes). This case report is relevant in that it adds to the ophthalmologic repertoire of findings in this rare syndrome.

Neurofibromatosis Type 1-Associated Optic Pathway Glioma in Children: A Follow-Up of 10 Years or More.
Michael Kinori, Sharon Armarnik, Robert Listernick, Joel Charrow and Janice Lasky Zeid.
American Journal of Ophthalmology, 2021 Jan; 221: 91-96.

This retrospective observational case series of 45 children with neurofibromatosis type 1 (NF1) associated optic pathway gliomas (OPGs) with follow up of 10 years or longer was performed at one academic institution. The goal of the study was to better understand the long term follow up in patients with NF1- associated OPGs. The authors reviewed charts of patients over a 22 year period and included only those with at least 10 years of follow up or longer (mean 14 years). They found that a third of patients had moderate to severe visual impairment in one eye and 11% in both eyes. Optic nerve appearance and visual acuity at presentation were the factors that could predict longer term outcomes and that virtually all patients who were asymptomatic at presentation did very well. This paper is unique in that it has very long follow up period. The data in this paper further supports deferring neuroimaging in patients with NF1 who have normal acuity and exam findings. This paper is relevant to the pediatric ophthalmologist because it contributes to a growing but compelling body of literature reminding us that not all patients with NF1 need neuroimaging, and this point is made stronger by this paper due to it's very long follow up period.

Visual field outcomes in children treated for neurofibromatosis type 1-associated optic pathway gliomas: a multicenter retrospective study.
Heidary G, Fisher MJ, Liu GT, Ferner RE, Gutmann DH, Listernick RH, Kapur K, Loguidice M, Ardern-Holmes SL, Avery RA, Hammond C, Hoffman RO, Hummel TR, Kuo A, Reginald A, Ullrich NJ.
J AAPOS. 2020 Nov 20:S1091-8531(20)30228-7. doi: 10.1016/j.jaapos.2020.07.013. Epub ahead of print. PMID: 33221469.

Optic pathway gliomas associated with neurofibromatosis type 1 (NP1-OPGs) can have a negative effect on both visual acuity and visual field. Practical difficulties of performing formal visual field testing in young children limits outcome data of visual field function after treatment with chemotherapy. The authors performed a retrospective, international, multicenter study of visual field outcomes in patients treated with chemotherapy for NF1-OPGs. Of the children who underwent testing at the initiation and completion of treatment, 44% had a stable visual field, 19% showed improvement and 38% had worsening of visual field. Change in visual field did not always correlate with visual acuity. Involvement of optic tracts and radiations was associated with increased and more profound visual field defect. The study demonstrates the need to spend extra time trying to assess formal visual fields in young children since visual acuity may not correlate with visual field defects. These defects may be important for accommodations for education and activities of daily living such as sports, ambulation and driving for older children. Additional studies would be helpful to determine if visual field defect should be an independent outcome metric for treatment planning.

Enhanced Depth Imaging Optical Coherence Tomography of Optic Nerve Head Drusen in Children.
Sim PY, Soomro H, Karampelas M, Barampouti F.
J Neuroophthalmol. 2020 Dec;40(4):498-503.

Recent work by the Optic Disc Drusen Consortium provided a consensus protocol for identification of optic disc drusen in adults using enhanced depth imaging OCT. Determining whether EDI OCT may be a useful modality in children has not been performed to date and the purpose of this study was to examine the value and feasibility of EDI OCT in a cohort of pediatric patients ≤ 16 years old. Specifically the authors compared conventional OCT non EDI, fundus autofluorescence, and EDI OCT in a group of 15 patients with optic nerve drusen confirmed by B scan ultrasonography. Between standard OCT and EDI

OCT, the authors did not find a significant difference and EDI OCT revealed optic disc drusen in 86%. The failure to detect optic disc drusen in all patients was attributed to the inability of EDI OCT to identify buried drusen as effectively as in B scan ultrasonography. However EDI OCT was superior to fundus autofluorescence (64%) in detecting optic disc drusen. This study is important as it establishes that EDI OCT is feasible in children in spite of a potentially longer image acquisition time, and that it allows for quantification of size and structure of optic disc drusen.

Real-World Clinical Experience With Idebenone in the Treatment of Leber Hereditary Optic Neuropathy
Catarino CB, von Livonius B, Priglinger C, Banik R, Matloob S, Tamhankar MA, Castillo L, Friedburg C, Halfpenny CA, Lincoln JA, Traber GL, Acaroglu G, Black G, Doncel C,Fraser CL, Jakubaszko J, Landau K, Langenegger SJ, Muñoz-Negrete FJ, Newman NJ, Poulton J, Scoppettuolo E, Subramanian P, Toosy AT, Vidal M, Vincent AL, Votruba M, Zarowski M, Zermansky A, Lob F, Rudolph G, Mikazans O, Silva M, Llòria X, Metz G, Klopstock T.
J Neuroophthalmol. 2020 Dec;40(4):558-565.

Idebenone has been shown in clinical trials to be an effective medication in the treatment of Leber Hereditary Optic Neuropathy. In this study, the authors collate the experience of use of the medication beyond the clinical trial in an effort to examine the “real-world clinical experience” with the medication. The cohort consisted of 111 genetically confirmed LHON patients treated within 1 year of diagnosis with idebenone at 900 mg/day who participated in the expanded access program established through the European manufacturer of idebenone Santhera. Primary analyses included evaluation of clinical recovery or clinical stabilization of the final included cohort of 87 patients. The authors also cumulated adverse events of which the most common was diarrhea. Clinically relevant stabilization occurred for 50% of the cohort and clinically relevant recovery occurred for 46% of the cohort with a higher proportion of the cohort with the T14484C doing better as expected based on the genetic mutation. The duration of treatment of 18-24 months was recommended. This study importantly extends the outcomes from the placebo controlled LHON trial and provides further data on the value of idebenone treatment within 1 year of diagnosis.

Optic Nerve Topography in Multiple Sclerosis Diagnosis: The Utility of Visual Evoked Potentials.
Vidal-Jordana A, Rovira A, Arrambide G, Otero-Romero S, Río J, Comabella M, Nos C, Castilló J, Galan I, Cabello S, Moncho D, Rahnama K, Thonon V, Rodríguez-Acevedo B, Zabalza A, Midaglia L, Auger C, Sastre-Garriga J, Montalban X, Tintoré M.
Neurology. 2021 Jan 26;96(4):e482-e490. Epub 2020 Dec 16.

In this retrospective study comprised a subset of the Barcelona Clinically Isolated Syndrome (n=388) (CIS) cohort, the authors examined whether the diagnosis of multiple sclerosis could be improved by incorporating optic nerve involvement as part of the criteria. Specifically, the authors explored whether optic nerve involvement as dissemination in space would be valuable towards improving sensitivity and specificity of the McDonald 2017 criteria for MS. To define optic nerve involvement VEP was used. The primary analyses were to determine risk of second attack and analysis of the diagnostic performance with the modified criteria of optic nerve involvement. The addition of optic nerve involvement as a unique region in the diagnostic criteria improved risk assessment and diagnostic performance. This study is important because enhancing the ability to accurately predict multiple sclerosis is valuable for counseling patients about risk. Some patients may present with CIS involving the optic nerve and therefore, incorporation of optic nerve involvement as part of the McDonald criteria for MS may expand the ability to give insight as to risk of MS in this setting.

Longitudinal Changes in the Retinal Microstructures of Eyes With Chiasmal Compression
Lee G, Son KY, Park K-A, Kong D-S, Oh SY.
Neurology. 2021 Jan;96(1):e131-e140. Epub 2020 Oct 22.

In this case-control study, the authors retrospectively reviewed the longitudinal impact of chiasmal compression on the visual pathways through evaluation of retina structure using OCT. OCT measurements prior to surgery for chiasmal decompression and 1 year following surgery were compared with a focus on RNFL, GCL, and IPL. Inclusion criteria was age > 20 years, chiasmal lesion undergoing trans sphenoidal decompression with 87 patients and 100 controls. Preoperative RNFL and IPL thicknesses were predictive of visual field recovery post operatively. In spite of treatment, retinal thickness continued to decline in patients with chiasmal compression. This study provided insight into use of RNFL and IPL thickness preoperatively to help counsel patients about the potential for visual field recovery after a compressive optic neuropathy from a chiasmal lesion is identified.

Cranial Nerve Disorders Associated With Immune Checkpoint Inhibitors
Vogrig A, Muñiz-Castrillo S, Joubert B, Picard G, Rogemond V, Skowron F, Egri M, Desestret V, Tilikete C, Psimaras D, Ducray F, Honnorat J.
Neurology. 2021 Feb 9;96(6):e866-e875. Epub 2020 Dec 14.

Immune checkpoint inhibitors (ICIs) are a new class of medication for the treatment of cancers such as malignant melanoma. This study evaluated the frequency and type of cranial neuropathy occurring as an adverse event secondary to treatment. The authors retrospectively evaluated 67 cases of ICI-associated cranial neuropathy. The median time to adverse symptom development was 3 months. Isolated cranial nerve palsies included involvement of the optic nerve, abducens nerve, and oculomotor nerve in additional to the facial nerve. Immunosuppressive treatment including IVIG, plasma exchange or corticosteroid was successful in facilitating a partial or complete improvement in cranial neuropathy. Among the cases, 2 had a persistent optic neuropathy in spite of treatment. This paper raises awareness of potential side effects from these novel medications and the modes of treatment when adverse events occur.

Opthalmic Technology Assessment: Imaging Methods for Differentiating Pediatric Papilledema from Pseudopapilledema
Melinda Y. Chang, Gil Binenbaum, Gena Heidary, David G. Morrison, Jennifer A. Galvin, Rupal H. Trivedi, Stacy L. Pineles
Ophthalmology; 2020 Oct;127(10):1416-23

This study reviewed the evidence supporting the use of OCT, fundus photography, multicolor confocal scanning laser ophthalmoscopy, ultrasound, fluorescein angiography to distinguish between papilledema and pseudo-papilledema in children. Despite an extensive literature search, only six articles with a level III significant (case series/reports or case-control studies) were found. The studies reported a broad range of positive and negative predictive values, but none actually measured the intracranial pressure directly in all patients diagnosed as pseudo-papilledema, instead relying on a stable clinical exam over time for most patients. Fluorescien angiography with disk leakage appeared the most reliable, while the various OCT studies relied upon multiple arbitrary measures to distinguish true papilledema. The authors' conclusion appears justified that more rigorous study is required to determine the best imaging technique to distinguish pseudo-papilledema from true papilledema.

Neuroanatomy and Imaging Assessment in Traumatic Brain Injury
Strominger, M.
Journ J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):119-121.

Concussion is a common injury in childhood with an estimated 1.4 million children sustaining concussions annually in the United States. While many concussions occur in the sports and recreation setting, it is important to recognize that non-sports and recreation activities are also common causes of concussion in childhood. Since neurologic projections associated with the afferent and efferent visual system are widely distributed throughout the brain and thought to comprise over 50% of brain function, it is not surprising

that the diffuse shear injury associated with concussion often produces visual dysfunction. However, the redundancy within the system prevents easy demonstration clinically except perhaps with vergence. Thus, different testing strategies need to be developed to isolate more subtle findings. Also given that standard magnetic resonance imaging is normal, the use of functional imaging gives the best chance of demonstrating pathway changes and isolating vulnerable populations that might have long-term effects. The author notes that this information can lead to the development of ways to prevent concussion or limit certain activities at high risk of concussion within these groups.

Introduction to Traumatic Brain Injury in Children
Bacal, D.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):116-118.

Over the last decade, the reported rates of traumatic brain injury (TBI) have increased dramatically in all age groups, but particularly in children. However, these reports likely underestimate the scope of the problem for several reasons. There is no uniformly accepted definition of mild TBI (concussion). There are often no outward and obvious physical signs of TBI. Interpersonal and psychological issues, which may be significant, may be misdiagnosed or misinterpreted. And there is no uniformly accepted neuroimaging protocol as well as a lack of universal recommendations for management and treatment. The author notes that there is a need need to have concrete data on symptom resolution rates for all of the various parts of the visual system that can be affected. Delineating the best ways to follow recovery will allow a better protocol for reintegration, with recommendations for step-wise return to normal activities. Post-concussive syndrome (PCS) needs to be recognized and the individuals who suffer from PCS may require a very different protocol toward recovery.

Traumatic Brain Injury in Children: Do the Eyes Have It? The Orthoptic Evaluation of Traumatic Brain Injury
Arnoldi, K.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):122-127.

Because the neuropathological changes caused by mild traumatic brain injury (mTBI) more often manifest as functional impairments than structural abnormalities, the clinical diagnosis of mTBI may rely too heavily on a combination of history and self-reported symptoms. The mechanism of injury in mild traumatic brain injury (mTBI) predicts that supranuclear pathways controlling eye movement systems would be vulnerable to damage, and diagnostic tests of these systems would be high-yield. In fact, tests of oculomotor function have proven to be highly sensitive in detecting neurological soft signs, but may require expensive, specialized equipment. Fortunately, Certified Orthoptists (COs) are skilled at the evaluation of accommodative dysfunction, abnormalities of saccades, smooth pursuit, and vestibular eye movements, and vergence errors using standard ophthalmic equipment. Because COs are accustomed to adapting the sensorimotor exam to infants and pre-verbal children, they are able to modify or design objective methods, the results of which may be difficult for the patient with a functional overlay to decipher and deceive. When the patient with a history of mTBI presents to the ophthalmologist with visual symptoms and a normal routine eye exam, it is important to order a sensorimotor examination by a CO to confirm the diagnosis. The mechanism of injury in mTBI predicts that supranuclear pathways controlling eye movement systems would be vulnerable to damage, and evaluation of these systems would provide the highest-yield diagnostic tests when routine CT and MRI are negative. However, the clinician must keep in mind that the eye movement dysfunctions described here are not specific to mTBI. Neurodegenerative diseases and frontal lobe brain disorders lead to similar visuomotor dysfunctions. Therefore, though not discussed here, a thorough medical history is essential in interpreting the test results. There is no single test of ocular motor function that can be used alone to reliably confirm mTBI or monitor recovery from mTBI. Tests of multiple monocular and binocular visuomotor functions are still required. Clinicians should test for accommodative dysfunction, abnormalities of saccades, smooth pursuit, and vestibular eye movements, and vergence errors. Fortunately, for the most part, these may be qualitatively evaluated using standard ophthalmic equipment, to yield objective results that may be difficult for the patient to

decipher and deceive, and with a minimum amount of extra exam time. If an abnormality is found on more than one test, and the patient has a history of head trauma, the likelihood of mTBI is high.

Traumatic Brain Injury in Children: Sport-related Concussions in Children
Hiasat JG, Nischal KK.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):128-133.

Concussion is a worldwide health concern among children and adolescents. Over the decades concussion has been gradually better recognized as an entity that accounts for a significant disability post head trauma in patients. Patients present with cognitive, somatic and oculo-vestibular symptoms that can be incapacitating. Most concussion symptoms are transient and resolve within 1–2 weeks but can persist for years. Concussion pathophysiology is complex and may not be fully understood but it involves numerous mechanisms including cellular metabolic derangements, cerebral blood inflow, and axonal disruption. With no associated objective biomarkers or visible pathologic brain changes, diagnosis of concussion can be challenging. Many organizations and collaborative groups have suggested numerous definitions and diagnostic criteria for concussion in an attempt to improve the evidence-based clinical assessments and therapies for concussion. Proper assessment and evaluation is crucial starting from counseling of the patient, gradual return to cognitive and physical activity in an individualized treatment plan to ensure a timely return to daily activities and full sport participation. This report provides a grasp over the current state of sport-related concussion knowledge, diagnosis, and clinical evaluation in children and adolescent, with a focus on the ocular symptoms and signs.

Traumatic Brain Injury in Children: The Psychological Effects of Mild Traumatic Brain Injury
Whitecross, S.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):134-139.

Concussion, or mild traumatic brain injury (mTBI), results from a force to the head and can cause acute physical, cognitive, and psychological symptoms. The majority of concussion symptoms will resolve within a month, but upward of a third of patients will have persistent, chronic symptoms. When these symptoms become chronic and persist beyond 1–3 months, this is termed post-concussion syndrome (PCS). Psychological changes associated with PCS may in part be due to a traumatic event and the injury itself and therefore post-traumatic stress reactions may contribute. In addition, alterations to daily life and alteration of lifestyle as a result of the injury can cause feelings of disconnection which in turn can feed anxiety and depression symptoms. A preinjury diagnosis or history of psychiatric or mood disorder, migraine, or family history of psychiatric illness is one the greatest risk factors for the development of PCS. It is recommended that evaluation of concussion and those with PCS take a multidisciplinary approach including evaluation by psychology, psychiatry, and/or neuropsychology. While most concussions do not require treatment, those with PCS will not likely see the resolution of their physical and psychological symptoms without intervention. Treatment is limited, but cognitive behavioral treatment has shown promise in the management of PCS symptoms. It is important to recognize the role psychology plays in the development and persistence of PCS and to recognize and seek collaborative care when treating these patients. Post-concussion syndrome occurs when concussion symptoms persist beyond the acute stage following a head injury and is a complex myriad of symptoms including somatic, cognitive, and emotional reactions. Those with preexisting psychiatric or mood disorders or a family history are at the highest risk of developing post-concussion syndrome following a concussion. Both physical and psychological symptoms associated with PCS can be exacerbated by post-traumatic stress reactions, anxiety, and depression, and it is unlikely for symptoms to resolve without intervention. It is important that families and children understand the potential role of psychological factors with PCS and associated symptoms as it may be assumed that the symptoms experienced are purely a result of brain damage from the injury itself. [4] Collaborative care or a multidisciplinary approach to treatment and management is imperative for a successful recovery from PCS. It is important to continue to develop an awareness of concussion and brain injury and educate society to further refine approaches to assessment and academic function and accommodation. This will further help gain a better understanding of the potential long-term effects of untreated, unmanaged mild traumatic brain injuries.

Management and Treatment Modalities in Traumatic Brain Injury
Jenkins PT.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):140-146.

Traumatic Brain Injury (TBI) is a very broad diagnosis. Some TBI patients have minimal complaints for a short period of time. Other TBI patients suffer from drastic life-altering, permanent brain damage. One particularly troubling class of TBI patients arises from people who experience one or more concussions in their youth. Later, as adults, the TBI manifests as multiple learning difficulties or even personality changes. As ophthalmic professionals, we are often the first to see potential TBI patients as they complain of visual disturbances. It is of utmost importance to find ways to help these people, but first we have to find the deficits. Brain impairment can be devastating at any age, but symptoms and disabilities may be life-long and far-reaching in children with TBI, or any patient with a history of more than one traumatic event. An important key to recovery is to have active-rest following the traumatic event. Eye complaints and various treatment modalities for several, often dissimilar, disorders are often the only tangible therapy a patient can do to improve themselves following the traumatic brain injury. The orthoptic evaluation leads us to areas where we can give positive reinforcement. Fresnel prisms and Gunnar filters can be tremendously therapeutic for those with diplopia, oscillopsia, VF defects, or photophobia associated with brain injuries. Convergence therapy, building of fusional amplitudes and accommodative management are also used in the treatment for pediatric and adult TBIs. ERGs, Hyperbarics, LASER/LED phototherapy and nutrition were also discussed in this paper. Orthoptists are and should be included to help in so many different capacities as a team member. Certainly, inter-disciplinary and collaborative work will continue to be the best answer for these folks who have had head trauma. This paper discusses some therapeutic measures given to TBI patients and the examinations that will provide vital information.

Schwannoma Masquerading as Recurrent Painful Ophthalmoplegic Neuropathy: A Diagnostic Dilemma
Shaza N Al-Holou, Crystal DeLuca, Regina E Gatteau, Richard H Legge
J Pediatr Ophthalmol Strabismus. 2020 Aug 19;57:e68-e70

Recurrent painful ophthalmoplegic neuropathy “ophthalmoplegic migraine” is characterized by cranial nerve paresis following a headache. During episodes neuroimaging may show enhancement of the cranial nerve, though the absence of a structural lesion is required for diagnosis. In this report of two cases, both patients presented similarly with recurrent oculomotor nerve paresis. In case one, MRI revealed enhancement initially thought to be consistent with schwannoma. Similarly, in the second case, the initial MRI revealed a mass consistent with schwannoma. Both of these studies were performed during the ophthalmoplegic episode. Follow up imaging performed between episodes found no evidence of schwannoma in the first case, while it re-demonstrated the oculomotor nerve mass consistent with schwannoma in the second. The authors recommend MRI to better characterize the presence or absence of a schwannoma between episodes, when it is feasible.

The risk of a serious etiology in pediatric Horner syndrome: indications for a workup and which investigations to perform.
Graef S, Chiu HH, Wan MJ.
J AAPOS. 2020 Jun;24(3):143.e1-143.e6.

Horner syndrome in children can present as an isolated benign entity or can be a harbinger of serious pathology. The goal of this retrospective study was to assess the incidence of serious etiology in pediatric Horner syndrome in a group of 48 patients diagnosed between age 1 month and 17 years. In their cohort, a serious etiology was discovered in 15% of patients including neuroblastoma, nasopharyngeal carcinoma, and desmoid tumor. All of the neuroblastoma patients presented with an isolated Horner syndrome and the tumor was only discovered in the workup of the Horner syndrome. In children without a known cause of Horner syndrome, such as birth trauma, the authors recommend urine catecholamines

and imaging of the sympathetic chain to rule out serious etiologies, with an estimate risk (based on this study and their review of prior studies) being around 13%, or 1 in every 8 cases.

Differences of megalopapilla and normal sized disk with age-an optical coherence tomography analysis.
Gama R, Relha C, Gaspar S, Esteves C, Nascimento F.
J AAPOS. 2020 Feb;24(1):14.e1-14.e4.

Megalopapilla is a congenitally anomalous enlarged optic disk with surface area >2.50 mm^2. The purpose of the study was to compare the optic discs of children and adults with megalopapilla to controls using optical coherence tomography (OCT). This was a case–control study conducted at a single hospital in Lisbon, Portugal. A total of 168 eyes of 168 subjects were included: 78 with megalopapilla (39 children/39 adults) and 90 (45 children/45 adults) controls with normal sized discs. For the same optic nerve head area, children had a higher rim area, a smaller cup:disc ratio, and a smaller cup volume compared to adults (all three comparisons had $P<0.001$). For both children and adults, megalopapilla had a larger cup:disc ratio and a larger cup volume than a normal sized disc. These findings suggest that enlargement of the cup of the optic disc and reduction of the rim area can occur through life.

Visual snow syndrome: A clinical and phenotypical description of 1,100 cases
Puledda F, Schankin C, Goadsby PJ
Neurology 2020 Feb; 94:e564-e574.

In this retrospective study of a large cohort of patients with visual snow, the authors review clinical diagnostic criteria and describe the clinical phenotype of this poorly understood phenomenon. Among the patients with visual snow, age of onset was in early life with characteristic “black and white” static in vision. Risk factors for more severe visual symptoms included concurrent tinnitus and migraine. There was no predilection for gender in terms of who was affected but data analysis suggested that female patients were more likely than male patients to have more visual symptoms beyond static and may have therefore a more severe presentation.

Retinal defect in children with infantile spasms of varying etiologies
An observational study
McFarlane MT, Wright T, McCoy B, Snead OC, Westall CA
Neurology. 2020 Feb;94(6):e575-e582.

Vigabatrin is an important medication used for the treatment of infantile spasms but this medication has been associated with the development of retinal abnormalities, ERG abnormalities and peripheral vision loss. In this study, the authors evaluated a cohort of 312 patients with infantile spasms who had never been treated with vigabatrin in an effort to define the prevalence of retinal defects that may be unrelated to vigabatrin. Primary outcome measure was a reduction in the 30 Hz flicker amplitude on ERG. Of the cohort, 18.9% demonstrated an ERG abnormality. The group which most commonly had retinal changes were those patients with a history of a perinatal ischemic event including periventricular leukomalacia from intraventricular hemorrhage in prematurity or hypoxic ischemic encephalopathy. In this group, 24.4% of patients had abnormal ERG. This study is important because it emphasizes the need to do baseline ERG testing prior to initiation of vigabatrin in an effort to more carefully distinguish vigabatrin induced toxicity from baseline retinal dysfunction distinct from exposure to vigabatrin.

Visual field deficits following laser ablation of the hippocampus
Donos C, Rollo P, Tombridge K, Johnson JA, and Tandon N
Neurology. 2020 Mar;94:e1303-e1313.

In this article, the authors evaluate several techniques for the treatment of refractory epilepsy with a primary outcome measure of induced visual field defects. The study included 57 patients with mesial

temporal lobe epilepsy who required laser ablation for treatment. Specifically, the authors examined the impact of laser interstitial thermal therapy (LITT) and its application to the amygdala/hippocampal complex. Patients were tested post treatment using HVF 30-2. In this cohort 37.5% of patients developed visual field deficits which were more commonly associated with treatment of the left hemisphere compared with the right. This study provides support for the minimally invasive technique of LITT and also highlights anatomic differences between the two hemispheres allowing for more effective counseling prior to treatment.

Repetitive ocular vestibular evoked myogenic potentials in myasthenia gravis
Robert H.P. de Meel, Kevin R. Keene, Magdalena A. Wirth, Konrad P. Weber, Umesh A. Badrising, Jan J. Verschuuren, Martijn R. Tannemaat
Neurology. 2020 Apr;94(16):e1693-e1701.

The current techniques for the diagnosis of myasthenia gravis are sometimes limited insofar as antibody testing is often negative and single fiber EMG is both cumbersome and can be unrevealing. In this study, the authors evaluate the effectiveness of a new diagnostic test RoVEMP to diagnose myasthenia gravis. This test utilizes ocular vestibular evoked myogenic potentials. The unique feature of this test is that it allows direct testing of the neuromuscular junction in extraocular muscles which are predominantly affected thereby enhancing the ability to positively diagnose disease. The response of the test was compared among patients with known MG, other neuromuscular disease, healthy controls, congenital MG, and Lambert Eaton. In 6/7 patients with seronegative MG, the RoVEMP was positive. Further, the authors found the sensitivity to be 80% for ocular MG and 67% for systemic MG.

Steroid-sparing maintenance immunotherapy for MOG-IgG associated disorder.
Chen JJ, Flanagan EP, Bhatti MT, Jitprapaikulsan J, Dubey D, Lopez Chiriboga ASS, Fryer JP, Weinshenker BG, McKeon A, Tillema JM, Lennon VA, Lucchinetti CF, Kunchok A, McClelland CM, Lee MS, Bennett JL, Pelak VS, Van Stavern G, Adesina OO, Eggenberger ER, Acierno MD, Wingerchuk DM, Lam BL, Moss H, Beres S, Gilbert AL, Shah V, Armstrong G, Heidary G, Cestari DM, Stiebel-Kalish H, Pittock SJ.
Neurology. 2020 Jul;14;95(2):e111-e120.

Myelin oligodendrocyte glycoprotein-immunoglobulin G (MOG-IgG) associated disorder is a CNS demyelinating disease distinct from multiple sclerosis and aquaporin-4-IgG neuromyelitis optica spectrum disorder. Its clinical features include optic neuritis, transverse myelitis and, in children, acute demyelinating encephalomyelitis. This multicenter, retrospective study evaluated long-term immunotherapy for MOG-IgG associated disorder and the relapse rate on a variety of treatments. 70 patients age 3-61 were included in the study with one third of the cohort aged < 18 years. The authors calculated the annualized relapse rate for patients on treatments including mycophenolate mofetil, rituximab, azathioprine, and IVIG. Among these patients, those who were on chronic IVIG showed the lowest rate of relapse suggesting that this steroid-sparing approach should be considered for long term maintenance in patients with MOG-IgG associated disease.

Progression Over 5 Years of Prelaminar Hyperreflective Lines to Optic Disc Drusen in the Copenhagen Child Cohort 2000 Eye Study.
Malmqvist L, Li XQ, Hansen MH, Thomsen AK, Skovgaard AM, Olsen EM, Larsen M, Munch IC, Hamann S.
J Neuroophthalmol. 2020 Sep;40(3):315-321.

The authors continue to provide information on children ages 11-12 who were enrolled in a prospective study evaluating the natural history of optic nerve head drusen. This paper describes the 5 year outcomes in this cohort. In the original cohort of 724 children, 11 children presented with drusen and subsequently in the 5 years, 5 more children developed drusen for a total of 16 children. Importantly the authors found a difference in scleral canal size between children with drusen 1364 microns versus

controls 1457 microns (P<0.001). The authors try to better define the relevance of prelaminar hyperreflective lines which were present on the OCT of all children with optic disc drusen and in 24 additional children without optic disc drusen at 5 year follow up. The continued monitoring of these children will be important to determine whether those with hyperreflective lines go on to develop optic disc drusen and the paper defines a new risk factor for drusen development as a narror scleral canal opening.

Population-based Incidence of Pediatric and Adult Optic Neuritis and the Risk of Multiple Sclerosis
Ju-Yeun Lee MD, Jinu Han MD, Mi Yang MS, Sei Yeul Oh MD
Ophthalmology. 2020 March; 127(3):417-425.

This study took place in South Korea where health claims of all patients with optic neuritis or retrobulbar optic neuritis were reviewed from 2010 to 2016. Both inpatient and outpatient data were a part of the health claims. Fourteen years of age was used as the cutoff to define pediatric versus adult patients (15-65 years old). 531 pediatric patients were diagnosed with optic neuritis with mean age of 9.8±3.2 years. 49.3% were male and 50.7% female. Of these patients, 5.8% were diagnosed with multiple sclerosis, 1.1% with NMO and 1.1% with ADEM with the rest (91%) being idiopathic. The annual incidence was 1.04 per 100,000 people in both sexes with peak incidence occurring at 10-14 years of age. Adults had an incidence which was 3.2 times higher than in the pediatric population. In the age group 0-4 years, the incidence was higher in males but for all other age groups, the incidence was similar or higher in females. Conversion to MS in the pediatric patients was 13.8%. Limitations of this study include possible misdiagnoses/miscoding of optic neuritis in the claims data as well as potential misdiagnoses of underlying conditions such as NMO or MS. Also, the results of this study are specific to the Korean population which may explain why incidence of optic neuritis in adults is lower than what has been reported in other western countries though incidence for pediatric patients in Korea was similar to that reported in western countries.

Reproducibility of macular retinal nerve fiber layer and ganglion cell layer thickness measurements in a healthy pediatric population.
Jiménez Santos M, Acebal Montero A, Sáenz-Francés San Baldomero F, Valverde-Megias A, Gómez de Liaño R.
Eur J Ophthalmol. 2020 Aug 1:1120672120947614. doi: 10.1177/1120672120947614. Epub ahead of print. PMID: 32744092.

The use of SD-OCT has been increasingly used in the pediatric population. As this technology has improved, the use of analyzing the retinal ganglion cells (RGCs) and their axons that constitute the RNFL. These have become invaluable in the adult population, but normative data has not been studied in the pediatric population. The goal of this study is to evaluate the reproducibility of the Spectralis SD-OCT segmented GCL and macular RNFL (mRNFL) measurements in healthy pediatric population. This is an observational, prospective, cross-sectional study. The authors included healthy full term children after the BCVA, stereopsis, refraction, color vision, alignment, slit lamp and indirect fund examination was done. Children with family history of retina or optic nerve disease, previous trauma, congenital malformations, pre term, amblyopia, high refractive errors were excluded. All children had scans by a novel and experienced operator with the Heidelberg explorer Software to include multiple measurements including RNFL, GCL, etc. The interobserver and intraobserver reproducibility were defined by the intraclass correlation coefficient (ICC) and coefficients of variation (COV). The results of the intraoperator GCL thickness were highly reproducible and reliable. When compared to a novel and experiences examiner, lower ICC and higher COV were found. The authors were not able to demonstrate that age plays a role in the reproducibility or repeatability.

Prenatal or Perinatal Injury? Diagnosing the Cortically Blind Infant.
Ho ML, Mansukhani SA and Brodsky MC.
Am J Ophthalmol. 2020 Mar; 211:56-62.

This retrospective case series of eight children over 2 years was performed with the purpose of describing the association of prenatal brain disruption with perinatal distress in children with cortical visual impairment (CVI). The authors point out that CVI is the leading cause of blindness in developed countries and while often thought to be due to hypoxic ischemic injury (HIE), that there are increasingly more complex pathophysiologic explanations to this condition. The 8 children who were studied were diagnosed with CVI based on a history of perinatal distress, poor visual responsiveness, normal eye structure, and coexisting neurologic dysfunction. The outcomes were perinatal history, visual and neurologic findings and MRI results. The authors go on to describe each of the 8 cases and then discuss that while infants with a known perinatal distress event are often labeled as HIE, there is actually more complex etiologies and many of these patients have MRI findings other than the watershed infarcts expected in HIE. The authors discuss a comparison with cerebral palsy and the overlap in proposed mechanisms for these conditions. This is an interesting read for those of us who still are confused by the giant spectrum of CVI. In the end the authors point out the utility of MRI in patients with CVI since many patients in their series had other brain findings pointing to etiologies other than direct injury to the visual cortex.

6. NYSTAGMUS

Horizontal Transposition of the Vertical Rectus Muscles to Correct a Head Tilt in 5 Patients With Idiopathic Nystagmus Syndrome
Alexander de Castro-Abeger, Nancy M. Benegas, Burt Kushner and Sean P. Donahue
American Journal of Ophthalmology, 2020 Sep;217:68-73.

This is a retrospective case series of five patients who underwent horizontal transposition of the vertical rectus muscles to correct a head tilt due to nystagmus. Two of these patients previously had a Kestenbaum procedure. The authors describe the procedure in this paper: To correct a right tilt, nasal transposition of the right superior rectus and left inferior rectus was performed. Alternatively, temporal transposition of the right inferior rectus and the left superior rectus can be performed. This will lead to excyclotorsion of the right eye and incyclotorsion of the left eye to correct a right tilt. The patients were between 5 and 8 years old. 3 of the 5 patients had near resolution of the tilt. Neither patient with previous surgery had anterior segment ischemia. This paper, while only five patients, is the largest of it's type for this type of surgery. The authors discuss different options for eye muscle surgery for head tilt in INS, which is important since these cases are often challenging. This case demonstrates another surgical tool that we have to help some of our most difficult patients with INS and AHP.

Post audio-visual biofeedback training visual functions and quality of life in paediatric idiopathic infantile nystagmus: A pilot study.
Daibert-Nido M, Pyatova Y, Markowitz M, Taheri-Shirazi M, Markowitz SN.
Eur J Ophthalmol. 2021 Jan 26:1120672121991048. doi: 10.1177/1120672121991048. Epub ahead of print. PMID: 33499653.

Patients with idiopathic infantile nystagmus syndrome (IINS) can have a decreased visual acuity, contrast sensitivity, stereopsis and other visual functions that can negatively impact the quality of life. With the use of microperimeters, audio-visual biofeedback training (BT) modules have become available. These have been used for years in patients with low vision to help improve near and distance vision. The authors hypothesize that this can optimize visual function in pediatric patients with IINS. They conducted a pilot observational study of 10 patients comparing visual functions and quality of life comparing baseline and pre BT visits to post BT data. They found an improvement in visual acuity both at distance and near, stereopsis, reading speed, and contrast sensitivity with the use of BT. No side effects occurred besides fatigue during training sessions. Quality of life scores also increased significantly post BT therapy. This shows further options for patients with IINS to improve their visual functioning, however a larger cohort study would need to be performed.

Characteristics of acute nystagmus in the pediatric emergency department.
Garone G, Suppiej A, Vanacore N, La Penna F, Parisi P, Calistri L, Palmieri A, Verrotti A, Poletto E, Rossetti A, Cordelli DM, Velardita M, d'Alonzo R, De Liso P, Gioè D, Marin M, Zagaroli L, Grosso S, Bonfatti R, Mencaroni E, Masi S, Bellelli E, Da Dalt L, Raucci U.
Pediatrics. 2020 Aug;146(2): e20200484; DOI: https://doi.org/10.1542/peds.2020-0484.

Summary: Acute nystagmus (AN) is an uncommon neurologic sign in children presenting to abstract pediatric emergency departments. The authors of this retrospective, multicenter, cohort study conducted in Italy describe the epidemiology, clinical features, and underlying causes of AN in a large cohort of children with the goal of identifying features associated with higher risk of severe underlying urgent conditions (UCs). The authors reviewed the clinical records of all patients aged 0 to 18 years presenting for AN to the pediatric emergency departments of 9 Italian hospitals over an 8-year period. Excluded were patients with: (1) abnormal eye movements other than nystagmus (such as ocular flutter, opsoclonus, and/or supranuclear gaze disturbances), (2) patients presenting to the pediatric emergency department because of head injury or (3) epileptic seizures, and (4) patients affected by an already known neurologic

condition explaining the nystagmus. Clinical and demographic features and the underlying causes were analyzed. A logistic regression model was applied to detect predictive variables associated with a higherrisk of UCs. Results: A total of 206 patients with AN were included (male-to-female ratio: 1.01; mean age: 8 years 11 months). The most frequently associated symptoms were headache (43.2%) and vertigo (42.2%). Ataxia (17.5%) and strabismus (13.1%) were the most common neurologic signs. Migraine (25.7%) and vestibular disorders (14.1%) were the most common causes of AN. Idiopathic infantile nystagmus was the most common cause in infants < 1 year of age. UCs accounted for 18.9% of all cases, mostly represented by brain tumors (8.3%). The logistic regression analysis showed that cranial nerve deficits, ataxia, or strabismus were strongly associated with an underlying UC. Presence of vertigo or attribution of a nonurgent triage code was associated with a reduced risk of UCs. The authors conclude that AN should be considered an alarming finding in children given the risk of severe UCs. Cranial nerve palsy, ataxia, and strabismus should be considered red flags during the assessment of a child with AN.

Importance: The diagnostic value of nystagmus in the emergency room setting has been unclear. This study found that migraine was the most common cause of AN in the emergency room setting. But almost 20% of children with AN had an urgent neurologic condition and this study reveals several “red flags” (see summary above) associated with higher risk that may expedite diagnosis of such an underlying condition.

Nystagmus associated with macular dysplasia.
Wang FB.
Strabismus. 2020 Mar;28(1):17-19.

This study examined macular abnormalities in patients with nystagmus using spectral-domain optical coherence tomography (SD-OCT). They included 29 eyes of 17 patients with various macular abnormalities whose diagnoses included albinism, foveal hypoplasia and macular coloboma. The anatomic findings were consistent with widely understood findings in each of the respective conditions. The authors concluded that absence of a normal foveal it on SD-OCT is associated with nystagmus and lower visual acuity.

Vertical Optokinetic Stimulation Induces Diagonal Eye Movements in Patients with Idiopathic Infantile Nystagmus
John R Economides, Young-Woo Suh, Joshua B Simmons, Daniel L Adams, Jonathan C Horton
Invest Ophthalmol Vis Sci. 2020 Jun;61, 14

This small study looked at the response patients with idiopathic infantile nystagmus without ocular misalignment to a vertical optokinetic stimulation. These patients were also compared to patients with strabismus, though without nystagmus. While the six patients with strabismus but without nystagmus presented with a normal response to the vertical optokinetic stimulation, those with idiopathic infantile nystagmus without ocular misalignment presented with a diagonal nystagmus. This response was recorded and noted not to be the sum of the horizontal and the presumed vertical trajectories, rather the slow phase was altered. This presents a very interesting opening to further research as the pattern of the nystagmus can be broken with presentation of a stimulus and can possibly be localized in the brain with treatment to that area to decrease the nystagmus.

Two-Dimensional Analysis of Horizontal and Vertical Pursuit in Infantile Nystagmus Reveals Quantitative Deficits in Accuracy and Precision
Lee Mcilreavy, Tom C A Freeman, Jonathan T Erichsen
Invest Ophthalmol Vis Sci. 2020 Jun;61:15.

This small study of twelve adult volunteers with idiopathic infantile nystagmus sought to measure the precision and accuracy of horizontal and vertical pursuits. The authors noted that there was a decrease in accuracy and precision in both horizontal and vertical pursuits for faster moving targets and targets that

moved further from the point of fixation. This shows the importance in understanding all limitations, not just visual acuity, in patients with idiopathic infantile nystagmus and other ocular diseases that cause a decrease in visual function. Limitations included lack of a control group and a small sample size. Also, as visual acuity was not stratified, these patients may have performed better if they had a larger fixation target.

Can Structural Grading of Foveal Hypoplasia Predict Future Vision in Infantile Nystagmus? A Longitudinal Study
Sohaib R. Rufai, Mervyn G. Thomas, Ravi Purohit, Catey Bunce, Helena Lee, Frank A. Proudlock, Irene Gottlob
Ophthalmology. 2020 Apr(4);127:492-500.

This study compared the usefulness of handheld OCT of the fovea versus preferential looking as predictors of future vision in preverbal children with infantile nystagmus. Foveal hypoplasia was graded using previously validated criteria that stratified the structural abnormalities into six levels. Only subjects for whom successful OCT images were obtained who could also provide a logMAR visual acuity were included. OCT typically required about 10 minutes per child and successful images were obtained in ~90% of subjects in at least one eye, while preferentially looking was only successful in ~70% of subjects. The structural grading was significantly better correlated than with future visual acuity (r=0.65) than preferential looking (r = 0.42). The authors also looked at quantitative measures, but found the overall structural grading had the best correlation with future visual acuity. The study both highlights the inadequacy of preferential looking in assessing future vision and emphasizes the importance of the foveal anatomy in visual function.

Comparison of Techniques for Correction of Chin-down Vertical Abnormal Head Position Associated with Infantile Nystagmus Syndrome
Law JJ, Zheng Y, Hold DG, et al.
Am J Ophthalmol. 2020 May; 213:57-61.

The authors of this retrospective interventional case series sought to evaluate the relative effectiveness of combined recession-resection of vertical muscles vs. superior rectus recession with inferior oblique weakening for patients with chin-down positions and infantile nystagmus syndrome (INS). They included 22 patients at one academic institution with a primary outcome of collapsing the head position and unfavorable outcome of repeat surgery, induced strabismus, and failure to collapse the head position. The authors found that the recession-resection procedure was more likely to result in a V pattern esotropia requiring operation, and that both surgeries had similar rates of collapsing the head position. The largest limitation of this paper is that it was retrospective and performed after the authors suspected that the standard recession-resection technique was resulting in more re-operation rates than expected, which could induce some bias. Overall this is an important paper because it helps guide the pediatric ophthalmologist when making difficult decisions about eye muscle surgery in the setting of a vertical null point.

The efficiency of biofeedback visual rehabilitation therapy in patients with infantile nystagmus syndrome: A retrospective study.
Caputo R, Febbrini Del Magro E, Amoaku WM, Bacci GM, Marziali E, Morales MU
Eur J Ophthalmol. 2020 Jul 6:1120672120940981. doi: 10.1177/1120672120940981. Epub ahead of print. PMID: 32627590.

Patients with infantile nystagmus syndrome (INS) can have reduced vision that can be mild to severe. Most patients with INS use low vision resources to enhance their vision. Microperimetry (MP) is a device that measurements retinal light sensitivity similar to a visual field analyzer. Modern MPS are equipped with software to perform biofeedback fixation training (BFT). The use of BFT has not been studied in patients with INS. The authors aim of this retrospective study is to see if the use of this technology can

obtain some visual function improvement and possibilities for larger studies. Patients (ages 6-12 years) with INS performed BFT with MP sessions overall a minimum of a 6 month period. Visual acuity and MP stabilities indices were analyzed. 12 patients completed the entire session. All patients showed improvement in some indices of fixation but no significant improvement in vision at any time point. Larger studies should be warranted to make a firmer conclusion.

Long-term Outcomes Following Surgery for Infantile Nystagmus Syndrome with Abnormal Head Positioning
Zheng Y, Law JJ, Holt DG, Morrison DG, Donahue SP.
Am J Ophthalmol. 2020 Feb;210:3-7.

This retrospective observational case series of 150 patients who had surgery for abnormal head position (AHP) associated with infantile nystagmus syndrome (INS) was performed at one academic institution. The goal of this study was to better understand the long term outcomes in these patients in terms of their head position, duction limitations, and strabismus. The authors defined success in head position as 10 degrees or less. Most (119) patients had surgery for horizontal head position, 31 for chin up/down position, and none in this series for torsional head positioning. Most patients had a 50-60% augmentation and 38 patients had a dose adjustment to account for strabismus. The authors found that at 10 years, there were no overcorrections and 7% of patients had an under correction. 9% of patients had surgery for over or under correction during that 10 year time period. There was also a 7% rate of induced strabismus after the surgery. While some patients had an initial duction limitation, at 10 years, no patients had any limitations the ductions. Overall there was a 21% reoperation rate. The authors concluded that their paper supports surgery as a long term solution for AHP in patients with INS. They pointed out the main limitations being the retrospective nature of the study as well as selection bias in the patients with return follow up may not represent entire cohort. The main take home message from this paper is that AHP can be treated long term by a Kestenbaum-Anderson procedure, though the risk of needing more eye muscle surgery for over or under correction or strabismus is about 20%.
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7. PREMATURITY.

Effect of Prematurity on Foveal Development in Early School-Age Children.
Semra Tiryaki Demir, Evrim Kiray Bas, Murat Karapapak, Mehmet Egemen Karatas, Hasan Sinan Uslu, Ali Bulbul and Dilek Guven.
American Journal of Ophthalmology, 2020 Nov;219:177-185.

This retrospective, cross-sectional quantitative and comparative cohort study of 126 eyes of 63 patients was performed to evaluate the foveal development in preterm children. The authors looks at children aged 6-8 years old who were born prematurely but did not require treatment for ROP. They lumped the children into groups based on gestational age at birth (<30 weeks, between 31-34 weeks, and compared to children born at term). The authors compared central foveal thickness (CFT), inner retinal thickness (IRT), outer retinal thickness (ORT), subfoveal choroidal thickness (CT), temporal and nasal CT, foveal avascular zone (FAZ) diameter, and vessel densities in different areas. The authors found that in the most premature children, they had a thicker CFT, IRT, ORT, vessel density was significantly greater compared to the other groups. Additionally, the temporal CT and FAZ diameter were lower than in the other groups. The authors concluded that the morphology of the fovea and the surrounding vasculature in school-age children who were born premature is different from those born at full-term. The authors did not compare visual acuities or other functional vision test and it is unknown or if this structural difference had any functional significance. The important take away from this paper is that prematurity does have some lasting effect on foveal development but that more studies are needed to determine if this has any clinical significance.

Birth Weight Is a Significant Predictor of Retinal Nerve Fiber Layer Thickness at 36 Weeks Postmenstrual Age in Preterm Infants.
Liangbo L. Shen, Shwetha Mangalesh, Brendan McGeehan, Vincent Tai, Neeru Sarin, Mays A. El-Dairi, Sharon F. Freedman, Maureen G. Maguire and Cynthia A. Toth.
American Journal of Ophthalmology, 2021 Feb; 222:41-53.

The goal of this prospective observational study of 83 infants (159 eyes) was to measure retinal nerve fiber layer thickness (RNFL) in preterm infants at 36 weeks post menstrual age. The authors imaged the patients awake with head held optical coherence tomography (OCT). The authors measured the RNFL and correlated it to sex, race, ethnicity, gestational age, birth weight, stage of ROP and presence of pre-plus or plus disease. They hypothesis was that intrauterine processes affect RNFL before any treatment for ROP, which is why the authors designed this study with the 36 week post menstrual age timeframe. The authors found that the right eye was slightly thicker than the left eye and that birth weight was the only predictor of RNFL thickness with extremely preterm infants more likely to have thinner RNFL. Not surprisingly, patients with periventricular leukomalacia had thinner RNFL The authors had solid intergrader reproducibility and this is the first study to report RNFL thickness in preterm babies such a narrow timeframe. They did not have a great explanation for the thicker RNFL in right eyes, but pointed out that other studies found the same. There were not enough patients with stage 3 ROP to make any conclusions about the relationship between RNFL thickness and ROP severity. The study had a few limitations, but the largest being that it only included infants born earlier than 32 weeks. Overall conclusion was that birthweight, rather than gestational age, was an independent predictor of RNFL thickness in premature infants. This data will be most useful to the pediatric ophthalmologist who is looking for normative data in this patient population.

Longitudinal Analysis of Refractive Errors in Premature Children during the First Three Years of Life
Hennein L, Camponanes A,
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):170-176.

This paper examines the longitudinal behavior of refractive errors in both retinopathy of prematurity (ROP) and non-ROP screened premature children during the first three years of life. This retrospective cohort included premature children (less than 37 weeks gestational age) born between 10/2011 and 8/2013 with ≥ two cycloplegic refractions. Cycloplegic refractions were converted into power vectors: *M* (spherical equivalent), J_0 [positive for with-the-rule (WTR) and negative for against-the-rule (ATR) astigmatism], and J_{45} (oblique astigmatism). Each power vector component was fitted by multilevel mixed-effects linear regression models; the mean change over time was analyzed. Mean J_0 was 0.59 (95% CI 0.53–0.66) at six months and 0.29 (95% CI 0.19–0.39) at 18 months; afterward, the change was <0.1 per year. J_0 decreased −0.32 (0.64 diopters) over three years. When analyzed in one-year increments, the mean change in J_0 and *M* was lowest at 24 months. *M* decreased 1.13 diopters over three years. WTR astigmatism and spherical equivalent decreased over the first three years of life. WTR astigmatism accounted for the majority of amblyopogenic refractive errors. The change in J_0 leveled after 18 months and the lowest rate of change was at 24 months in J_0 and *M*, thus it may be appropriate to screen this high-risk population around 18–24 months.

Morphological characteristics of early- versus late-onset macular edema in preterm infants.
Mangalesh S, Wong BM, Chen X, Tran-Viet D, Stinnett SS, Sarin N, Winter KP, Vajzovic L, Freedman SF, Toth CA.
J AAPOS. 2020 Oct;24(5):303-306.

This is a retrospective review of 185 premature premature infants comparing macular images of infants with early-onset edema (occurring at or before 33 weeks' postmenstrual age [PMA]) and infants with late onset edema (at or after 36 weeks' PMA). At first appearance, early-onset edema has a more severe morphology, with foveal bulging and elongated cystoid spaces than late-onset edema, which presents as small cystoid spaces outside the foveal center. Morphological variations may be an indicator of the underlying cause of edema in preterm infants. The presence of mostly parafoveal small cystoid spaces in the late-onset edema group may be suggestive of an association with neurological injury.

Macular thickness in children aged 3-6 years born preterm
Kiziloglu OY, Coskun Y, Guven NE, and Toygar O.
JAAPOS. 2020 Feb; 24:12.e1-5

This is a prospective case-control study looking at children 36 to 72 months of age born under 34 weeks and age-matched control children born at term. Macular thickness measurements were measured with spectral domain OCT. 45 preterm children and 44 controls were included in the study. Central macular thickness (CMT) was significantly higher (*P*=0.010) and perifoveal thickness was significantly lower (*P*=0.029) in the preterm compared with the control group. Moderate negative correlations of CMT with gestational age and birth weight were found in the preterm group. There was no significant difference in macular thickness found between subjects who had retinopathy of prematurity and those who did not. the results of this study are limited by the small number of overall cases and the single center, hospital-based design. Also, only full-thickness measurements of the macula were obtained, and retinal layer segmentation was not performed. This study suggests the preterm group have thicker retinas at the central macula and thinner perifoveal retinas.

Increased Foveal Ganglion Cell and Inner Plexiform Layer Thickness in Children Aged 6.5 Years Born ExtremelyPreterm
Rosen R, Hellgren K, Vekataraman A, Vicent A, Nilsson M
Retina. 2020 Jul; 40:1344–1352.

The aim of the study was to analyze the ganglion cell layer and inner plexiform layer (GCL+) thickness in children born extremely preterm and control children. The study included 6.5-year-old children born before the gestational age of 27 weeks and age-matched controls. The GCL+ thickness and foveal depth (FD) were analyzed in a single optical coherence tomography B-scan. Association with neonatal risk

factors and sex was investigated. Extremely preterm was divided into no, mild, and severe retinopathy of prematurity, retinopathy of prematurity treatment, and no, mild, and severe intraventricular hemorrhage. Adequate measurements were obtained from 89 children born extremely preterm and 92 controls. Extremely preterm children had increased total (5 mm, P , 0.001) and central (21 mm, P , 0.001) GCL+ thickness and reduced FD (253 mm, P , 0.001) compared with controls. Extremely preterm children receiving retinopathy of prematurity treatment had increased GCL+ thickness and reduced FD compared with other subgroups. Sex and gestational age were associated with increased central GCL+ thickness and reduced FD. Reduced total GCL+ thickness was associated with severe intraventricular hemorrhage. Extremely preterm birth can cause incomplete extrusion of the GCL+ and reduced FD. Retinopathy of prematurity treatment, gestational age, and male sex were associated to increased central GCL+ thickness and reduced FD, while severe intraventricular hemorrhage was associated with reduced total GCL+ thickness.

8. RETINOPATHY OF PREMATURITY

ROP Screening Tool Assessment and Validation in a Third-Level Hospital in Argentina: A Pilot Study.
Esposito E, Knoll E, Guantay C, Gonzalez-Castellanos A, Miranda A, Barros Centeno MF, Gomez Flores M, Urrets-Zavalia JA.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):55-61.

ROPScore12 is a free mathematical tool consisting of a logistic regression equation to calculate the risk of severe ROP. This risk calculator was evaluated retrospectively on 411 preterm infants born with a BW of 1,500 g or less and/or a GA of 32 weeks or younger seen over a six year period at a NICU in Argentina. ROPScore considers the following clinical paramaters: BW, GA, weight gain proportional to BW measured at 6 weeks of life (patient's weight measured at 6 weeks of life minus BW, divided by BW), the presence or absence of blood transfusion until 6 weeks of life, and the need for mechanical ventilation. The cut off values of 11 for any ROP and 14.5 for severe ROP as suggested by previous research were initially used in this study. These criteria applied to this patient population missed 28% of severe ROP. Therefore, new cut off criteria, 9.15 for any ROP and 12.05 for severe ROP were evaluated. These criteria performed well, with a PPV of 35% and NPV of 100% for any ROP. These cut off values did not miss any severe ROP and would have reduced screening examinations by 38%. This report demonstrates that risk calculators, and the cut off scores used with them, should be introduced with caution. When adapted to and validated in a specific NICU they could be useful tools, reducing unnecessary examinations without missing treatment requiring ROP.

Progression from preplus to plus disease in the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity (e-ROP) Study: incidence, timing, and predictors.
Cheng QE, Quinn GE, Daniel E, Baumritter A, Smith E, Ying GS; e-ROP Cooperative Group.
J AAPOS. 2020 Nov 16:S1091-8531(20)30293-7. doi: 10.1016/j.jaapos.2020.07.016. Epub ahead of print. PMID: 33212296.

Plus disease in retinopathy of prematurity (ROP) is characterized by vascular dilation and tortuosity of at least two quadrants of the posterior pole. The presence of plus disease is a major indicator for the need for treatment of ROP. Preplus was added in the 2005 ICROP classification to describe the condition in between normal and plus disease. It is a visual diagnosis and there can be variability between specialists. The authors sought to determine the incidence of and timing and predictors for progression from preplus to plus disease using telemedicine images. The authors identified that preplus occurs in 38% of premature infants and approximately 8% of preplus progresses to plus disease with a median time of 3 weeks. Several factors were found to be associated to predict a higher risk of progression: eyes with a higher stage and/or lower zone at time of detection as well as a larger number of quadrants with pre-plus at time of first detection of preplus. Limitations of the study are grading is subjective and possible technique issues of pressing too hard when performing the photos. Better knowledge of the transition of pre-plus to plus disease may allow for more effective management of ROP screening and better outcomes.

Long-term macular vascular density measured by OCT-A in children with retinopathy of prematurity with and without need of laser treatment.
Carreira AR, Cardoso J, Lopes D, Loureiro T, Sampaio A, Fonseca T, Vide-Escada A, Campos N.
Eur J Ophthalmol. 2020 Dec 29:1120672120983204. doi: 10.1177/1120672120983204. Epub ahead of print. PMID: 33372558.

The gold standard treatment for ROP is laser photocoagulation, however this is without risk of long tern visual complications. Recent students have used OCTA to assess retina vasculature in ROP,

demonstrating that former premature infants with ROP have a different foveal morphology and reduced retinal vascular density. The goal of the authors of this study was to evaluate the macular density and macular morphology measured by OCTA in preterm infants with and without laser treatment. In this observational study, the authors enrolled former premature children with stage 2 or 3 ROP over the last 10 years. They enrolled 34 eyes of 34 children (15 of which had no treatment and 15 which had laser treatment). The results showed that those who had laser treatment for ROP had lower best corrected visual acuity compared to those without treatment. Patients who had laser treatment on OCTA had a high mean macular thickness and lower circularity of the avascular zones. These changes in OCTA may demonstrate the lower visual acuity in patients treated with laser for their ROP. This is an important consideration when consenting families for laser treatment for advanced ROP, however the long term goal of vision preservation should be emphasized.

Favorable outcomes in the treatment of aggressive posterior retinopathy of prematurity.
Sahinoglu-Keskek N, Akkoyun I, Torer B.
Eur J Ophthalmol. 2021 Jan;31(1):179-183.

Aggressive posterior retinopathy of prematurity (AP-ROP) is a rapidly progressing form of ROP in zone 1 or posterior zone 2. The authors purpose was to report the anatomic outcomes of AP-ROP in cases initially treated with intravitreal ranibuzumab (IVR). 15 eyes of 8 patienets with ap-ROP were in this study. All patieents received a dose of IVR (0.25 mg in 0.025ml). All patients needed retreatment. All patients need laser treatment. Recurrence of the disease was noted all patients between 3-7 weeks. The authors concluded that initial treatment with anti-VEGF of AP-ROP followed by laser photocoagulation may be the gold standard.

Artificial intelligence for retinopathy of prematurity
Rebekah H. Gensure, Michael F. Chiang, and John P. Campbell
Curr Opin Ophthalmol. 2020 Sep 31:312-317

This is a review of the current state of artificial intelligence (AI) applications in the diagnosis and management of ROP. The article discusses the origins in computer-based image analysis (CIBA) which has largely evolved into the evaluation and application of convolutional neural networks (CNNs.) The CNNs use deep learning to classify as well as to learn without being explicitly told what to focus on. An ROP vascular severity score has demonstrated utility in monitoring disease progression, regression after treatment, and differentiating the pace of disease in posterior ROP. While these show promise, the authors discuss some of the challenges with this technology. Issues such as generalizability across camera systems, capturing images of sufficient quality for AI to interpret, and variability of ROP in different populations are concerns. Clinical integration may prove challenging with expense due to regulatory approval, as well as how to integrate it alongside clinicians. Finally, the authors discuss future directions for AI in ROP. AI may be able to be used in diagnosis of stage, vascular severity as well as increasing sensitivity of detecting severe ROP and reducing the chance of a missed diagnosis with an added layer of objectivity. This may be important as there is often disagreement among clinicians on treatment requiring ROP and could provide evidence-based guidelines for treatment. It may also be able to detect ahead of time patients who will not likely need treatment which may lead to fewer screening exams. In conclusion, this review gives insight into the potential utility in the future of screening and treatment recommendations for ROP, but there are limitations at this point in the reproducibility, uniformity and implementation of the technology in a clinical setting.

Fluorescein angiographic features post-intravitreal bevacizumab for retinopathy of prematurity: can they support rescue laser photocoagulation to the avascular retina
Gonzalez A, Agarwal-Sinha S.
Can J Ophthalmol. 2020 Oct;55(5):373-381.

Anti-VEGF medications have changed the course of ROP treatment, but there is still a risk of early and late recurrence of disease in treated infants. The retinal vascular changes and fluorescein angiography (FA) findings after anti-VEGF treatment are varied and there is not much evidence to guide clinicians on outcomes based on these changes. Therefore, the authors of this study wanted to evaluate retinal vascular changes after intravitreal bevacizumab (IVB) by FA and identify retinal features that may pose a risk of late reactivation of ROP. They performed a retrospective review of 26 infants (47 eyes) with type 1 ROP that were treated with IBV. All of the infants had RetCam photos and FA performed at an average of 68 weeks postmenstrual age (PMA). 19 infants later had images at average 98 weeks PMA, and 10 infants even later at average 120 weeks PMA. 8 eyes of 6 infants had recurrence of stage 3 disease at mean of 11.7 weeks after initial IVB. These infants all had repeat IVB injections. All eyes showed chronic vascular arrest in Zone 2, and after repeat IVB 7/8 showed persistent vascular arrest in zone 2. 25/26 showed FA findings that have been described previously, including peripheral avascularity, shunts, branches, and tangles. One eye of one infant was treated with repeat IVB at 63 weeks and later showed diffuse hyperfluorescence along the regressed proliferation site at 68 weeks PMA. This patient later presented with early stage 4 at 92 weeks PMA and was treated with laser. Overall, 98% of post-IVB eyes showed no late complications, with only 1 requiring barrier laser after reactivation. The authors conclude that peripheral avascular retinal ablation with laser after IVB is not mandatory.

Comparison of OCT angiography in children with a history of intravitreal injection of ranibizumab versus laser photocoagulation for retinopathy of prematurity.
Zhao J, Wu Z, Lam W, Yang M, et al.
Br J Ophthalmol. 2020 Nov; 104:1556-1560.

OCT angiography (OCTA) is a newer technique that can visualize the retinal vasculature without the need for dye injection. This study aimed to investigate the foveal microvascular structure and visual function in children treated with intravitreal ranibizumab (IVR) and laser photocoagulation (LP) for retinopathy of prematurity. This cross-sectional study included 37 children age 4 to10 with a history of IVR or LP monotherapy for ROP, all of which were initially diagnosed with zone II treatment-requiring disease. 17 (38 eyes) were treated with 0.25mg IVR and 20 (37 eyes) with LP. Spectral-domain OCTA was performed in all eyes. Eyes with IVR had a statistically significantly lower central foveal vessel length density and perfusion density compared to those with LP. There was no significant difference in the parafoveal area. Central foveal thickness was thinner in the IVR group, and the foveal avascular zone was higher in the IVR group. There was no significant difference in spherical equivalent refraction between the two groups, although the best-corrective visual acuity was worse in the IVR group. The authors explained that the lower vessel length density and perfusion density in the central fovea can be attributed to decreased VEGF. Laser photocoagulation can lead to prevention of peripheral migration and reorganization of infer retinal cells, leading to the smaller foveal avascular zone and thicker central foveal thickness seen in patients treated with LP. These findings reveal the changes in the retina that might be expected with these two treatments, and demonstrate that OCTA is a useful non-invasive modality for examining these children.

ANATOMICAL AND VISUAL OUTCOMES IN STAGE 5 RETINOPATHY OF PREMATURITY WITH MICROINCISION VITRECTOMY SURGERY
Sen P, Bhende P, Rishi E, Gopal L, Jain S.
Retina. 2021 Feb 1;41(2):331-337. doi: 10.1097/IAE.0000000000002837. PMID: 32349102.

The goal of the study was to report anatomical and visual outcomes and potential prognostic factors with microincision vitrectomy surgery in Stage 5 retinopathy of prematurity. The medical records of premature babies who underwent microincision vitrectomy surgery for Stage 5 retinopathy of prematurity using 23G, 25G, or 27G instrumentation and had a minimum follow-up of 6 weeks were, retrospectively, analyzed. Primary outcome measures were anatomical success at last follow-up defined as retinal attachment at the posterior pole and visual outcomes. Potential risk factors and complications influencing anatomical outcomes were also analyzed. One hundred seventy eyes of 115 infants underwent lensectomy and vitrectomy with microincision vitrectomy surgery. After a mean follow-up of 30.59 ± 33.24 weeks,

anatomical success was achieved in 56 eyes (33.7%) of 166 eyes that had a minimum follow-up of 6 weeks. Occurrence of vitreous hemorrhage was more with 23 gauge (62.27%) as compared to 25 gauge (37.73%) (P = 0.024). With increase in age with each week, the probability of achieving anatomical success was found to be significantly more (odds ratio 1.030; confidence interval = 1.010–1.060; P = 0.008). Presence of anterior segment pathology was associated with poor anatomical outcomes (odds ratio 2.480; confidence interval = 1.190–5.160; P = 0.010). Seventeen children with attached retina had a follow-up of 14 months–5 years, of which ambulatory vision was recorded in five eyes and the ability to identify objects close to face in 12 eyes. Although surgery for Stage 5 retinopathy of prematurity is challenging, anatomical success can be seen in one-third of cases with microincision vitrectomy surgery. Visual prognosis may be limited but still beneficial.

ULTRA-WIDE-FIELD IMAGING AND INTRAVENOUS FUNDUS FLUORESCEIN ANGIOGRAPHY IN INFANTS WITH RETINOPATHY OF PREMATURITY.
Mao J, Shao Y, Lao J, Yu X, Chen Y, Zhang C, Li H, Shen L.
Retina. 2020 Dec;40(12):2357-2365.

The study looked to determine the feasibility of ultra–wide-field imaging and ultra–wide-field intravenous fundus fluorescein angiography (UWF-IV-FFA) in infants with retinopathy of prematurity (ROP) using Optos 200Tx. The authors performed Optos 200Tx capturing on 32 premature infants (14 females) and UWF-IV-FFA with Optos 200Tx on 12 of the 32 infants between April 2017 and July 2018 at the affiliated eye hospital of Wenzhou Medical University and analyzed their fundus images. Ultra–wide-field color images were acquired from 32 infants (64 eyes). UWF-IVFFA was performed successfully in 12 premature infants (24 eyes). No adverse events were observed. The ultra–wide-field Optos 200Tx color images and UWF-IV-FFA images revealed Stages 1, 2, and 3 ROP and aggressive posterior ROP. Ultra–wide-field imaging and intravenous fundus fluorescein angiography using Optos 200Tx are feasible in infants with ROP, which have the potential to screen, diagnose, and follow-up for ROP. Technology to help with ROP mangement is described in this study.

ANATOMICAL AND FUNCTIONAL RESULTS OF INTRAVITREAL AFLIBERCEPT MONOTHERAPY FOR TYPE 1 RETINOPATHY OF PREMATURITY: One-Year Outcomes.
Chen YT, Liu L, Lai CC, Chen KJ, Hwang YS, Wu WC.
Retina. 2020 Dec;40(12):2366-2372.

The goal of the study was to evaluate the anatomical and functional outcomes of Type 1 retinopathy of prematurity 1 year after the intravitreal injection of aflibercept (IVA). This prospective cohort study enrolled Type 1 retinopathy of prematurity patients who had been treated with IVA as first-line therapy from July 1, 2015, to June 30, 2017. Patients were followed up for at least 1 year after injection. The primary outcomes were retinopathy of prematurity regression, progression, reactivation, and the occurrence of associated complications after the use of IVA. The secondary outcomes were visual acuity and refractive error at 1 year after IVA. Seventeen eyes of nine patients were enrolled in our study. A single IVA injection resulted in resolution in 15 eyes (88.2%), whereas 2 eyes (11.8%) needed retreatment. The mean Snellen visual acuity and refractive error were 6/13 ± 0.34 and 21.94 ± 2.97 D, respectively. No major ocular complications or systemic adverse effects were noted during the follow-up period, except one patient (11%) passed away at the age of 14 months due to a pulmonary infection. Aflibercept is effective and well tolerated for the treatment of Type 1 retinopathy of prematurity; it is a potential treatment option as it achieves good anatomical, visual, and refractive outcomes.

Slow progressive perifoveal vascular formation in an infant with aggressive posterior retinopathy of prematurity.
Chen X, Imperio R, Seely KR, Viehland C, Izatt JA, Prakalapakorn SG, Freedman SF, Toth CA.
J AAPOS. 2020 Oct;24(5):323-326.

A case report of the use of investigational bedside noninvasive optical coherence tomography angiography to visualize the slow and progressive perifoveal vascular formation in an infant with AP-ROP treated with bevacizumab. Aggressive posterior retinopathy of prematurity (AP-ROP) is a severe form of ROP occurring in preterm infants that is characterized by rapid progression and prominent vascularity. Extensive vascular shunts and morphological differences between arrested and growing retinal capillaries at the vascular wavefront was documented.

The early gut microbiome could protect against severe retinopathy of prematurity.
Skondra D, Rodriguez SH, Sharma A, Gilbert J, Andrews B, Claud EC.
J AAPOS. 2020 Jul 21. In press.

There is growing interest in the relationship between the gut microbiome and ocular disease, though little is known about the connection between this and retinopathy of prematurity. This is a study comparing 6 infants with type 1 retinopathy of prematurity to 4 premature infants without retinopathy of prematurity. The study found that there was a divergence in microbiome composition between groups (analyzed from collected stool samples). Pathway abundance analysis showed multiple enriched metabolism pathways in those without retinopathy of prematurity. This is a small preliminary study, but the authors conclude that certain metabolic pathways could be protective in premature infants and future studies are needed to better understand the connection between the gut microbiome and ocular disease in the developing neonate.

Retinopathy of Prematurity: Evolving Treatment With Anti–Vascular Endothelial Growth Factor
M. Elizabeth Hartnett
American Journal of Ophthalmology, 2020 Oct; 218: 208-213.

This perspective article involves a critical review and synthesis of the literature particular regarding anti-VEGF treatment for retinopathy of prematurity. The author is a leading expert in the field. Although this paper does not bring any new data to the field, it is a nice overview of the major studies using anti-VEGF therapies for ROP and discusses the differences in ROP across the world.

Current management of retinopathy of prematurity in sub-Saharan Africa.
Lloyd T, Isenberg S, Lambert SR.
J AAPOS. 2020 Jun;24(3):151.e1-151.e6.

Retinopathy of prematurity clinical presentations and treatment paradigms vary geographically based on availability of resources, patient demographics, and provider preferences. The goal of this paper was to report the results of a survey of ophthalmologists and neonatologists in sub-Saharan Africa around the current management trends for retinopathy of prematurity. This survey was completed by 28 of 97 neonatologists and 34 of 76 ophthalmologists (29% and 45% response rates, respectively). 90% of ophthalmologists surveyed personally screened for ROP and 30% had regional or national guidelines for screening. Nearly all screened based on gestational age and birth weight, which ranged from <32 to <37 weeks and <1500 g to <2500 g. Regarding treatment, 74% reported using intravitreal injections and 37% used laser photocoagulation. On average, ophthalmologists reported 2 infants per center who had lost vision due to retinopathy or prematurity the previous year. The results of this survey shed light on current retinopathy of prematurity practice patterns in sub-Saharan Africa and also can be used to illuminate the resource deficits which may drive certain practice patterns or contribute to poor outcomes.

The association between high levels of luteinizing hormone and proliferative retinopathy of prematurity in female preterm infants.
Movsas TZ, Gewolb IH, Paneth N, Lu Q, Muthusamy A.
J AAPOS. 2020 Jun;24(3):145.e1-145.e5.

Luteinizing hormone (LH), a reproductive hormone, has proangiogenic properties. Given that retinopathy of prematurity is essentially a disorder of dysregulated angiogenesis, the aim of this study was to assess the association between high levels of LH and proliferative retinopathy of prematurity in preterm infants (stages 3-5). This was a cross-sectional study of 45 preterm infants (18 with retinopathy of prematurity and 27 without) assessing hormone levels taken from dried blood spots. The authors found that female infants with ROP had higher LH levels at weeks 1 and 4 of life. They did not find any differences in LH levels in male infants with or without ROP. This is the first study to show a correlation between high levels of LH and proliferative retinopathy of prematurity in female infants and further studies are needed to better understand this relationship.

Evaluation of artificial intelligence-based telemedicine screening for retinopathy of prematurity.
Greenwald MF, Danford ID, Shahrawat M, Ostmo S, Brown J, Kalpathy-Cramer J, Bradshaw K, Schelonka R, Cohen HS, Chan RP, Chiang MF.
J AAPOS. 2020 Jun;24(3):160-162.

This is a retrospective evaluation of the ROP vascular severity score in an operational ROP screening program at one institution for the detection of type 2 or worse ROP. The authors report the first artificial intelligence (AI) for ROP screening and represents proof of concept. Of the 110 eligible infants admitted to the NICU from September 2015 to July 2018, there were 81 infants placed in deep learning analysis with 613 eye encounter images. From the 81 infants, there were 2 infants with ROP in telemedicine screening and 79 infants without ROP in telemedicine screening. The mean number of telemedicine examinations for each infant was 3.8, SD 2.3 (range 1-10). The mean PMA at birth for the 81 infants was 29.2 weeks, SD 2.1 weeks with mean BW of 1240g, SD 235g. Limitations of the study include small sample size based upon the selected NICU hospital as not necessarily representative of ROP in other regions/communities. In summary, these results show a proof of concept that AI may have a role in the screening of patients at risk for ROP. The authors suggest that with further validation, this AI technology may improve the accuracy, objectivity, efficiency of the diagnosis of ROP in our patients at risk for ROP progression.

Late visual outcomes in infants treated with primary bevacizumab for type 1 retinopathy of prematurity.
Rodriguez SH, Schechet SA, Shapiro MJ, Blair MP.
J AAPOS. 2020 Jun;24(3):149.e1-149.e5.

This was a retrospective review of the visual acuity in children at one institution who received 0.5mg (0.02cc) intravitreal bevacizumab (IVB) treatment for posterior type 1 ROP (zone 1 and posterior zone 2) between January 2011 and January 2014 during infancy at the NICU institution. Participants were only included if there was a follow-up exam after 4 years old. Results included 23 infants (46 eyes) with completion of visual acuity (VA) testing. Median age was 6 years. Median VA was logMAR 0.18. Normal VA was recorded in 39 (85%) of 46 eyes (VA of 20/40 or better). Of the 46 eyes, 42 eyes (in 21 patients) had an exam under anesthesia with FA and all 42 eyes showed peripheral capillary abnormalities (abnormal branching, shunts, tangles) with 90% with peripheral nonperfusion and 64% leakage. Limitations of the study include the retrospective study of a short time period regarding the progression of potential amblyopia in the children over age 4 years. Another limitation is the small number of eyes at a single institution. In summary, the authors report VA of 20/40 or better in 85% of the IVB treated infants with type 1 ROP; however, periperal vascular abnormalities were noted on FA and this is helpful to monitor potential visual function changes during the amblyopic age range of children with a IVB history of ROP treatment.

Myopia and anterior segment optical coherence tomography findings in laser-treated retinopathy of prematurity eyes.
Lenis TL, Gunzenhauser RC, Fung SS, Dhindsa YK, Sarraf D, Pineles SL, Tsui I.
J AAPOS. 2020 Mar;24(2):86e1-7.

The authors evaluated the visual outcomes and structural features in eyes with a prior history of laser treatment for retinopathy of prematurity (ROP) with the recruitment at one insitution of three groups of children: (1) control group born after 37 weeks' gestational age (GA); (2) preterm group born before 33 weeks GA but without ROP or with type 2 ROP that spontaneously resolved; (3) preterm treated group born before 33 weeks GA and treated with laser ablation. Of note, both preterm groups included extremely preterm (before 28 weeks GA) and very preterm (28-32 weeks GA) infants. Testing included the use of anterior segment optical coherence tomography (OCT) to evaluate structural features and in particular, the anterior chamber angle (ACA). Median age of patients was 9.05 years for full term controls, 9.20 years for ROP laser-treated, and 6.40 years for preterm monitored controls. Analysis included 50 eyes of 50 patients (19 full term eyes, 12 preterm monitored eyes, 19 laser-treated type 1 ROP eyes). Of the 50 eyes, 44 (88%) eyes had visual outcomes and 15 (30%) eyes had anterior segment data. There was no significant difference in age or gender at the final exam of the 3 groups. Compared with full term control group and preterm group without ROP, the laser-treated ROP group had measured narrower ACA and statistically significant more myopic refractive error (-0.88 D as compared to +0.50 D and 0.00 D, respectively with P=0.0186). Limitations of this study is the small cohort of 50 eyes of 50 patients analysis and lack of outcome measurements such as axial length, corneal curvature, lens thickness, anterior chamber depth. Another limitation is that the ACA was not evaluated in all 50 eyes when performing the anterior segment OCT. In summary, laser treatment may affect the ACA in ROP treated infants and anterior segment OCT is a valuable tool to include in evaluating the anterior segment development and refractive error of our patients with ROP.

ROPtool analysis of plus and pre-plus disease in narrow-field images: a multi-image quadrant-level approach.
Weinert MC, Wallace DK, Freedman SF, Riggins JW, Gallaher KJ, Prakalapakorn SG.
J AAPOS. 2020 Mar;24(2):89e1-7.

The authors analyzed images previously collected from a large prospective study where non-physician health care workers used narrow field imaging (Pictor) to obtain retinal images of infants being screened for ROP at one institution. Of note, previously, imagers had selected 1-3 images per eye at each imaging session for telemedicine image grading. So, for this study, one imaging session per eye per infant was chosen by the authors using a pre-defined selection algorithm that was used in a previous study to create an enhanced sample of images with disease. One of the authors, a masked non-ophthalmologist, performed all ROPtool analyses. Specifically, ROPtool was used to see if this semiautomated computer program could objectively measure retinal vascular characteristics such as pre-plus and plus disease in narrow-field images which combined quadrant-level data from multiple images of a single retina. Quadrant analysis with ROPtool included tortuosity index (TI), maximum tortuosity (Tmax), dilation index (DI), maximum dilation (Dmax), sum of adjusted indices (SAI), tortuosity-weighted plus (TWP). Analysis included 769 of 792 (98%) quadrants of 198 eyes from 99 infants imaged. The majority of eyes (98%) had 3-4 quadrants analyzed. The authors used 'area under the curve' (AUC) measurements to evaluate the ability of ROPtool indices of tortuosity, dilation, and a combination to identify pre-plus and plus disease in the images as compared to the clinical exam findings of a reference standard. All tortuosity or combination measures had an AUC of greater than 0.96 for identifying plus disease and greater than 0.94 for identifying pre-plus or plus disease. Limitations of the study is that it is a cross-sectional study using a subjective criteria of the clinical diagnosis of pre-plus or plus disease for ROP. Another limitation is the analysis of one image for each eye per infant. In summary, this ROPtool technology nees further validation in a longitudinal study of images to help assess which ROP infants will progress to needing treatment. However, this small study of the quadrant-level ROPtool analysis is valuable step to identify pre-plus and plus disease with high accuracy with this semiautomated computer program.

Refractive outcome of intravitreal bevacizumab injection in comparison to spontaneous regression of retinopathy of prematurity (ROP).
Etezad Razavi M, Shoeibi N, Hassanzadeh S, Kianmehr S, Bakhtiari E.
Strabismus. 2020 Mar;28(1):49-54.

ROP is a significant cause of visual impairment in children in developing countries. Even when appropriately treated, it can result in refractive error. The authors sought to compare the refractive outcomes in children with ROP who were treated with intravitreal bevacizumab (IVB) compared to children with spontaneous regression. In this prospective study, they enrolled 87 infants (174 eyes) and categorized the infants into group 1 who received IVB (38 infants, 76 eyes) and group 2 who did not require treatment (49 infants, 98 eyes). As expected the groups differed significantly by ROP zone and stage as well as gestational age and birth weight, but did not differ by gender. At one year of age, the spherical equivalent did not significantly differ, and neither gestational age nor birthweight affected the spherical equivalent. The authors recognize the limitations of the lack of long term follow up possibly affecting their results, especially as other studies have found refractive errors at 2.5 years old are a better predictor of refractive status. They also indicated that larger sample sizes at each of the ROP zones and stages would be helpful in determining with greater accuracy whether differences exist. Studies of longer duration and a greater number of infants would be helpful for determining the relationship between IVB and refractive error.

Conserved regression patterns of retinopathy of prematurity after intravitreal ranibizumab: a class effect.
Ji, M. H., Moshfeghi, D.M., Shields, R.A., Bodnar, Z., Ludwig, C.A., Callaway, N.F., Orazi, L., Amorelli, G. M., & Lepore, D.
Eur J Ophthalmol. 2020, E publication ahead of print. July 28.

Anti-VEGF therapies for ROP have been known to have late reactivation when compared to laser therapy. Patients who receive this therapy need longer and extended follow-ups after treatment. Recently, intravitreal bevacizumab (IVB) was demonstrated to adhere to a regression pattern related to the amount of non-perfused retina. The authors hypothesize that this is similar for all anti-VEGF agents, and a similar pattern should be noted for invitreal ranibizumab (IVR). This as an onbservational retrospective case series study of all infants with IVR for type 1 ROP between July 2016 and November 2018. FA images were analyzed and the peripheral avascular areas measured with ImageJ using a reference of a disc diameter. Based on the extent of avascular area and tortuosity, eyes were classified into 4 categories of complete vascular maturity, VAA (avascuare area>2dd of the ora serrata), VAT (avascar area >22 DD of ora with posterior tortuosity), and reactivation. Of the 13 eyes in the study, none of them reached complete vascular maturity at 60 PMA. 29% were VAA, 33% with VAT, and 37.5% reactivated. The authors concluded that IVR conforms to the previously described regression patterns for IVB.

Foveal thickness, foveal microvasculature, and refractive error in children with asymmetric involvement of retinopathy of prematurity
Celik G, Gunay M, Vural A, Kizilay O.
Eur J Ophthalmol. 2020, E publication ahead of print. May 19.

The current treatment efor ROP is laser photocoagulation. OCTA is a non -invasive imaging modality to obtain vascular imaing of the retina, choroid, and optic nerve without the need for intravenous dye. The authors which to seek out the difference in OCTA results in patients with unilateral laser treated ROP with the untreated spontaneously regressed fellow eye. 17 children (34 eyes) with a history of asymmetric course were assessed. Treated eyes were more myopic than non-treated eyes. Compared to non-treated eyes, treated eyes had a shallower AC depth. Es of these children.There was no significant difference regarding OCTA parameters between the two eyes except for a higher central foveal thickness in laser treated eyes. Future studies would be helpful to validate these results.

RATES AND RISK FACTORS FOR RECURRENCE OF RETINOPATHY OF PREMATURITY AFTER LASER OR INTRAVITREAL ANTI–VASCULAR ENDOTHELIAL GROWTH FACTOR MONOTHERAPY
LING K, LIAO P, WANG N, CHAO A, CHEN K, CHEN T, HWANG Y, LAI C, WU W
RETINA Sept 2020; 40:1793–1803.

The study aimed to determine the rates and risk factors of recurrent retinopathy of prematurity (ROP) treated by laser photocoagulation, intravitreal bevacizumab (IVB) monotherapy, or intravitreal ranibizumab (IVR) monotherapy. This was a retrospective cohort study, where consecutive infants with Type 1 ROP who received laser, IVB, or IVR treatments were followed for at least 75 weeks of postmenstrual age. Data analysis was performed between March 2010 and February 2017 in Chang Gung Memorial Hospital, Linkou, Taiwan. Results: A total of 176 infants (340 eyes) were included in this study. The mean follow-up was 197.3 ± 110 weeks. All of the baseline demographic and ROP characteristics among the laser, IVB, and IVR groups were similar. The overall recurrence rate after treatment was 44 of 340 eyes (12.9%). The IVB group had a recurrence rate of 10.0%, followed by the laser group (18.0%) and the IVR group (20.8%); however, these rates were not significantly different (P = 0.0528). Compared with the laser group, the IVB and IVR groups exhibited recurrence at later ages (43.4 ± 3.5 weeks for the IVB group, 42.3 ± 2.0 weeks for the IVR group, and 39.5 ± 2.8 weeks for the laser group; P = 0.0058). The mean interval of recurrence from initial treatment in the laser group was 3.6 ± 1.4 weeks compared with 8.8 ± 3.9 weeks and 8.3 ± 1.6 weeks in the IVB and IVR groups, respectively (P = 0.0001). Overall, the independent risk factors of recurrence included an early postmenstrual age at initial treatment (P = 0.0160), Zone I (P = 0.0007), low Apgar score (P = 0.0297), and multiple births (P = 0.0285). There was no significant difference in progression to retinal detachment among the three groups (laser: 3/61, 4.9%; IVB: 2/231, 0.9%;and IVR: 1/48, 2.1%; P = 0.2701). Laser, IVR, and IVB are effective for Type 1 ROP. Retinopathy of prematurity recurrence requiring re-treatment was encountered as late as 50 weeks of postmenstrual age after IVB or IVR but earlier after laser. Longer follow-up for infants treated with anti–vascular endothelial growth factor is needed, especially in patients with significant risk factors such as an early postmenstrual age at initial treatment, Zone I ROP, low Apgar score, and multiple births. As newer therapies emerge for ROP treatment, it's very important to consider the recurrence rates and potential long term outcomes when deciding on treatment.

TEN-YEAR EPIDEMIOLOGY OF RETINOPATHY OF PREMATURITY TREATMENT IN TAIWAN
KANG E, HSU K, CHU S, LIEN R, WANG N, LAI C, CHEN K, HWANG Y, LIN C, WU W
RETINA Sept 2020; 40:1804–1811.

The study aimed to understand the epidemiology of retinopathy of prematurity (ROP) requiring treatment in Taiwan from 2002 to 2011. This retrospective cross-sectional study enrolled 11,180 premature patients with a length of stay .28 days who survived during hospitalization. The incidence of the first ROP treatment was analyzed. Among ROP patients (n = 4,096), 6.5% (n = 265) received treatment. The most frequently performed treatment was laser administration (n = 199), followed by intravitreal anti–vascular endothelial growth factor (VEGF) injection (n = 38), scleral buckle or pars plana vitrectomy (n = 14), and cryotherapy (n = 14). The incidence of ROP requiring treatment increased during the study period, as did the use of intravitreal anti-VEGF injection. Shifts in the treatment modality from cryotherapy and scleral buckle/pars plana vitrectomy to laser treatment after 2003 and from laser treatment to intravitreal anti-VEGF injection after 2010 were observed. In Taiwan, the incidence of the use of intravitreal anti-VEGF injection for treating ROP increased between 2002 and 2011. Laser treatment was less frequently used than intravitreal anti-VEGF injection in 2011.

POTENTIAL UTILITY OF FOVEAL MORPHOLOGY IN PRETERM INFANTS MEASURED USING HAND-HELD OPTICAL COHERENCE TOMOGRAPHY IN RETINOPATHY OF PREMATURITY SCREENING
ANWAR S, NATH M, PATEL A, LEE H, BROWN S, GOTTLOB I, PROUDLOCK F.
RETINA Aug 2020; 40:1592–1602.

The study aimed to investigate dynamic foveal morphology with postmenstrual age, in preterm infants with and without retinopathy of prematurity using hand-held optical coherence tomography, adjusting for gestational age (GA) and birthweight (BW). This was a prospective mixed cross-sectional/longitudinal observational study of 87 participants (23–36 weeks GA; n = 30 with, n = 57 without retinopathy of prematurity) using hand-held optical coherence tomography images (n = 278) acquired between 31 weeks and 44 weeks postmenstrual age excluding treated retinopathy of prematurity. Measurements

included foveal width, area, depth, central foveal thickness, maximum slope, and parafoveal retinal thickness at 1,000 mm nasal and temporal to the central fovea. Retinopathy of prematurity was significantly correlated with only foveal width in either GA or BW adjusted statistical models. In contrast, severity of prematurity (GA, BW) correlated with foveal area (P , 0.005), depth (P # 0.001), and slope (P , 0.01), although central foveal thickness (P = 0.007) and parafoveal retinal thickness (P , 0.001) correlated with GA, but not with BW. Foveal width is independent of GA and BW with potential in retinopathy of prematurity screening assessment using hand-held optical coherence tomography. Foveal morphology could be graded in prematurity during development, with possible implications for future management of preterm infants. Paper looked at parameters that can help us understand future ocular findings of babies with history of ROP.

THE EVOLUTION OF ISOLATED NEOVASCULAR TUFTS ("POPCORN") IN RETINOPATHY OF PREMATURITY
XUE K, HUANG X, XU S, ZHANG T, WANG X, ZHANG M, RUAN L, NI Y
RETINA Jul 2020; 40:1353–1358.

Goal of the paper was to explore the natural evolution of isolated neovascular tufts ("popcorn") in retinopathy of prematurity (ROP) and its significance in the progression of acute ROP. In this retrospective case series, 89 infants (89 eyes) in total having acute ROP were analyzed during serial retinal examinations with a RetCam III wide-angle fundus imaging system, among which 53 eyes were observed to have popcorn and 36 eyes did not. The clinical outcomes of the popcorn (+) group and the popcorn (2) group were compared. Popcorn was located only in Zone II, Stage 2 ROP, primarily in the temporal field (65%). It appeared at a mean postmenstrual age of (37.6 ± 1.3) weeks, disappeared at (41.0 ± 2.2) weeks, and lasted for (2.8 ± 1.1) weeks. The popcorn (+) group had a significantly higher natural regression incidence than the popcorn (2) group (P , 0.05). The laser treated eyes in the popcorn (+) group had earlier presentations (36.4 ± 0.7 vs. 38.2 ± 1.3 weeks) and shorter existences (1.5 ± 0.5 vs. 3.2 ± 0.9 weeks) of popcorn than the regressed eyes (P , 0.01, respectively). Popcorn is generally a "benign" indicator of the regression of ROP. The early presentation (postmenstrual age 37 weeks) and short duration of popcorn require further observation.

New modifications of Swedish ROP guidelines based on 10-year data from the SWEDROP register
Holmstrom G, Hellstrom A, Granse L, Saric M, Sunnqvist B, et al
Br J Ophthalmol. 2020 Jul;104:943-949.

Currently all infants in Sweden with gestational age (GA) <31 weeks are screened for ROP, and results are registered in a we-based register called the Swedish National ROP Register. This study aimed to analyze incidence and treatment of ROP to enable modifications if needed of the existing guidelines. 7249 infants were analyzed over the period of 2008-2017, of which 31.9% (2310) had ROP and 6.1% (440) were treated. No infants with GA 30 weeks was treated. Total incidence of ROP remained similar over the time of the study, although over time the infants with ROP had lower GA and BW. In eyes treated with anti-VEGF alone, recurrence occurred in 66.7% (58/87), with retreatment performed a mean of 8.5 weeks. Recurrence after laser as first treatment was 25.7% (199/773), with mean retreatment occurring 2.6 weeks after first treatment. Overall based on the results of the study, proposed changes to the screening guidelines include screening infants with GA of less than 30 weeks, which would have spared 1681 out of 7249 infants from exam.

Aggressive Posterior Retinopathy of Prematurity: Clinical and Quantitative Imaging Features in a Large North American Cohort
Kellyn N. Bellsmith, James Brown, Sang Jin Kim, Isaac H. Goldstein, Aaron Coyner, Susan Ostmo, Kishan Gupta, R. V. Paul Chan, Jayashree Kalpathy-Cramer, Michael F. Chiang, J. Peter Campbell
Ophthalmology. Aug 2020(8);127:1105-12.

This study analyzed differences between treatment requiring ROP with or without aggressive posterior ROP from an ongoing imaging and informatics study of ROP patients. The goal was to test the predictive value of the quantitative vascularity score generated by deep learning AI in classifying aggressive posterior ROP. The strengths are the standard protocols, de-identified and masked data, and multiple readers for the images. As might be predicted, lower birth weight and earlier onset of ROP was correlated with need for treatment, but additional factors included more rapid progression and a high vascular severity score. Even among experienced readers, however, the diagnostic agreement on aggressive posterior ROP was only fair, making future comparative studies on outcomes difficult since the study groups will likely be quite variable. The authors' conclusion that early onset of ROP is associated both with more posterior disease and earlier time to treatment is likely accurate, since earlier onset suggests more aggressive disease. The authors' conclusion that pace of disease progression is a significant risk factor is also likely accurate, since more rapidly progressive retinal changes are worrisome for more severe ROP. Finally, the authors' conclusion that image-based AI might more consistently diagnose posterior ROP is both accurate and also unsurprising, since a single computer-based algorithm should be more consistent that a group of readers with different clinical backgrounds and experiences.

Early Vitamin A Supplementation Improves the Outcome of Retinopathy of Prematurity in Extremely Preterm Infants
Sun H, Cheng R, Wang Z
Retina. Jun 2020; 40:1176–1184.

This study assessed the efficacy and safety of early vitamin A (VA) supplementation to improve outcomes of retinopathy of prematurity in extremely preterm infants. A total of 262 eligible extremely preterm infants underwent randomization; of these, 132 were assigned to the VA group and 130 to the control group. The infants were administered a solution of VA (1,500 IU/day), added to their enteral feeds as soon as minimal feeding was introduced and continued for 28 days or until discharge. With no adverse effects occurring, serum VA of the VA-supplemented infants on Days 14, 28, and postmenstrual 36 weeks was higher than that of the placebo group (P , 0.001). No signs of VA toxicity or increased intracranial pressure were reported. The VA group had lower unadjusted rates of Type 1 retinopathy of prematurity (1.6 vs. 6.9%, P = 0.030) and bronchopulmonary dysplasia (18.9 vs. 33.8%, P = 0.008) than the control group. Regression analysis revealed an association between serum VA levels and risk of Type 1 retinopathy of prematurity (beta = 22.37). Vitamin A supplementation reduced VA deficiency in extremely preterm infants; it was associated with a decreased incidence of Type 1 retinopathy of prematurity and may also have a positive impact on reducing bronchopulmonary dysplasia. The study introduces a potential method to help decrease risk of ROP progression but needs to be repeated on a larger scale.

Lens-sparing vitrectomy for stage 4A retinopathy of prematurity in infants with aggressive-posterior ROP: anatomic and functional results.
Macor S, Pignatto S, Capone A Jr, Piermarocchi S, Lanzetta P.
Eur J Ophthalmol. 2020, E publication ahead of print. August 8.

With improved survival of very prematuring infants, there has been an increase in AP-ROP. These very young infnats can develop stage 4 and 5 ROP rapidly in the absence of intervention. Early intervention with laser photocoagulation for AP-ROP, however some eyes progressive to retinal detachment. Early lens sparing vitrectomy (LSV) may have favorable functional outcomes, regression of neovascular activity and retina reattachment. The authors of this study is to report the long term anatomic and functional outcomes of early LSV for stage 4A ROP in infants with AP-ROP in a retrospective chart review. Of the 10 eyes on 7 patients identified for this study, all eyes received laser therapy before LSV. The mean follow-up was 36 +/- 13.4 months. At the last follow up, anatomic successive was 100% with a mean vision of 20/80. 80% of the eyes had a high myopic refractive correction. The authors concluded that early LSV for stage 4A ROP was effective in terms of anatomic and functional outcomes, despite a high myopic shift in refractive error.

9. STRABISMUS

Assessing Variability of Control Within a Single Day in Intermittent Exotropia.
Prile SM, Kim J, Moon Y, Lim HT.
J Pediatr Ophthalmol Strabismus. 2020 Nov 1;57(6):378-383.

This prospective observational study of 95 pediatric patients with intermittent exotropia evaluated control over time during a single office visit. Two or three assessments of control were obtained an average 1.6 hours apart using the Look and Cover and Ten seconds of Observation Scale for Exotropia (LACTOSE) tool. This reliable and validated scale measures control over 5 points (0-4) at distance and near. The highest combined distance and near score, 8, indicated poor control and exotropia noted throughout the assessment. Variability, defined as a change of one point or more on the scale, was observed in 47% of patients. Of these, 60% had a change of only one point and the remaining 40% showed a 2 point change. Good control at near was associated with less variability. Patients with LACTOSE scores associated with excellent (<2) and poor (>6) control had less variability compared with patients who had intermediate scores. In conclusion, the initial evaluation of patients with good near control, and either overall excellent or poor control is likely to represent control throughout the day. In contrast, patients with moderate initial control scores are more likely to have variable control. The study is limited by taking all measurements during a single office visit, which may not be representative of an entire day.

The Effect of Age on Binocular Vision Normative Values.
Sánchez-González MC, Sánchez-González JM, De-Hita-Cantalejo C, Vega-Holm M, Jiménez-Rejano JJ, Gutiérrez-Sánchez E.
J Pediatr Ophthalmol Strabismus. 2020 Nov 1;57(6):363-371.

This prospective cross-sectional study evaluated the relationship between horizontal heterophoria, fusional vergence amplitudes, vergence facility, and age. The subjects were aged 18 to 65 years, and the population was divided into a non-presbyopic group (n=49) and a presbyopic group (n=63). All variables were tested at distance and near. Positive fusional amplitudes were measured using base out prism to identify the blur and brake point. Negative fusional vergence was determined using base in prism. Vergence facility was determined by counting the number of times the subject could resolve the fixation image with 3 base in prism alternating with 12 base out prism in one minute. Exophoia increased while near positive horizontal fusional vergence and vergence facility decreased with increasing age. The authors suggest that a larger study could better determine normative values, which would likely be dependent on age. From the results presented, the wide range each variable demonstrated after controlling for age could limit the usefulness of these normative values. The range did seem to decrease in the 60-plus aged subjects, and if it would be interesting to see if this continued into advanced age.

Binocular Interference vs Diplopia in Patients with Epiretinal Membrane.
Hatt SR, Leske DA, Iezzi R, Holmes JM.
JAMA Ophthalmol. 2020 Sep;138(11):1121-1127.

This is a retrospective medical record review of an adult strabismus clinic at a tertiary referral center from 2010 to 2019 who completed the Adult Strabismus (AS)-20 questionnaire. The authors identified two groups, those who reported eye closure sometimes and those who reported no eye closure (control group). Authors included in the review 124 patients with epiretinal membrane (ERM), with 58 (47%) women with mean age of 70 years old reporting monocular eye closure. The authors also evaluated the frequencies of (1) central-peripheral rivalry (CPR)-type diplopia (dragged fovea diplopia), (2) binocular interference (monocular eye closure but no diplopia or strabismus), and (3) other (associated with monocular eye closure). In addition, the authors compared the quality of life between control patients and patients with CPR-type diplopia and/or binocular interference. Results showed that compared to 11 control patients with ERM, they found 36 (29%) patients with binocular interference, 34 (27%) patients

with CPR-type diplopia, 54 (44%) patients with other (primarily strabismus). Compared to the control patients with ERM, patients with ERM and binocular interference had a worse quality of life on AS-20 reading function (P=0.007) and general function (P=0.01) domains. Compared to the patients with CPR-type diplopia, patients with binocular interference had poorer worst-eye visual acuity [median 20/63 (0.50 logMAR) versus 20/40 (0.30 logMAR); P=0.03] and larger interocular visual acuity difference [20/58 (0.46 logMAR) versus 20/30 (0.19 logMAR); P=0.004]. The authors suggest that for patients with binocular interference, who close one eye (without having strabismus or diplopia), this review shows the negative impact affecting the quality of life in patients with ERM. Limitations of the study include the retrospective medical chart review, the referral from only retina clinicians at one ophthalmology department, and the lack of measurement of both monocular and binocular visual acuity and contrast sensitivity in patients. While the authors were not able to comment about the differences between binocular inhibition and binocular interference, the study was helpful to evaluate what patients with ERM are experiencing. In summary, this retrospective medical review from Mayo Clinic is helpful for our evaluation of adult strabismus patients with ERM and how diplopia, quality of life, and visual acuity is impacted.

Bilateral Occlusion Reduces the Ocular Deviation in Intermittent Exotropia
John R Economides, Daniel L Adams, Jonathan C Horton
Invest Ophthalmol Vis Sci. Jan 2021;62, 6

This small study investigated 18 individuals with well-controlled intermittent exotropia. They measured prismatic deviation with monocular occlusion as well as binocular occlusion. They noted that 11 of the 18 patients had a smaller prismatic deviation under binocular occlusion than monocular occlusion. They state that this is due to the lack of ability to fixate under binocular occlusion. This is most likely secondary to lack of neural input to yolk muscles. If confirmed in larger studies, these types of measurements may be useful in preoperative measurements to potentially change the amount of correction needed for patients with intermittent exotropia.

Finite Element Model of Ocular Adduction by Active Extraocular Muscle Contraction
Somaye Jafari, Yongtao Lu, Joseph Park, Joseph Demer
Invest Ophthalmol Vis Sci. Jan 2021;62, 6

This study made a three-dimensional model of the globe, horizontal recti muscles, and the optic nerve. Based on magnetic resonance imaging of the orbit in multiple gazes, calculations were made to approximate the tension and strain on the horizontal recti and optic nerve in twenty six and thirty two degrees of adduction. With further imaging and inclusion of all extraocular muscles, similar models will help us better understand the interrelationship of all of the tissues within the orbit.

Pseudostrabismus in the First Year of Life and the Subsequent Diagnosis of Strabismus
Timothy T. Xu, Cole E. Bothun, Tina M. Hendricks, Sasha A. Mansukhani, Erick D. Bothun, David O. Hodge and Brian G. Mohney.
American Journal of Ophthalmology, 2020 Oct; 218: 242-246.

The goal of this retrospective population-based cohort study was to report the prevalence of pseudostrabismus in the first year of life and the subsequent diagnosis of true strabismus. The authors looked at all the residence of Olmsted county Minnesota under the age of 1 who were diagnosed with pseduostrabismus over a ten year period using medial record linkage system. They found that 1/113 children had a diagnosis of pseudostrabismus in the first year of life. Most of these patients were diagnosed by a non-ophthalmolgist, but confirmed by an ophthalmologist. Approximately half of the infants had at least one follow up and 9 of those (5%) were diagnosed with strabismus at a mean age of 4.5 years. The authors concluded that pseudostrabismus was a common diagnosis but that the prevalence of true strabismus in the cohort of patients diagnosed with pseudostrabismus was lower than in previous reports which range from a rate of 9.6 to 19%. The methods of this paper, while retrospective, are expectedly strong and the authors point out that this population may not be representative of the

country as a whole. Based on previous studies, the authors expected rates of true strabismus in the patients initially diagnosed to have pseudostrabismus to be closer to 10%, which they were not. The authors hypothesize that previous studies had selection bias since those patients with follow up tended to be those where the families or pediatricians noted eye deviation. This paper is important to the pediatric ophthalmologist because it suggests that the rate of true strabismus might be lower than we think in patients with pseudoesotropia and perhaps the surveillance that man of us do after diagnosing pseudoesotropia is not necessary.

Functional Anatomy of Muscle Mechanisms: Compensating Vertical Heterophoria.
Joseph L. Demer and Robert A. Clark.
American Journal of Ophthalmology, 2021 Jan; 221:137-146.

This prospective case series of 8 patients uses MRI of the extraocular muscles to evaluate the role of extraocular muscles in compensating for large vertical fusional vergence (VFV). The authors sought to use MRI to obtain an objective measure of the extraocular muscles contractile function to better understand what is happening in these muscles in patients with large vertical fusional amplitudes. Part of the goal was to better understand if patients with large VFV really had decompensated superior oblique palsies or sagging eye syndrome, or something else. The authors used a specialized, research focused MRI technique while viewing monocular and binocularly. Contractility of the extraocular muscles was determined from changes in the muscle volume. The authors found that 5/8 patients could sustain fusion while in the MRI scanner. And of those scans they could analyze, they found that the compensation from VFV was due to relaxion of the inferior rectus. The authors suggest that this should guide the surgeon to weaken the medial portion of the inferior rectus in the hypotropic eye. This paper has a small sample size and since some of these patients had had previous inferior oblique weakening, I think it detracts from any of their conclusions. While this paper does contribute to our understanding of patients with VFV, the small sample size and previous surgery in this cohort of patients doesn't convince this reader that the suggested surgical plan in these patients is the only solution.

Strabismus After Ahmed Glaucoma Valve Implantation.
Laura Robbins, Toshiaki Goseki, Simon K. Law, Kouros Nouri-Mahdavi, Joseph Caprioli, Anne L. Coleman, Joann A. Giaconi, Joseph L. Demer, Federico G. Velez and Stacy L. Pineles.
American Journal of Ophthalmology, 2021 Feb; 222:1-5.

This retrospective review of 732 patients at one institution over 5 years who had an Ahmed glaucoma valve (AGV) implanted aimed to describe strabismus in patients after this procedure. The authors found that 29 of the patients (4%) developed new-onset strabismus after AGV and of those 21 (72%) had diplopia. Three patients had esotropia, 11 had exotropia,6 had a vertical deviation, and 9 had combination horizontal and vertical strabismus. Mean follow up was about 3 years in both the strabismic and non-strabismic group and the patients with strabismus tended to be younger. The authors concluded that this number is comparable to the strabismus risk of other glaucoma drainage devices and encouraged this risk to be discussed preoperatively. Of note the patients included in the strabismus group were those who complained of double vision or strabismus. As this is a large retrospective study, the patients were not evaluated before and after surgery to determine any changes, however all patients with strabismus or diplopia were referred to pediatric ophthalmology. The authors suggest that the mechanism for strabismus in these cases is restrictive based on the location of the AGV and type of strabismus observed. The limitations of this paper are due to the fact that it was a chart review and not actual patient exams, which could have eliminated patients who were asymptomatic or did not report symptoms. Nonetheless, this paper is important as it has very large numbers of patients.

Measuring health-related quality of life in individuals with cyclodeviation using the Adult Strabismus 20 (AS-20) questionnaire.
Flodin S, Rydberg A, Pansell T, Grönlund MA.
Journal of AAPOS (2021), doi: https://doi.org/10.1016/j.jaapos.2020.08.011.

The negative influence of strabismus on a patients's well-being has been documented in studies evaluating health-related quality of life (HRQol) or vision-related quality of life (VRQol).The Adult Strabismus-20 (AS-20) assess HRQol in adults with strabismus and has shown to have test-retest reliability. The authors used this tool to assess HRQol in patients with cyclodeviation and to evaluate change after surgical treatment and how the scores compared to nonstrabismic patients and those with other types of strabismus. The patients were divided into two groups: those requiring Harada-Ito for correction of cyclodeviation and those only requiring vertical deviation correction. Previous studies have shown surgery has a positive effect on quality of life and greater positive effect in psychosocial scores. The authors of this study showed a different result with the improvement in scores after surgery were observed mainly in the functional subsection. The authors suggest that this is explained by the fact that the misalignment in this group is not apparent to others therefore not causing a stigma that would cause distress in the patient while the functional aspect was disabling. The Harada-Ito group had greater improvement of scores especially the functional subscale when compared to the vertical group. The authors suggest that this Implies a greater effect of cyclodeviation on function. Limitations of the study were: a small number of individuals in the vertical group as well as the fact that the study relies on only patient reported outcome measures with no correlation of objective clinical findings. The study is important in demonstrating the effect of cyclodeviation on function which may be important in making decisions for surgery planning and managing patient expectations.

Outcomes in accommodative esotropia with a high AC/A ratio.
Reynolds MM, Diehl NN, Mohney BG.
Eur J Ophthalmol. 2020 Dec 24:1120672120977831. doi: 10.1177/1120672120977831. Epub ahead of print. PMID: 33356527.

Accommodative esotropia with high AC/A ratio occurs in 1/5 children with accommodative esotropia. These patients are typically treated with bifocals to improve alignment at near. This is a large population based cohort to describe the outcomes of high AC/A ratio esotropia over a 30 year period in Olmsted County, Minnesota. About 20.7% of patients with accommodative esotropia had high AC/A ratio. There was no significant initial or final clinical differences between those who wore bifocals and those who did not. At a mean follow up of 4 years, there was no difference in the rate of amblyopia, angle of deviation at both distance and near, and stereoacuity. More than half of children were able to discontinue bifocal use in their teenage years. Esotropic children who wore bifocals were no. more likely to require strabismus surgery than those who did not wear bifocals. The authors did specify that the number of children who did not wear bifocals in their cohort was small, but this observation does require further investigation.

Accuracy of anterior segment optical coherence tomography for pre-operative localization of insertions of extraocular recti muscles.
Jayaraj S, Singh A, Agrawal A, Panyala R, Samanta R, Mittal SK, Kumar B.
Eur J Ophthalmol. 2020 Nov 3:1120672120971192. doi: 10.1177/1120672120971192. Epub ahead of print. PMID: 33143475.

Imaging such as CT, US, and MRI have been used to determine the measurement of an extraocular muscle (EOM) insertion from the limbus but are limited due to low accuracy and image resolution. The purpose of this study was to evaluate the accuracy of the ASOCT functionality of the Cirrus OCT to determinte the distance of the four rectus muscles in children compared to intraocular measurements. This was a prospective, double-masked, observational study and included 46 patients ages 5-40 yo who were undergoing primary strabismus surgery during the study period. 92.3% of superior rectus muscles were within 1 mm difference. 95.7% of IR muscles were within 1 mm difference. 100% of medial rectus muscles were within 1 mm difference. 96.5% of lateral rectus muscles were within 1 mm difference. Overall, 96.9% came within 1 mm difference. The AS OCT may be a good way to determine the location of the rectus muscles, even in children. The next step would be to see if this is the case for reoperated muscles.

Reduced stereacuity as a predictor for clinically significant convergence insufficiency
Leshno A, Stolovitch C, Zloto O, Meirovitch S, et al.
Br J Ophthalmol. 2021 Jan; 105:37-41.

The association between convergence ability and stereoacuity has not been rigorously studied. This large cohort study examined the association between convergence amplitude and stereoacuity in children. A retrospective chart review of 2200 was conducted for children age 6-17. Patients with amblyopia, manifest strabismus or visual acuity <20/30 were excluded. Randot stereoacuity and convergence amplitudes using base-out prism bars were measured. Overall there was an increased prevalence of normal stereoacuity as convergence ability improved. There was a negative correlation between stereoacuity and the break point on convergence amplitudes. Trends were seen even after excluding refractive errors and children with convergence insufficiency symptoms. There were no sex differences, but the mean age of children with convergence insufficiency was higher than the normal convergence group (but not significantly so). A small group of 21 patients had longer-term follow-up (at least 2.5 years) and were treated for CI. Convergence improved in 66% of these patients and the rate of normal stereoacuity increased from 29% to 76%. This was, however, a retrospective study and further studies are warranted, but children with poor convergence accompanied by low stereoacuity should be considered for referral for orthoptic treatment.

Analysis of the quality, reliability, and popularity of information on strabismus on YouTube.
Mangan MS, Cakir A, Yurttaser Ocak S, Tekcan H, Balci S, Ozcelik Kose A.
Strabismus. 2020 Oct 19:1-6. doi: 10.1080/09273972.2020.1836002.

Given the popularity of information-sharing via YouTube, the authors sought to evaluate the videos available on the website that address strabismus. The authors included 84 unique videos in English that were longer than 60 seconds. The main publishers were patients (27) or ophthalmologists (24). Most videos were about patient experience (30) or patient information (22). The majority of patient experience videos had adult female patients (90%, 27 of 30). The authors also found that YouTube videos provide only fair quality information for strabismus and the highest quality educational videos were posted by academic centers. The authors acknowledge that the results of the study may differ if analyzed by a patient or lay person, as compared to a physician as there are different expectations regarding content.

Increased myofiber size and reduced satellite cell numbers in medial rectus muscle of patients with intermittent exotropia.
Kim CZ, Lee SJ.
Strabismus. 2020 Oct 21:1-7. doi: 10.1080/09273972.2020.1832546.

The authors investigated the muscle fiber arrangement and diameter of the medial rectus muscle in patients with intermittent exotropia to investigate the pathogenesis of strabismus. The authors enrolled 17 patients (15 exotropes, 2 controls) over a 2 year period for whom the medial rectus muscle was resected. The tissue subsequently underwent H&E staining and immunohistochemical analysis. The average age of the intermittent exotropia group was younger than the control group (17.33 vs 22.0 years) and had a different gender composition (male:female ratio 10:5 exotropes vs 2:0 controls). The mean myofiber diameter was significantly thicker ($p < .01$) in the intermittent exotropia group. Additionally the ratio of PAX7 and PCNA positive cells to number of muscle fibers per unit area was lower in exotropes than normal controls. However the study has significant limitations, which include the small number of tissues, the limited number of controls, and difficulty obtaining tissue in children. Future studies to confirm these findings in different population and comparable control groups is necessary.

Comparison of the Efficiency of the Botulinum Toxin for the Treatment of Esotropia in Children with and without Neurological Disease and/or Prematurity
Mangan MS, Basar E.

J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):163-169.

The goal of this paper is compare the effect of botulinum toxin injection for the management of esotropia in patients with and without neurological disease and/or prematurity. This study was a single-center, retrospective, nonrandomized controlled study was performed on botulinum toxin in 87 children divided into two groups: study group of esotropia in 56 children with neurological disease and/or prematurity and, control group of 31 healthy children with infantile esotropia. All patients were followed for at least 24 months after injection. Success was defined as motor alignment with 10^{Δ} of orthotropia after single bilateral botulinum injection. Mean age at treatment was similar in both groups (15.5 vs 14.8 months; $p = .555$). Mean pretreatment deviation was similar in both groups (50.8^{Δ} vs 50^{Δ}; $p = .855$). The success rate was better in the control group (61.2% vs 51.7%, $p = .265$) at 24 months after injection, but the change in the mean angle of deviation was not statistically significant between the groups at 12 and 24 months after injection ($p = .264$ and $p = .547$, respectively). Multivariate regression analysis showed that pretreatment angle of deviation and presence of retinopathy of prematurity were significant predictors at 12 months after injection ($p = .0001$ and $p = .004$, respectively), while pretreatment angle of deviation was found to be a predictor at 24 months after injection ($p = .0001$). The authors found that decreased angle of deviation and absence of retinopathy of prematurity were associated with a better result. There was no difference in motor alignment of esotropia in children with and without neurological disease and/or prematurity. In these patients, botulinum injection may be used as an alternative to surgery.

Extraocular Muscle Palsy in Patients with Chronic Orbital Myositis
Akbari M, Mirmohammadsadeghi A, Eshraghi B, Amoli FA, Mehrpour M.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):177-181.

Orbital myositis (OM) is a subgroup of idiopathic orbital inflammation. It can involve single or multiple extraocular muscles and result in restriction or paresis of extraocular muscles. This paper reports two unusual cases of extraocular muscle paresis in the fibrotic stage of chronic OM and reviews the literature related to this finding. The first case was of a 38-year-old woman with chronic OM with large-angle right eye exotropia and right medial rectus paresis. She received a botulinum A toxin injection into the right lateral rectus muscle as a first treatment, but it was unsuccessful in correcting her deviation. Subsequently, she underwent two strabismus surgeries, which successfully resolved her diplopia in primary gaze. The second case was of a 35-year-old woman with chronic OM and left lateral rectus palsy, which was managed with a botulinum A toxin injection. The authors conclude that OM can cause extraocular muscle palsy in the chronic fibrotic stage of the disease.

Histopathological features and satellite cell population characteristics in human inferior oblique muscle biopsies: clinicopathological correlation.
Baytaroğlu A, Taylan Şekeroğlu H, Erkan Turan K, Orhan D.
J AAPOS. 2020 Oct;24(5):285.e1-285.e6.

This is a prospective study investigating the correlation between clinical and histopathological and immunohistochemical features of inferior oblique muscles in patients with priary and secondary interior oblique overaction. Inferior oblique muscle specimens of 51 patients who underwent inferior oblique–weakening procedures for primary or secondary inferior oblique overaction were recruited. Subjects were mainly divided into two groups, each of which was further divided into two subgroups: group 1 included patients with primary inferior oblique overaction (subgroups, infantile esotropia vs acquired V-pattern esotropia), and group 2 included patients with secondary inferior oblique overaction (subgroups, congenital vs acquired trochlear nerve palsy). Inferior oblique overaction was graded between 0-4. Histopathologic changes, such as angular fibers, endo- and perimysial fibrosis, and vacuolization were categorized from mild to severe. Immunohistochemical markers Pax7, NCAM, and MyoD1 were used to detect satellite cells, a unique stem cell population in muscles presumably responsible from myofiber regeneration and maintenance, and their activity. Results were reported as stained cells per cross-section ratio. Satellite cell distribution and activity was significantly higher in group 1 (P\0.001). The angular fiber

count and the degree of perimysial fibrosis was higher in the secondary group (P \ 0.001 and P 5 0.01, resp.). There was no correlation between clinical amount of inferior oblique muscle overaction and immunohistochemical markers. This study suggests that satellite cell population behavior varies among strabismus types.

Pulled-in-two syndrome in a patient with heavy eye syndrome.
Oltra EL, Levy RL.
J AAPOS. 2020 Oct;24(5):314-316.

A case report of a 73-year-old woman diagnosed with heavy eye syndrome who underwent loop myopexy of the superior rectus and lateral rectus muscles after suffering pulled-in-two syndrome caused by exploration of the medial rectus muscle, which could not be recovered. Given that intraoperative forced ductions remained positive after loss of the muscle, a loop myopexy of the superior rectus muscle and lateral rectus muscles was performed. Postoperatively the patient regained full adduction, and her esotropia improved notably.

Esotropia Outcomes and the Influence of Delay to Wearing Full Hypermetropic Correction
Brennan, Rosie; McCance, Patrick; Jian Lee Yeong; Adamson, Gary; Mallett, John.
J Pediatr Ophthalmol Strabismus 2020 Mar;57(2): 85-89.

The authors prospectively evaluated new esotropic patients (age <7) over a one year period. Etiology, clinical characteristics, management and outcome data were recorded for these patients. 117 patients were included in the study, of which 49% had partially accommodative esotropia and 44% had fully accommodative esotropia. The authors were interested to learn if a delay in prescribing and/or wearing full hyperopic correction decreased the chance of a fully accommodative esotropia outcome. Increased time between esotropia diagnosis by an orthoptist or esotropia noticed at home and glasses wear was associated with a deceased chance of a fully accommodative esotropia outcome. Additionally, increased hyperopia was associated with fully accommodative esotropia. In multivariate analysis only spherical equivalent remained uniquely predictive of fully accommodative esotropia outcome. The authors suggest that time between identification of esotropia and hyperopic correction should be minimized. One limitation of the study is that in some patients partial verses fully accommodative esotropia could be different diseases and time between diagnosis and correction of hyperopia irrelevant to the final outcome.

Acquired Comitant Esotropia in Children and Young Adults: Clinical Characteristics, Surgical Outcomes, and Association With Presumed Intensive Near Work With Digital Displays
Pinar Topcu Yilmaz, MD; Özlem Ural Fatihoglu, MD; E. Cumhur Sener, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul ;57(4):251-256.

This was a retrospective review of 27 patients with acquired esotropia and diplopia, which described their clinical characteristics and surgical outcomes. 5 additional patients with acquired esotropia and diplopia were excluded from the study due to less than 6 months of follow up. Neurological evaluation, myasthenia gravis work up, and brain magnetic resonance imaging with contrast were normal in all patients. Mean age at onset of esotropia and diplopia was 17.8 ± 10.3 years (range: 6 to 44 years). A history of excessive near work (≥ 4 hours a day) with digital displays was present in 21 (78%) patients. Myopia was more common than hyperopia in this cohort: eighteen patients had simple myopia (range: -0.25 to -7.75 diopters [D]), 5 patients had hypermetropia (range: 0.50 to 1.50 D), and 4 patients had emmetropia. The angle of deviation prior to surgery was 35.6 ± 10.3 prism diopters (PD) for far and 38.0 ± 10.5 PD for near fixation. After prism adaptation, there was a significant increase in the mean angle of esotropia at distance (49.1 ± 11.6 PD) and at near (52.2 ± 10.6 PD) (P < .001). The prism adapted angle of esotropia was used as the surgical target angle, and this was higher than the angle obtained by alternate prism cover test . A variety of surgical approaches was used, and all surgeries were done by one surgeon. Diplopia resolved and 40-100 arc seconds of stereopsis was achieved in all patients postoperatively. Three patients had recurrence of esotropia in long-term follow-up.

The authors suggest that inquiring about intensive near activities with use of digital displays may avoid time-consuming and costly investigations for other causes of acquired esotropia. However, this study was not designed to actually answer this question. The baseline rate of excessive near work and use of digital displays may be similar in people who do not develop esotropia.
This study is helpful in showing that surgery targeting an augmented prism-adpated angle of deviation restores binocularity in most patients with acquired esotropia and diplopia.

Assessment of Refractive Error Changes and Factors for Decompensation in Patients With Fully Accommodative Esotropia
Selcen Çelik, MD, Osman Bulut Ocak, MD; Aslı İnal, MD; Ebru Demet Aygıt, MD; Ceren Gürez, MD; Zahid Hüseyinhan, MD; Birsen Gökyiğit, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):217-223.

The purpose of the study was to study the factors affecting the risk of deterioration and to evaluate the refractive error change in patients with fully accommodative esotropia. Patients diagnosed as having fully accommodative esotropia (esotropic deviation that started before 7 years of age and less than 8 to 10 prism diopters [PD] of esotropia with full hyperopic correction and/or bifocals) were included in this retrospective population-based cohort study. Deterioration of accommodative esotropia was defined as developing esotropia deviation>10 PD with full hyperopic correction on simultaneous prism cover test, and these patients went on to surgery.
Two hundred and twenty-three patients met the inclusion criteria. The mean follow-up time was 5.94 ± 0.31 years (range: 5 to 8 years). Deterioration occurred in 30 of 223 patients (13.5%). Male gender, higher near distance disparity, and presence of inferior oblique overaction were significantly higher in patients who decompensated compared to those who did not. Hyperopic error increased from the initial level until 7 years of age, followed by a (small) myopic shift thereafter: 0.13 D per year between age 7 to 12 and 0.06 D per year from age 12 to 17. Few children had resolution of fully accommodative esotropia and could discontinue spectacle therapy.
The study is helpful in showing the natural history of initially accommodative esotropia, as patients had long follow up. Decompensation requiring surgery occurs in approximately 13% of patients, and most patients are not able to discontinue spectacles. Grouping patients into three age categories (<7, 7-12, and 12-17 years) to study changes in refractive error over time is statistically problematic.

Comparison of a New, Filter-Free Stereopsis Test (BEST) With the Randot Stereotest in a Pediatric Cohort
Lagstein, Oded; Hecht, Idan; Anteby, Irene.
J Pediatr Ophthalmol Strabismus 2020 Mar;57(2):129-135.

In this retrospective study the Bernell Evaluation of Stereopsis Test (BEST) (Bernell Corporation, Mishawaka, IN) was compared to the Randot Stereotest (Randot) (Stereo Optical, Inc., Chicago, IL). The Randot test requires wearing polarized glasses and occasionally can be difficult to administer in young children. The BEST uses cylindrical lenses that refract light from the target thereby forming binocular parallax and the illusion of depth without the need for wearing glasses. In this study, included patients were aged 3-18 and were both orthophoric (64%) and strabismic. Patients with intellectual disability or no sterovision on either test were excluded. 100 patients met inclusion criteria and were assessed with both Randot and BEST on the same clinic day in unmasked fashion during a single clinic visit. Both tests performed similarly with the exception low stereoacuity, where BEST scores were better generally than Randot scores. Knowing that BEST and Randot perform similarly could be useful if BEST is easier to administer to a larger group of patients compared to the more commonly used Randot test.

Comparison Between Parental Observations and Clinical Evaluation Findings in Korean Pediatric Patients With Intermittent Exotropia
Son, Wonyung; Kim, Won Jae.
J Pediatr Ophthalmol Strabismus ; 2020 May 1;57(3):199-203.

This study is the first to compare parental observations with clinical observation specifically in patients with intermittent exotropia. The authors developed a questionnaire for parents that consisted of one open ended question and three multiple choice question questions. One hundred patients of 95 children participated in the study. Patients with basic exotropia who had deviations of greater than 18 PD were included. Patients with vertical deviations, prior history of strabismus surgery or neurologic impairment were excluded. The concordance between clinical observation and parental observation regarding the deviating eye was 74%. Seventy six percent of parents had a high degree of awareness of the deviation and 24 percent had low awareness, this not related to the amount of deviation. Awareness did correlate with control noted in the office at distance. Previous studies have found little concordance between parental observation and clinical findings but included multiple types of strabismus. In cases of intermittent exotropia, the most common type of strabismus in some populations, degree of control is an important indication for surgery. Furthermore when the deviation is intermittent and a child may not be cooperative in the office, parental observation could be useful.

Exotropic heavy eye syndrome in unilateral high axial myopia.
Awadein A, Hassanein DH.
J AAPOS. 2020 Jun;24(3):131.e1-131.e6.

This is an observational study of 13 patients with unilateral exotropia and hypotropia in the presence of unilateral high axial myopia (> 26.5mm) at one institution from 2013 to 2017. The authors evaluated all 13 patients' ocular motility, orbital imaging, visual acuity, refraction, previous surgeries. Median age was 27 years, SD 14.6 years. In the deviated eyes, mean SE was -13.6 D, SD 9 D, mean AL 28.3mm, SD 1.7mm. All patients had a V pattern with limitation of elevation in abduction. MRI indicated no displacement of the LR in all patients and in turn, no radiologic evidence of heavy eye syndrome (HES). Pre-operative horizontal angle was 46.5 PD, SD 12.1 PD and vertical angle was 21.1 PD, SD 6.5 PD. Six (46%) of 13 patients had surgery and in 5 of 6 patients, the LR was displaced inferiorly (mean of 2.5mm and range of 2.0-4.0mm). The SR in all patients had a normal path, with surgical exploration. The authors suggest that intraoperative findings were suggest of HES versus the radiologic findings in the 13 patients not being typical for HES. Hence, the authors suggest that these 13 patients had exotropic heavy eye, with a different pathogenesis than HES. Furthermore, the authors suggest that exotropic heavy eye in their patients is associated with the dense amblyopia noted in the unilateral anisometropia axial myopia. Limitations of the study include the very small number of patients observed and in turn, a new clinical syndrome, such as exotropic heavy eye cannot be fully explained from these 13 patients. In summary, the authors share insights about the strabismus intraoperative findings and radiologic findings in unilateral axial myopia with a combined exotropia and hypotropia.

When pediatric acute acquired comitant esotropia is not caused by a neurological disease
Dotan G, Keshet Y, Qureshi HM, Friling R, and Yahalom C.
J AAPOS. 2020 Feb; 24:5.e1-5

This is a retrospective study reviewing the medical records of patients age >4 with acute acquired comitant esotropia (AACE) examined by a single practitioner from 2014 to 2018 and measuring the presence of neurological disease. A total of 20 children (11 males; mean age, 9.8$\pm$ 4.1 years) were included. Mean esodeviation was 29.5$^{\Delta}$ $\pm$ 14.8$^{\Delta}$ (range, 10$^{\Delta}$-55$^{\Delta}$). All had an otherwise normal ophthalmological and neurological evaluations. Of the 20, 19 (95%) had normal brain neuroimaging. One child that did not have neuroimaging was followed over 2 years without developing any neurological sequelae. In this study cohort, pediatric AACE was not accompanied by other ophthalmic and neurological abnormalities and was not a manifestation of an intracranial pathology. The study is limited in the retrospective design and small number of patients and 1 patient who elected not to have neuroimaging. This study suggests acquired neurological pathology as a cause for AACE is rare. The decision to perform neuroimaging or to monitor closely may be considered on a case-by-case basis after discussion with the child's caregivers and the treating physicians.

Longitudinal changes in binocular coordination of smooth pursuit in patients with intermittent exotropia after strabismus surgery
Mihara M, Hayashi A, Kakeue K, and Tamura R.
J AAPOS. 2020 Feb; 24:20.e1-7

This is a prospective study reviewing video records of the smooth pursuit of patients with intermittent exotropia before, 1 week after, 1 month, 3 month and 6 months after strabismus surgery. Subjects were asked to track a step-ramp target moving at $\pm$ 6.1°/sec horizontally as accurately as possible under binocular viewing. The difference in gain (eye velocity divided by target velocity) and amplitude of smooth smooth pursuit between right and left eyes before and after surgery were compared. A total 9 patients (mean age 22.2, 10-45 years, 7 females) were included. The mean preoperative ocular alignment at near was $59.1^{\Delta} \pm 34.7^{\Delta}$. The difference in gain between the left and right eyes before surgery was 0.23 $\pm$ 0.1; in amplitude, 3.0 $\pm$ 3.7. These values were improved at 1 week after surgery (gain, 0.08 $\pm$ 0.06; amplitude, 0.9 $\pm$ 0.65) and continued to improve for 6 months after surgery; however, ocular alignment at near reverted from $5.9^{\Delta} \pm 10.5^{\Delta}$ to $18.9^{\Delta} \pm 17.5^{\Delta}$ by 6 months after surgery. Limitations of the study is the wide age range, and the small cohort. This study suggests in this small patient cohort that surgical correction of ocular alignment improved binocular coordination of smooth pursuit in intermittent exotropia in the first 6 months.

Motor skills in children with strabismus.
Hemptinne C, Aerts F, Pellissier T, Ruiz CR, Cardoso VA, Vanderveken C, Yüksel D.
J AAPOS. 2020 Mar;24(2):76e1-6.

The authors performed a prospective case-control cohort study at one institution between February 2019 to December 2019 to evaluate if specific parameters of childhood strabismus was associated motor difficulties, using the Movement Assessment Battery for Children, Second Edition (MABC-2). Participants included 40 children with strabismus (mean age 7.25, SD 3.83 years; 19 females) and 18 controls (mean age 8.33, SD 5.42 years; 6 females) with no ophthalmic disease. For the strabismic children, results from the MABC-2 indicated that 19 (47.5%) had no motor disability and 21 (52.5%) were at risk or already presented with significant motor disabilities. MABC-2 results were significantly lower for strabismic children without binocularity compared to children with binocularity (P=0.002). Moreover, lack of binocularity was associated with lower motor performance of static balance (P=0.003) and catching tasks (P=0.042). Limitations of the study include the small sample size and the fact that the strabismic and control groups were not the same size and were not matched for age or sex. In summary, the authors found in their small study that lack of binocularity and stereopsis in strabismic chidren as compared to controls is associated with a significant motor skills impairment, especially with catching tasks and static balance.

Relationship between stereopsis outcome and timing of surgical alignment in infantile esotropia.
Yagasaki T, Yokoyama Y, Tsukui M.
J AAPOS. 2020 Mar;24(2):78e1-5.

This was a retrospective review of children (8 years and under) undergoing strabismus surgery for infantile esotropia from 1997 to 2015 at one large community health care organization and hospital. Results included 76 patients divided into three groups: very early surgery (under 8 months old), early surgery (between 8 months and 24 months old), and late surgery (24 months old and up). The authors sought to evaluate the medical records for the timing of surgery and stereopsis outcome in infantile esotropia. Of the 76 patients in the study, 22 (2.6%) patients in the very early surgery group, 30 (39.4%) patients in the early group, and 24 (31.5%) patients in the late group. Surgery for infantile esotropia was the same for all 76 patients, BMR recession. Outcome measures for the binocular response was evaluated using the Bagolini lenses at distance and at near and stereoacuity measured using Randot stereotest or Titmus stereotest. Of note, there was no significant differences between the three groups for pre-operative strabismus angle deviation at initial assessment, at 1 month, or at final post-operative visit.

The final exam averaged at 9.40 months, SD 4.72 months post-operatively for all three groups. Positive binocular response was statistically signficant and reported in 96% patients of the very early group and in 80% patients of the early group as compared to 50% of the late group ($P < 0.001$ and $P<0.05$, respectively). Positive stereopsis was statistically significant and reported in 77% of the very early group compared to 20% of the early group and in 13% of the late group ($P < 0.001$). The authors also reported a correlation between earlier strabismus surgery (especially under 8 months old) and improved stereopsis ($P <0.001$). Limitations of this cohort study include the retrospective evaluation and the fact that although the authors evaluated 18 years of data, only 76 patients were included in the analysis. Another limitation is the evaluation of stereoacuity and Bagolini lenses in all children across all age groups. It is unknown how consistent this documentation was for the cohort. In summary, as the authors report in their discussion section, there study is similar to earlier studies by Wright et al and Birch et al reports of early surgery in patients with infantile esotropia and improved high-grade stereopsis.

Epidemiology of childhood manifest strabismus in the Republic of Moldova.
Paduca A, Arnaut O, Cardaniuc C, Spinei L, Bendelic E, Bruenech JR, Lundmark PO.
Strabismus. 2020 Aug 3:1-8. doi: 10.1080/09273972.2020.1791912. Online ahead of print.

The authors characterized the prevalence of newly detected strabismus in children in Moldova by performing a retrospective chart review of patients seen between 2011-2017. The prevalence ranged from 1.26-1.3%. The rate was highest in children 3-10 years old at 11.7/10,000 children. The rate of esotropia was approximately 16:10,000 and the rate of exotropia was approximately 4:10,000. The authors subsequently compared their findings to studies conducted in other groups, finding lower prevalence in the Moldovian population. However, they note that the limitations of the study include the different inclusion criteria by age and the lack of ophthalmologists in some areas to conduct the exam which could affect the rates.

Young patients with divergence insufficiency related to excessive near work.
Xia Y, Cao L, Peng X, Wang L.
Strabismus. 2020 Jul 10:1-6. doi: 10.1080/09273972.2020.1789676. Online ahead of print.

The purpose of this study was to identify the relationship between divergence insufficiency esotropia and near work characteristics in young adults. The authors prospectively enrolled 12 adults (aged 21-35 years, mean 28.17± 4.06 years) over a 5 year period with DI esotropia measuring at least 10 prism diopters. Esodeviations at initial presentation measured 27.5 PD (range 18-35 PD) at distance and 15 PD (8-20 PD) at near. Most patients (10 of 12) had low fusional amplitudes at distance. After reducing the amount of near work per day to no more than 1 hour for a period of 3 months, all patients noted a significant decrease in the esodeviation to 20 PD (range 10-25 PD) at distance and 8 PD (range 2-13 PD) at near. One patient resolved spontaneously and the other 11 resolved with prism (6 patients) or surgery (5 patients). This study suggests that excessive near work may be a factor in the development of this subtype of esotropia in young adults and that behavior modifications may aid the treatment in conjunction with prisms and strabismus surgery.

Evolving trends in strabismus following retinal surgery: is there still a role for botulinum toxin?
Moorthy S, Theodorou M, Hancox J, Adams GG.
Strabismus. 2020 May 12:1-6. doi: 10.1080/09273972.2020.1752263. Online ahead of print.

Ocular motility disturbances after retinal detachment repair have decreased as vitrectomy has become the preferred method of treatment. The authors performed a retrospective review of medical records for received botulinum toxin between January 2006 and August 2017 at Moorfields. 32 patients with a mean follow up of 20 months (range 1-132 months) were included. They found an equal number of good (50% or greater reduction in baseline angle and/or resolution of diplopia) and poor (<50% reduction in baseline angle) responded. There were an equal number of vitrectomies compared to scleral buckles in each group. Of note, the macula was detached at presentation in 75% of cases, both across the board and in

each group. Repeat injections were needed with patients requiring a mean of 6-8 injections. The authors correctly identify a selection bias, as patients who received botulinum may have had a complex retinal surgery history and thus were less likely candidates for strabismus surgery. Additionally they highly that poor baseline visual acuity and multiple retinal procedures limit fusional potential. With that in mind, botulinum injections could be considered in patients who are poor candidates for strabismus surgery to restore binocularity in those with good fusional reserves and limited macular pathology.

Prism treatment of acute acquired concomitant esotropia precipitated by visual confusion.
Chang F, Wang T, Yu J, Li M, Lu N, Chen X.
Strabismus. 2020 Mar;28(1):7-12.

This study characterized the clinical findings in patients with acute acquire concomitant esotropia. Of the 30 patients enrolled, the average age was 29.7 years old (range 14-52). The amount of deviation ranged from 12-60PD at distance and 10-46PD at near. Most patients (28) were myopic. All patients underwent neuroimaging and neurologic evaluations were normal in all patients. All patients were fitted with Fresnel prisms and diplopia resolved in 27 of the patients with prism treatment. The remaining three patients underwent surgery, although the specific outcomes were not defined. All patients regained stereopsis. The authors speculate that increasing near work demands increase medial rectus tone and thus disrupt convergence and divergence mechanisms. The authors suggest that a complete motility exam, neuroimaging and a neurologic evaluation performed in patients presenting with acute acquired concomitant esotropia to rule out paresis, but once the diagnosis is confirmed, prism therapy is highly successful.

The prevalence of tropia, phoria and their types in a student population in Iran.
Hashemi H, Pakzad R, Nabovati P, Azad Shahraki F, Ostadimoghaddam H, Aghamirsalim M, Pakbin M, Yekta A, Khoshhal F, Khabazkhoob M.
Strabismus. 2020 Mar;28(1):35-41.

This study determined the prevalence of tropias and phorias in university students at a specific site in Iran. Of the 752 students who participated, the prevalence of tropia was 1.5% (1.2% exotropia, 0.3% estropia). The prevalence of phoria was 12.9% (11.7% exophoria, 1.2% esophoria). Exodeviations were higher in myopic individuals. The authors concluded that the prevalence was similar to the general Iranian population but lower than the general population. This study offers a limited scope of information on a small sub-population that has limited generalizability in and of itself but could be combined with other studies in different populations or a sub-analysis of those with ashthenopia to have a greater impact.

Longitudinal Development of Ocular Misalignment in Nonhuman Primate Models for Strabismus
Apoorva Karsolia, Emily Burns, Mythri Pullela, Vallabh E. Das
Invest Ophthalmol Vis Sci. April 2020;61, 8

This small study of 8 infant monkeys sought to determine if there were long lasting effects of induced strabismus by using Fresnel prisms at an early age. After using prisms for 4 months, starting at age 3 days, the monkey with prisms were all noted to have moderate to large angle strabismus. After 16 weeks without prisms, all monkeys that received prismatic treatment continued to have an average of 7 degrees of exotropia which was clinically significant from the 2 monkeys without prismatic treatment. This study shows a continued binocular and strabismic deficit when binocularity is disrupted at a very young age even when corrected afterwards.

Morphological Differences in the Inferior Oblique Muscles from Subjects with Over-elevation in Adduction
Jolene C Rudell, David Stager, Jr, Joost Felius, Linda K McLoon
Invest Ophthalmol Vis Sci. June 2020;61, 33

This small study of immunohistological staining of inferior oblique muscles from patients with primary overaction of the inferior oblique and Apert Syndrome sought to determine the histological differences in the muscles when compared to controls from donor eye bank eyes. In both the patients with primary overaction of the inferior oblique and those Apert Syndrome, changes were noted in the myosin heavy chain isoform patterns and an increase in neuromuscular junctions and nerve fiber densities were also noted. There were other histologic changes in the muscles from the Apert patients showing continuous changes over time. Future studies may look to compare the clinical grading of overaction and potential MRI images of the inferior oblique muscles to their immunohistological staining.

Reflexive Fusional Vergence and Its Plasticity Are Impaired in Convergence Insufficiency
Ian M Erkelens, William R Bobier
Invest Ophthalmol Vis Sci. Aug 2020;61, 21

This small study compared 10 patients with convergence insufficiency and 10 control patients. Reflexive vergence responses to an accommodative target were measure for both convergence and divergence. While there was no significant difference in divergence, there was a notable decrease in reflexive fusional convergence in the convergence insufficiency group along with increased response durations and settling times. This may give some extra insight into the complaints of patients with convergence insufficiency. Much else from the study is difficult to extrapolate due to the sample size, though this will lead to further studies with larger samples in order to not only get a better understanding of the neural inputs in patients with convergence insufficiency, but also to treatments based on these neural inputs.

Prevalence of Strabismus and Its Impact on Vision-Related Quality of Life: Results from the German Population-Based Gutenberg Health Study
Achim Fieß, Heike M. Elflein, Michael S. Urschitz, Konrad Pesudovs, Thomas Münzel, MD,5,8 Philipp S. Wild, Matthias Michal, Karl J. Lackner, Norbert Pfeiffer, Stefan Nickels, Alexander K. Schuster
Ophthalmology. Aug 2020(8);127:1113-22.

This study analyzed the prevalence of manifest strabismus and quality of life in older adults (35 to 74 years) as part of an ongoing health survey. Strabismus was diagnosed by Hirschberg light reflex by an ophthalmologist and further subdivided into comitant or inconcomitant (paralytic). Subjects also completed the VRQ-25 quality of life survey. Out of slightly less than 15,000 participants, the overall rate of manifest strabismus was 2.9%, with 1.6% esotropia and 0.8% exotropia as the predominant forms and only two subjects were diagnosed with paralytic strabismus. Lower visual acuity in both eyes, anisometropia, and hyperopia had increased odds of strabismus, while older age had decreased odds for strabismus. Subjects with strabismus had small but significant decreased overall and socioemotional quality of life. A weakness is the upper age limit of 74 years, since sagging eye syndrome tends to cause esotropia in older adults, and the lack of quantification of the magnitude of the strabismus. Larger angles of strabismus might be associated with greater quality of life issues.

Everything You Need to Know in 2020 About Compartmental Strabismus
Pineles SL, Chang MY, Velez FG.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3): 71-78

Recent reports confirm innervational compartments of select rectus extraocular muscles as well as the superior oblique. Histopathological and orbital imaging studies demonstrate well defined compartmental innervation of the horizontal rectus muscles with less differentiation in the vertical rectus muscles. Acquired vertical misalignment not associated with cyclovertical muscle dysfunction has been associated with horizontal rectus muscle compartment dysfunction. Pattern and other forms of strabismus have been associated with segmental or compartmental abnormal innervation of the extraocular muscles. Taking advantage of segmental function and innervation, selective weakening and strengthening procedures have been used to treat patients with incomitant near/distance disparities, incomitant vertical and torsional strabismus, and patients with A- and V-pattern strabismus. Because compartmentalization is

present in some muscles and not in others, the effect that it has in surgery may differ depending on the deviation. Computational biomechanical models (such as the program Orbit 1.8 by Eidactics) of the extraocular muscles may be helpful to predict muscle forces and directions generated by the muscle.

Differences of a Single Injection of Botulinum Toxin A between Infantile and Nonaccommodative Esotropia
Gama R, Santos JC, Nom TY, de Costa DC.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):98-102

The purpose of this study is to compare the results of a single injection of botulinum toxin A (BTA) between children with infantile esotropia (IET) and nonaccommodative esotropia (NAET) during the first 2 years after treatment. This retrospective study that included 23 children with IET and 25 with NAET. Administration of BTA was delivered in both eyes in all children. The dose administered was 2.5 units (U) BTA ®/muscle in patients younger than 2 years of age, and 2.5 U BTA ® on the fixing eye and 5.0 U on the non-fixing eye patients with 2 years of age or older (concentration: 5 U/0.1 ml). At 6 months, 1 and 2 years after treatment, the deviation and stereoacuity were evaluated. At 6 months and 1 year after treatment there was no difference in ocular alignment between the two groups. Success criteria were achieved in 36.8% in IET group and 60.0% in NAET at 6 months $p = .129$, and 57.9% in IET group and 68.0% in NAET group at 1 year $p = .352$. Two years after treatment, there were statistical differences between motor alignment (IET group 21,1% and NAET group 60.0%, $p = .007$) and stereoacuity (IET group 40% and NAET group 90%, $p = .004$) between the two groups. Although side-effects affected most children during the first week (in the first week, overcorrection was present in 16 (84.2%) children with IET, and in 19 (76.0%) children with NAET; and ptosis affected 15 (78.9%) children with IET and 17 (68.0%) children with NAET), at 6 months all the effects have disappeared on both groups. The authors recommend BTA as an alternative, but not as definite treatment in IET if the surgeon/parents are not comfortable with an early strabismus surgery; but retreatment or surgery will have to be considered after 1 year. On the contrary, the authors feel that BTA may be a first-line treatment of NAET because it is an easy, safe and has a long-lasting effect. A study comparing the outcomes of BTA to surgical correction would be helpful to directly compare the two techniques.

Late Surgical Correction of Longstanding Constant Strabismus in Adults: Is Fusion Possible in All Successfully Aligned Patients?
Tomac S, Uyer E, Akin T, Mutlu M, Altinsoy.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):109-114.

The goal of this study was to determine whether late surgical correction provides fusion in adults who have constant strabismus beginning in early childhood. This was a prospective study that included 34 consecutive adults with a history of early onset strabismus who had not previously undergone surgery. They were tested with the Bagolini striated glasses (BSG), Worth four-dot (W4D) test, cover test, and four-prism diopter (4-PD) test, preoperatively, and 6 weeks after surgery. The mean age of the patients was 23.8 years; 17 patients had esotropia and 17 patients had exotropia. Preoperatively, all patients demonstrated a manifest horizontal deviation ranging from 30^{Δ} to 60^{Δ} and had suppression. At 6 weeks postoperatively, 33 patients had a horizontal manifest deviation of $<15^{\Delta}$ (range, 2^{Δ}-14^{Δ}; median, 6^{Δ}), and none were orthotropic as determined by the cover test together with the 4-PD test. All of these 33 patients achieved anomalous retinal correspondence (ARC) with the BSG at near, and 25 (75%) had ARC with the W4D test at near, although none demonstrated stereopsis. This study had a limited number of patients its findings suggest it is possible to develop ARC after surgery in many adult patients with childhood-onset strabismus associated with suppression, and who have not previously been operated upon, if satisfactory alignment is achieved in adulthood, even if the first surgical alignment is performed at 20 years of age or greater. Anomalous retinal correspondence provides an anomalous type of fusion in natural visual conditions even though it is weaker than normal fusion. A larger study to evaluate this concept would be interesting and beneficial.

Objective cyclodeviation measurement in normal subjects by means of Cyclocheck application.
Simiera J, Ordon AJ, Loba P.
Eur J Ophthalmol. 2020 Feb 14:1120672120905312. doi: 10.1177/1120672120905312. Epub ahead of print. PMID: 32054328.

Cyclodeviation is an important assessment in a motility disorder. A variety of subjective and objective techniques have been used to evaluate this. Subjective methods are limited due to the sensory and psychological adaptions and not suitable for children and patients without binocularity. Standard assessments have been proposed based on the anatomic alignment of the globe around the antero-posgerior axisis based on the measurement of the disc-foveal angle (DFA). The purpose of this study is to assess the use of the Cyclocheck application for an objective assessment of cyclodeviation. Healthy subjects with normal muscle balance and good stereopsis and vision acuity. Two fundus photographs were taken of each eye and the DFA was calcuolated using the Cyclocheck applications. A total of 131 patients met includsion criteria. The man DFA for the whole group was 6.39+-2.72 degrees for the right eye and 7.52 +/-2.39 degrees for the left eye. These results fit within the normative values of the DFA reported on the literature of 0-13 degrees. This study did find a significant difference between the two eyes. The study did find the software to be efficient and repeatable, however further studies need to e done to take variables into account of the utility of this software.

Association of Strabismus With Functional Vision and Eye-Related Quality of Life in Children.
Hatt SR, Leske DA, Castaneda YS, Wernimont SM et al.
JAMA Ophthalmol. 2020 May;138(5): 528-535.

The relationship between strabismus and eye-related quality of life in children and their families was evaluated using the Pediatric Eye Questionnaire (PedEyeQ). This was a cross-sectional study from December 2017 to October 2019 at Mayo Clinic in Rochester, MN and the Retina Foundation of the Southwest in Dallas, TX. 91 children with strabismus and 166 visually normal (non-amblyopic) controls across three age groups (0-4 years, 5-11 years, 12-17years) were included. Participants and their parents completed either the child PedEyeQ or the proxy PedEyeQ and/or parent PedEyeQ and Rasch-calibrated PedEyeQ scores were calculated for each domain and converted to 0 (worst) to 100 (best). The PedEyeQ addresses functional vision, bothered by eyes/vision, social, frustration/worry, as well as impact on parent and family, worry about child's eye condition, worry about child's self-perception and interactions, and worry about child's functional vision domains. Results of the child PedEyeQ domain scores were lower with strabismus participants versus visually normal controls among children 5-11 years with the greatest mean difference in functional vision (12 points, SD 14 points; P=0.001). For children 12-17 years, the greatest mean difference in frustration/worry (27 points, SD 13 points; P<0.001). The proxy PedEyeQ scores were also lower in children with strabismus. Of note, for children 0-4 years and 5-11 years, the greatest mean difference was in functional vision (13 points, SD 9 points; P<0.001 and 26 points, SD 10 points; P<0.001), respectively. For children 12-17 years, the greatest mean difference was in functional vision (21 points, SD 12 points; P<0.001) and social (21 points, SD 13 points; P<0.001) and frustration/worry (21 points, SD 13 points; P<0.001). Similar to child and proxy PedEyeQ, parent PedEyeQ domain scores were lower with strabismus and the greatest mean difference was in worry about child's eye condition (38 points, SD 14 points; P<0.001). Limitations of the study include the racial homogenity with 81.3% white participants. Another limitation is that the authors didn't design the study with regard to other amblyopia treatment (ie spectacles) and its relationship to strabismus and eye-related quality of life in children. In summary, the PedEyeQ findings of this study report that strabismus is associated with a reduced functional vision and eye-related quality of life in children and their families. This study helps recognize the quality of life issues surrounding strabismus in children and their longitudinal management.

Incidence of Strabismus and Amblyopia Among Children Initially Diagnosed With Pseudostrabismus Using the Optum Data Set.
Ryu WY and Lambert SR.
Am J Ophthalmol. 2020 Mar; 211:98-104.

This is a very large population based retrospective cohort study. The goal of this study was to determine the frequency of strabismus among children originally diagnosed with pseudostrabismus. The data was taken from a large set of 17,885 children initially diagnosed with pseudostrabismus at or before the age of 3. Of those patients, 9.6% (1,725) went on to be diagnosed with strabismus, with esotropia being the most common form of strabismus. About 21.9% of these patients went on to need strabismus surgery. The authors concluded that patients diagnosed with pseudostrabismus are at increased risk of developing strabismus and needing strabismus surgery. The paper's main strength is the giant data set, but that also contributes to it's weakness as being unable to validate each data point since data collection was based on ICD9 codes. Nonetheless this is the largest paper defining the rate of true strabismus in this specific patient population. This is a really important for the pediatric ophthalmologist trying to council their patients on need for follow up exams and future risk of needing eye muscle surgery.

Automated Diagnosis and Measurement of Strabismus in Children.
Yehezkel O, Belkin M and Wygnanski-Jaffe T.
Am J Ophthalmol. 2020 May; 213:226-234.

This prospective, masked, inter-rater reliability study included 69 pediatric patients and compared manual prism alternating cover test (PACT) at a distance of 50cm to an automated system to measure strabismus. The purpose of this test was to determine the efficacy of this automated system, and the amount of time needed to perform this measurement. The reason to do this is that manual measurements of strabismus have a subjective component, are time consuming, and can vary with factors such as patient age and examiner experience. In their study, the authors found a high correlation between the automated and manual tests for horizontal and vertical deviations. The system studied is a an eye tracking based device called the EyeSwift system using near infrared illumination. To do this, the patient ears the wireless glasses (can be done over their prescription glasses) with a liquid crystal displace active shutter glasses that performs an automated alternate cover test and cover uncover test. This system is not designed to measure torsion, could not be easily used in patients with nystagmus, and cannot distinguish DVD from a vertical deviation. Nevertheless, this is an interesting contribution to the growing data on automated strabismus measurements.

The Effect of Axial Length on Extraocular Muscle Leverage.
Clark RA and Demer JL.
Am J Ophthalmol. 2020 Aug; 216:186-192.

The goal of this prospective observational case series of 36 orthophoric adults was to use MRI imaging to determine the effect of axial length (AL) on globe rotational axis and horizontal extraocular muscle leverage during horizontal duction. The authors at a single academic center studied patients with a range of ALs and performed high resolution axial orbital MRs in large controlled adduction and abduction. They measured the ALs in planes with maximum cross section and used area centroids to calculate the globe centers. Lever arms were calculated as distanced between published extraocular muscle insertions and rotational axes. The authors found that the increase in axial length did not change the rotational axis position and concluded that the globe rotates around a point nasal and anterior to its geometric center – this gives the lateral rectus more leverage than the medial rectus. Since the rotational axis remains the same, the per-millimeter dose /response in longer eyes will be reduced. This reduction in dose per millimeter may decrease the effect of tendon repositioning in patients who are highly myopic and have longer axial lengths.

10. STRABISMUS SURGERY

Medial Rectus Advancement for Secondary Exotropia
Allison C. Umfress, Alexis M. Flowers, Yuhan Liu, Yuxi Zheng, Qingxia Chen and Sean P. Donahue.
American Journal of Ophthalmology, 2021 Jan; 221: 65-74.

The authors of this retrospective interventional case series studied patients who had medial rectus advancement for the treatment of consecutive exotropia. In this study of 221 patients, 98 patients had unilateral medial rectus advancement (UMRadv), 89 patients had UMRadv with lateral rectus recession, and 34 patients had bilateral BMRadv. Almost 40% of patients were found to have a stretched scar at the time of surgery and in those patients the stretch scar was resected at the same time that the muscle was advanced. The stretched scar found intraoperatively was significantly associated with a preop adduction deficit. The authors found that the larger preoperative duction deficits, the larger the stretch scar that was found. The authors calculated the prism diopter change for each of the surgeries, notably those with stretched scar had less prism diopter correction per millimeter. They found that many patients had abduction deficits at week one that were gone by month two. This study's limitations include the fact that it was done from a single surgeons patients. The authors concluded that medial rectus advancement had good results as post op month two and that this is a really important surgery in cases of a stretched scar. The highlight of this study to me was the importance of a generous resection on medial rectus muscles that have a stretched scar when planning surgery in consecutive exotropia.

Contralateral Surgery for the Treatment of Third Nerve Palsy with Aberrant Regeneration.
Fouad HM, Kamal AM, Awadein A, Del Monte MA.
Am J of Ophthalmol 2021 Feb; 222: 166-173.

This retrospective case series from 2 different centers describes the results of contralateral recession-resection of the horizontal muscles in oculomotor nerve palsy with aberrant regeneration to correct both the strabismus and ptosis in one procedure. Patients were included if they had both exotropia and aberrant regeneration with a ptosis that improved on adduction. All patients had contralateral lateral rectus recession and medial rectus resection. Ductions, versions, angle of misalignment, and degree of ptosis were evaluated before surgery and at last follow-up. Eleven patients had surgery at a mean age of 15.0 ± 9.2 years. Five patients were male (45%) and the etiology of the CNIII palsy was trauma in 8 (72%) of the cases. The mean angle of exotropia was 42 ± 14 prism diopters. The mean degree of ptosis was 3.9 ± 1.6 mm. The mean lateral rectus recession was 8.2 ± 1.1 mm, and the mean medial rectus muscle resection was 6.7 ± 0.9 mm. The mean follow-up was 6.4 ± 2.5 months. After surgery, none of the patients had residual exotropia >10 prism diopters. The mean degree of ptosis after surgery was 0.9 ± 0.8 mm. None of the patients required further surgery for ptosis or strabismus.

Importance: Contralateral eye muscle in third nerve palsy with aberrant innervation offers the advantage of simultaneous correction of both strabismus and ptosis through a single procedure. A disadvantage is that this technique involves operating on the sound eye—which may not be acceptable to some patients—and could reduce ductions of the sound eye.

Hummelsheim procedure combined with medial rectus recession in complete sixth nerve palsy and esotropic Duane Retraction Syndrome
Bagheri A, Veisi A, Tavakoli M.
Eur J Ophthalmol. 2020 Nov 23

Complete cranial neve 6 palsy (CN6p) and esotropic Duane Retraction Syndrome (DRS) are the most common causes of esotropia with limited abduction. The authors of this study propose the effects of half tendon vertical rectus muscle transposition (HVRT) combined with medial rectus recession (MRc) on

esotropia, face turn, and abduction deficiency in patients with CN6p and DRS in this retrospective single center study. A total of 55 patients underwent this combined surgical procedure and 16 were excluded due to prior surgery. Of the 39 patients, 22 had CN6p and 17 had DRS. In the CN6p group, all patients had a stable deviation for at least 12 months prior to surgery but did have botox 1-2 times prior to surgery. There was a significant improvement in alignment outcome with this surgical procedure. In the DRS group, there was significant improvement in alignment however, one patient had an overcorrection and developed consecutive exotropia. The authors had improvement in head position and also described an improvement in abduction with this surgical procedure in both groups. Larger cohort studies need to be done to validate these findings.

Peribulbar anesthesia for strabismus surgery in adult patients.
Vagge A, Simonetti F, Marenco M, Burtolo C, Musolino M, Traverso CE.
Eur J Ophthalmol. 2020 Nov 22

Most strabismus surgeries are done under general anesthesia and some under retrobulbar anesthesia, however both forms of anesthesia have their respective risks. The aim of this study was to evaluate the efficacy and safety of peribulbar anesthesia in adult strabismus. The authors had 510 patients in their study group with a variety of strabismus surgeries (muscles not specified). 40.6% of their patients had bilateral surgery. There were no permanent complications observed with this block up to 6 weeks post operatively. 0.7% of patients required supplemental injection because of pain during the procedure despite topical anesthetic. This is an option for anesthesia in adult strabismus cases with low risks.

Outcome of surgery for near angle in patient with incomitant distance/near esotropia and without manifest deviation at distance.
Scaramuzzi M, Serafino M, Nucci P.
Eur J Ophthalmol. 2020 Nov 2

Different approaches have been used to manage partially accommodative esotropia with high AC/A ratio. The authors aim of the study was to investigate how patients with a manifest deviation <10 PD at distance and an angle larger than 10 PD at near would respond to a surgical approach for the near deviation. This was a prospective case series of 6 patients. There was no significant difference in the angle of esotropia at distance at follow up and no consecutive exotropia post-surgery. All patients developed different degree of stereopsis. The authors showed good post-surgical condition at least 6 months post-operatively. They did consider that all patients did show an increase in their distance angle after a patch test to confirm the hypothesis that these patients may have strong fusional divergence at distance to mask the real deviation. This is helpful in considering how to proceed surgically in the management of such patients.

Outcomes of symmetric bilateral medial rectus recession in large-angle esotropic Duane syndrome.
Nabie R, Manouchehri V, Azad B.
Eur J Ophthalmol. 2020 Nov 4

When esotropic duane syndrome (EDS) has a large primary position of deviation (larger than 20 PD), surgical planning becomes more complex. Options include medial rectus recession of both eyes, or transposition of the vertical muscles. Jampolsky was the first to propose the idea of asymmetric bilateral medial rectus recession with more recession in the uninvolved eye to induce “fixation duress” via introducing adduction limitation in the normal eye. However, this could lead to convergence insufficiency. The authors hypothesize that symmetric bilateral medial rectus recession for deviations larger than 20 PD to help improve primary position deviation, abnormal head posture and ocular ductions. They analyzed 30 patients with this criteria and surgery. 76.7% of patients had a successful outcome. No cases of consecutive exotropia occurred. This provides one option to correct large deviations without the risk of inducing vertical deviations or torsion by operating on the vertical rectus muscles.

Modified Y- split and recession of medial rectus muscles in convergence excess esotropia.
Bagheri A, Abbasnia E, Tavakoli M.
Eur J Ophthalmol. 2020 Oct 23

Convergence excess esotropia (CEET) is characterized as near esotropia greater than distance by 10 PD of deviation. Traditionally bifocal glasses have been used as a first-line treatment in a clinical setting. Besides bifocals, a variety of surgical procedures have been introduced to address CEET. The authors introduce another technique, a modified Y-splitting technique combined with the recession of MR muscles in patients with CEET. 14 patients were enrolled. The mean deviation before surgery was 31 PD at distance and 45 at near. These decreased to 2.4 PD at distance and 3.6 PD at near after surgery. The success rate in terms of alignment was 78.6%. All patients except one could remove the bifocal glasses. Stereopsis improved in 5 patients. This provides another surgical technique for this type of strabismus. A comparative analysis of non-surgical and surgical varieties would be important as a next step.

Lateral rectus advancement versus medial rectus recession for consecutive esotropia.
Fard MA, Ghahvehchian H.
Eur J Ophthalmol. 2021 Jan;31(1):258-262.

Surgical options for consecutive esotropia following bilateral lateral rectus recession for intermittent exotropia include lateral rectus advancement or medial rectus recession. The authors aim was to compare the effect of these surgeries. This was a single center retrospective review comparing medial rectus recession to lateral rectus advancement for consecutive esotropia with a minimum follow up of 6 months. The goal outcome was defined as a esophoria or exophoria <8 PD not requiring a third surgery. 43 cases were identified. The post-operative success rate for LR advancement was 90.9%. The post-operative success for MR recession was 71.4%. The authors concluded that LR advancement led to significantly less post-operative undercorrection than MR recession. This is an important consideration as re-operations can be less predictable. They concluded that the operation on a previous LR based on ¼ the angle of deviation might correct the consecutive deviation without clinically evident abduction limitation.

Lateral rectus resection versus lateral rectus plication in patients with residual esotropia.
Rajavi Z, Sabbaghi H, Kheiri B, Sheibani K.
Strabismus. 2020 Oct 21:1-7. doi: 10.1080/09273972.2020.1832544.

The goal of this study was to compare lateral rectus plication to lateral rectus resection in patients with residual esotropia. Of the 57 patients, 27 were randomized into the plication group and 30 into resection group. The demographics and clinical characteristics of the group were similar. The results showed no statistically significant difference in the postoperative mean angle of deviation at 1, 3 and 6 months postop. There was a slightly larger postoperative esoshift in the plication group at months 3 (11%) and 6 (14.8%), than in the resection group (3 and 6.7%, respectively). There were no cases of consecutive exotropia in either group. The authors conclude that either procedure is safe and effective, but suggest plication may be preferred in patients at risk of anterior segment ischemia.

Evaluation of single stage adjustable strabismus surgery (SSASS) under topical anesthesia in patients with symptomatic diplopia.
Ganesh SC, Rao SG, Narendran K.
Strabismus. 2020 Oct 19:1-8. doi: 10.1080/09273972.2020.1832545.

Single stage adjustable strabismus surgery (SSASS) has the advantages of using topical anesthesia, faster rehabilitation, and better cost-effectiveness. The authors performed a prospective observational case series of 16 adult (mean 28.12 years, range 19-65 years) patients undergoing SSASS during a 1 year period. Surgical procedures included single muscle recession (4) or recession/plication in the same

eye (12). Prior to adjustment, 10 of 16 patients were diplopic post-operatively and required adjustment. Of note, topical anesthesia was well-tolerated and the only complaint was discomfort hooking the muscle. No patient required supplemental sub-Tenons anesthetic. No patients had an oculocardiac reflex requiring atropine injection. Patients with esotropia attained orthotropia. Patients with exotropia tended to have a recurrent exodrift over time. The authors concluded that SSASS is safe and has good outcomes, however a small overcorrection may be the target for exotropic patients even if it were to result in diplopia at the time of adjustment.

Surgical treatment for small-angle vertical strabismus.
Sanz PM, Osuna V, Gómez de Liaño Sánchez P, Torres HED.
Strabismus. 2020 Oct 16:1-5. doi: 10.1080/09273972.2020.1832543.

Surgical intervention for patients with small angle vertical strabismus (<10PD) has become more popular as patient demand to be spectacle free has increased. The authors performed a retrospective review of medical records to assess the success of partial recession of the vertical rectus muscles with a formula of 1 mm of partial correction to correct 1.5 PD of deviation. Seventeen patients with a mean age 69.1 years (range 54-85 years) were reviewed. The diagnoses were varied, including paralytic and restrictive etiologies of strabismus. The mean preoperative deviation was 6.11 PD (range 4-10). The operation was performed on the SR in 11 patients (7 temporal, 4 nasal) and IR in 6 patients (3 temporal, 3 nasal). The mean post-operative deviation was 2.05 PD (range 0-6) at mean follow up of 10 months, for a 76% success rate. There were no overcorrections. The limitations of the study are the retrospective design, short follow up and varied etiologies of strabismus, however the authors emphasize that partial recession was successful in most cases and has the advantages of short operating time and reduced risk of anterior segment ischemia.

Surgical outcomes of augmented bilateral lateral rectus recession with conjunctival recession in patients of intermittent exotropia.
Verma R, Singh A, Agrawal A, Samanta R, Panyala R, Waghamare S, Mittal SK, Kumar B.
Strabismus. 2020 Oct 16:1-7. doi: 10.1080/09273972.2020.1832541.

The purpose of this study was to evaluate the surgical outcomes of an augmented bilateral lateral rectus (BLR) recession with conjunctival recession to the insertion in children and young adults with basic intermittent exotropia in the first six months after surgery. The authors noted that the augmented surgical dose is 1.5mm greater than Park's table. This prospective study enrolled 15 patients (mean age 19.6 years, range 9-31 years) with a mean preoperative deviation measuring 30 PD (range 16-42). On POD 1, 93.3% of patients were orthophoric. At POM 6, all patients were ortho at distance and 3 patients had an over (2 patients) or under (1 patient) correction. The authors conclude that performing the augmented BLR recession and adding conjunctival recession improved outcomes as it reduces undercorrection/recurrence. However the study is limited by a small sample size and lack of a control arm to accurately compare the effect of conjunctival recession.

Outcomes of pediatric accommodative esotropia with botulinum toxin A treatment in Thailand.
Wangtiraumnuay N, Surukrattanaskul S, Surakiatchanukul T, Masaya-Anon P, Hiriotappa J.
Strabismus. 2021 Jan 6:1-8. doi: 10.1080/09273972.2020.1871379.

In this retrospective study, the authors investigated the efficacy of botulinum toxin injections in the medial rectus muscle of children with accommodative esotropia from 2010-2017. Of the included 102 patients, the pre-op mean angle of deviation of 40PD decreased to 11PD at 2 weeks, 19 PD at 3 months and 25 PD at 6 months. The authors report that 67.0% of patients had satisfactory (50.0%) or excellent (ortho to esotropia < 10PD, 17%) at the 6 month visit. Complications were fairly common and included ptosis (37.25%), exotropia (11.76%), and hypertropia (4.9%), although these were reversible. This suggests that botulinum toxin may be a treatment methodology in children with accommodative esotropia who do not cooperation with glasses.

Single horizontal rectus muscle vertical augmented transposition with posterior fixation suture in management of monocular elevation deficiency.
Chen AC, Velez FG, Silverberg M, Bergman M, Pineles SL.
Strabismus. 2021 Jan 7:1-6. doi: 10.1080/09273972.2020.1871376.

This case series describes the clinical outcome of 3 patients with acquired monocular elevation deficiency who underwent superior transposition of the lateral rectus (LR) muscle with or without simultaneous inferior rectus (IR) weakening. Of note, 1 patient had IR recession and 1 patient had a botulinum injection to the IR. The mean hypotropia was reduced from 35 prism diopters (PD) (range: 20 to 60 PD) to 4.67 PD (range: 0 to 14 PD) with a mean correction of 32.57 ± 9.34 PD after 9 months. The authors conclude that the transposition of the LR appears to be successful with or without the IR weakening but emphasize that the position along the spiral of Tillaux must be maintained so as to not recess the muscle.

Horizontal rectus muscle transplantation for recurrent and residual strabismus.
Kannam M, Sutraye J, Kapoor R, Tibrewal S, Kekunnaya R, Sachdeva V.
Strabismus. 2021 Jan 20:1-9.

This study reported the outcomes of a retrospective multi-center, observational study of patients who underwent transplantation of resected muscle for re-operation for residual or recurrent strabismus in 7 patients. The patients had a mean age of 24 year and 6 presented with XT. The median pre-operative primary position deviation reduced from 40 prism diopters (PD) (range: 30 to 55 PD) to 8 PD (range: 6 PD ET to 10 PD XT) at six-weeks follow-up. For the results, the authors excluded 2 patients as they had additional large re-recessions. Of the remaining patients, 60% (3/5) achieved surgical success (≤ 8 PD) and all (100%) achieved cosmetic success (≤12 PD) at six-weeks-follow-up. The median correction obtained per mm of muscle transplantation at 6-weeks followup was 2.8PD, however there was a very wide range (range: 1.1 to 7.5 PD). No post-operative diplopia was noted, although the authors state that all patients had a sensory strabismus, which would make the risk of diplopia much lower. Although muscle transplantation does have the potential advantages of avoiding re-operations on multiple muscles and decreasing the risk of over weakening a muscle due to a large recession, the small number of patients in the series, surgeon variation, operating on previously operated vs naïve muscles and the variable amount of correction per millimeter of the transplanted segment should be considered.

Strabismus Surgery in Thyroid-Associated Ophthalmopathy; Surgical Outcomes and Surgical Dose Responses
Akbari M, Bayat R, Mirmohammadsadeghi A, Mahmoudzadeh R, Eshraghi B, Salabati M.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):150-156.

The authors state that the goal of their paper is to investigate the success rate and surgical dose responses in strabismus surgery of thyroid-associated ophthalmopathy (TAO). Thirty-three patients (26 men) were included in this study and underwent strabismus surgery. The mean follow-up time was 11.3 ± 6.5 months. Success was defined as the proportion of patients with a horizontal deviation of less than 10 PD, vertical deviation of less than 4 PD, and no subjective diplopia in primary and downgaze. After the final follow-up visit, strabismus surgery was successful in 87.8% of patients. Pre-operative factors (age, gender, smoking, corticosteroid usage, radioactive iodine, orbital decompression, optic neuropathy, baseline deviations, extorsion, type of strabismus, TAO duration) were not statistically correlated with success. Dose responses were calculated to be 3.44 ± 0.66 PD/mm of medial rectus recession and 4.83 ± 1.48 PD/mm for vertical rectus recession. Patients with deviation ≥25 PD had significantly larger surgical dose response compared to the group with deviation<25 PD (p value = .003 for horizontal and p-value <0.05 for vertical deviations). In eyes with predominant hypotropia, we found 1.64 ± 1.37 PD decrease in esotropia for each millimeter recession of inferior rectus muscle. Surgical dose responses in large deviations were significantly higher than the moderate angle of deviation. The reported mean for vertical dose responses may vary in different patients based on the laterality and

involvement of superior rectus muscles. The recession of inferior rectus muscle may correct mild-to-moderate esotropia without the need for horizontal muscle surgery.

Modified Anterior Superior Oblique Tuck: A Case Series
Solanes F, Velez FG, Robbins L, Pineles SL.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):157-162.

Selection of the ideal procedure to correct symptomatic excyclotropia depends on several factors including the degree of torsion and associated vertical, horizontal and pattern deviation. Selective tuck of the anterior temporal torsional fibers of the superior oblique (SO) tendon is an alternative procedure to the classical Harada-Ito. The purpose of this study is to report its stability and results. This was a retrospective review of consecutive patients with symptomatic excyclotorsion of at least 5º (degrees) treated by selectively splitting and tucking the anterior temporal fibers of the SO tendon. Torsion in primary position was measured using the double Maddox Rods. Patients with additional symptomatic vertical or horizontal diplopia underwent simultaneous surgery on other extraocular muscles. Five patients were studied. Mean age was 60 ± 8 years (47–67). Mean postoperative follow-up was 10 ± 8 months (3–21). The mean preoperative torsion of 11º±4º (7º-15º) significantly decreased to 3º±2º (p = .03) at the first postoperative visit (16 ± 9 days) and 3 ± 2º during the last visit (P = .03). The procedure corrected 1.4º±0.9º per mm of tuck. Postoperatively no patient complained of torsion. No undesirable vertical or horizontal deviations were noted. The authors conclude that this technique is a simple alternative to manage symptomatic excyclotorsion, with significant and stable relief of moderate amounts of torsion and without inducing unexpected vertical or horizontal deviation.

Adjustable graded augmentation of superior rectus transposition for treatment of abducens nerve palsy and Duane syndrome.
Dagi LR, Elhusseiny AM.
J AAPOS. 2020 Oct;24(5):268.e1-268.e7.

This is a retrospective review of 8 medical records of patients who underwent adjustable graded augmented superior rectus transposition (SRT) with or without adjustable medial rectus recession (MRc) from February 2017 to December 2019 at Boston Children's Hospital by a single surgeon, to evaluate postoperative vertical or torsional diplopia. The patients included those who underwent surgery for abducens nerve palsy or esotropic Duane syndrome. Patients with prior vertical muscle surgery or post operative follow up less than 2 months was excluded. Torsion was measured using double Maddox rod. A corneal toric marker was used to mark 6 and 12 o'clock and a straight ruler extending the marks to skin and drapes. The 4, 6, 8 and 10 mm myopexy sites along superior and inferior border of lateral rectus was marked. The augmentation sutures were placed in these positions according to pre-surgical measurements and cut if there was unwanted vertical or torsional change in the immediate postoperative period. Postoperative vertical and torsional diplopia and consecutive exotropia resolved in 7 or 8 cases. The 1 patient without resolution had 3 prior strabismus surgeries. The study is limited in the retrospective design and small number of cohort. This study suggests in this specific cohort, the adjustable graded augmentation of SRT may be a useful technique in treating complex strabismus disorders with torsion and vertical diplopia.

Incidence of symptomatic vertical and torsional diplopia after superior rectus transposition for esotropic Duane syndrome and abducens nerve palsy.
Escuder AG, Kazlas MA, Heidary G, Hunter DG, Zurakowski D, Dagi LR.
J AAPOS. 2020 Oct;24(5):270.e1-270.e5.

This is a retrospective review of medical records of patients with esotropic Duane syndrome or abducens nerve palsy at Boston Children's Hopsital (2006-2018) treated with unilateral superior rectus transposition (SRT) with or without augmentation to evaluate the incidence of symptomatic vertical and torsional diplopia after SRT surgery. Of 69 patients (32 with abducens palsy and 37 with esotropic duane

syndrome) 7% had postoperative vertical diplopia in primary position and none had torsional diplopia. This study is limited by its retrospective design and the technical differences in procedures performed by multiple surgeons. This study suggests there is minimal risk for postoperative torsional diplopia and the incidence of symptomatic vertical diplopia is low.

Ipsilateral gaze deviation as a risk factor for surgical overcorrection in two-muscle surgery for unilateral superior oblique palsy.
Nash DL, Diehl NN, Mohney BG.
J AAPOS. 2020 Oct;24(5):272.e1-272.e4.

This is a retrospective review of medical records of patients with presumed unilateral moderate angle trochlear nerve palsy who underwent two-muscle surgery to investigate the angle of deviation in various gaze positions as a risk factor for over-correction. The most common two-muslce surgery performed was a weakening of ipsilateral inferior oblique and contralateral inferior rectus muscle. 45 patients (age range, 12-77 years; 24 [53%] males) with deviation ranging from 14^{Δ} to 25^{Δ} in primary position underwent two-muscle surgery, of whom 8 (18%) experienced surgical overcorrection by 6 weeks' follow-up. The preoperative angle of deviation was similar between overcorrected and non-overcorrected patients for eight of nine cardinal distance positions and near gaze; however, patients with smaller deviations in ipsilateral gaze were more likely to be overcorrected with two-muscle surgery (8.5 vs 16.0 [$P = 0.029$]). Cut point analysis determined that an ipsilateral gaze of $\leq 9^{\Delta}$ was significantly associated with overcorrection. Greater lateral incomitance also trended toward overcorrection (15.0 vs 9.0 [$P = 0.059$]). Torsion was not a clinically significant indicator of overcorrection (3.5 vs 6 [$P = 0.083$]). The limitation of this study is the small case series, incomplete data of certain fields of gaze and postoperative torsion measurements, and the short postoperative follow-up and retrospective nature of the study. This study suggests that ipsilateral gaze measurements may guide surgeons to one or two-muscle surgery in patients with presumed unilateral trochlear nerve palsies and hyperdeviation of 14 to 45^{Δ} in primary position.

Augmented medial rectus muscle recession versus medial rectus recession with posterior scleral fixation in partially accommodative esotropia: a randomized clinical trial.
Al-Hayouti H, Awadein A, Gawdat G, Elhilali H.
J AAPOS. 2020 Oct;24(5):274.e1-274.e7.

This is a prospective study of 60 children with partially accommodative esotropia (PAET) without convergence excess, comparing postoperative alignment after medial rectus posterior fixation versus augmented recession. The patients were randomly assigned to either procedure. The ductions, versions, angles of deviation, and difference between angles were analyzed before and 6 months after surgery. Complete success was defined as orthotropia to within 8D of esophoria/tropia for both distance and near, with spectacle correction, at 6 months. Patients who developed any exophoria/tropia with their original spectacles and needed reduction of their hyperopic correction to achieve successful outcome were defined as qualified successes. 25 in the augmented group and 28 in the posterior fixation group completed follow-up. The mean age at surgery was 4.90 $\pm$ 2.34 years. The complete success rate was 48% and 64% in the augmented and posterior fixation groups, respectively ($P = 0.15$); the qualified success rate was 80% and 92.9%, respectively ($P = 0.17$). Success rate was significantly higher ($P = 0.04$) in the posterior fixation group (56%) than in the augmented group (18%) when the preoperative angle disparity was $\geq$20D. This study reports there was no statistically significant difference in the post operative distance angle with either surgery, but suggests that there may be a benefit of better motor alignment when combining posterior fixation to standard recession specifically to larger angle PAET with normal AC/A ratio.

Suture loop myopexy versus silicone band loop myopexy in the management of myopic strabismus fixus.
J AAPOS.
Farid MF.

2020 Oct;24(5):276.e1-276.e6.

This is a retrospective study comparing medical records of patients with myopic strabismus fixus who underwent surgical management with either superior rectus – lateral rectus loop myopexy suture (SLM) or silicone band loop (SBM) over a 4 year period. . The primary outcome measures were improvement of primary position esotropia, hypotropia, and limitations of abduction and elevation. The angle between the displaced superior rectus and lateral rectus muscles (angle of globe dislocation) was also assessed by orbital imaging before and after surgery. A total of 21 patients were identified, of whom 10 underwent SLM and 11 underwent SBM. Mean age at surgery was 65.4 $\pm$ 5.7 years in the SLM group and 68.5 $\pm$6.4 years in the SBM group. Both procedures significantly improved esotropia, hypotropia, angle of globe dislocation, and limitation of abduction and elevation (P<0.0001), with no significant statistical difference between procedures (P> 0.05). Intraoperative muscle splitting occurred in 2 cases in the SLM group, and transient foreign body sensation was documented in 3 cases in the SBM group. The limitations of this study are the small cohort and retrospective design. The study suggests in this study cohort, both techniques achieved significant correction of ocular deviation, limitation of ocular ductions, and angle of globe dislocation associated with myopic strabismus fixus, with no statistically significant difference between procedures.

Muscle belly union surgery with or without medial rectus recession for the treatment of high myopic strabismus fixus.
Çelik S, İnal A, Ocak OB, Aygıt ED, Hüseyinhan Z, Gürez C, Paşaoğlu I, Gökyiğit B.
J AAPOS. 2020 Oct;24(5):278.e1-278.e5.

This is a retrospective review of medical records of patients who underwent suerperior rectus and lateral rectus muscle belly union with or without medial rectus recession (MRc) for treatment of high myopic strabismus fixus over a 20-year period. A total of 50 eyes of 40 patients were included. Mean esotropia decreased from $57.27^{\Delta} \pm 25.45^{\Delta}$ (range, 8^{Δ}-100^{Δ}) before surgery to $11.67^{\Delta} \pm 13.85^{\Delta}$ (range, 18^{Δ} to 45^{Δ}) after (P < 0.001); mean hypotropia, from $6.05^{\Delta} \pm 9.13^{\Delta}$ (range, 0^{Δ}-13^{Δ}) before to $1.20^{\Delta} \pm 3.03^{\Delta}$ (range, 0^{Δ}-10^{Δ}) after (P < 0.001). Mean abduction improved from 2.82 $\pm$ 1.17 (range, 4 to 0) before to 0.75 $\pm$ 0.92 (range, 3 to 0) after (P < 0.001); mean elevation, from 1.62 $\pm$ 1.62 (range, 4 to 0) before to 0.57 $\pm$ 0.90 (range, 3 to 0) after (P < 0.001). Preoperative esotropia and postoperative limitation in abduction were significantly lower in the group where MRc was performed after muscle union surgery (P 5 0.03; P 5 0.01). This study is limited by the retrospective design. The strength of this study is the single surgeon with a large sample size. This study suggests that muscle union surgery may be used to successfully correct restrictive esotropia and hypotropia.

Effects of corrective strabismus surgery on social anxiety and self-consciousness in adults.
Estes KJ, Parrish RK, Sinacore J, Mumby PB, McDonnell JF.
J AAPOS. 2020 Oct;24(5):280.e1-280.e4.

This reports the results of a questionnaire-based interventional study to evaluate the effects of strabismus surgery on private self-consciousness, public self-consciousness, and social anxiety using a validated self-consciousness survey instrument. Patients who underwent strabismus surgery completed a demographics and a self-consciousness scale form both pre- and postoperatively. The total and subscale (private self-consciousness, public self-consciousness, and social anxiety) summative scores were compared using the Wilcoxon signed-rank test, with statistically significant relationships defined as P < 0.05. Total and subscale summative scores were analyzed as such and by strabismus type, years of education, and marital status. Overall improvement was found postoperatively in total scores (P = 0.012), public self-consciousness scores (P = 0.009), and social anxiety scores (P = 0.028). Although improvement was noted for the private self-consciousness subscale (P = 0.188), it did not reach statistical significance. Subdivided according to strabismic and demographic subgroups, significant improvement was only noted in esotropic patients, college graduates, married/living partner/widowed patients, and separated/divorced patients. There were 95 patients that completed the survey. The limitations of the study was that the study was masked, the patients completed the same questionnaire twice, and there

was a self-selection bias, given only those patients who were willing to participate were included. The results of this study suggests that strabismus surgery can result in improved public self-consciousness and social anxiety, with greatest effect noted in esotropic, college graduates, and nonsingle patients.

Acute, severe dystonia after strabismus surgery in a patient on propofol, ondansetron, and bupropion.
Elhusseiny AM, Grush A, Dagi LR.
J AAPOS. 2020 Oct;24(5):312-314.

This is a case report of acute, severe dystonia is a frightening and potentially lifethreatening surgical complication. A 41- year-old woman experienced postoperative drug-induced dystonia after elective strabismus surgery. In this case, the medications likely responsible were propofol, ondansetron, and, possibly, bupropion.

Comparison of different tendon transposition techniques for the treatment of monocular elevation deficiency type 2
Ocak OB, Inal A, Aygit ED, Celik S, Ocak SY, Gurez C, Pasaoglu IB and Gokyigit B
JAAPOS. 2020 Feb 24:8.e1-4

This is a retrospective study reviewing medical records of patients with type 2 monocular elevation deficiency (MED type 2) operated at a single institution from 2000 to 2016. The patients were divided into three vertical transposition groups: (1) full tendon width, (2) augmented surgery and (3) partial tendon width. Surgical success was defined as not having severe limitation of upgaze, hypotrpia of < 6^{Δ}, and without hypertropia in primary position. 39 patients were included. Pre- and postoperative deviations in group (1) were $22.50^{\Delta} \pm 4.78^{\Delta}$ and $3.5^{\Delta} \pm 1.27^{\Delta}$, respectively; in group (2) $23.75^{\Delta} \pm 4.78^{\Delta}$ and $1.75^{\Delta} \pm 1.14^{\Delta}$; and in group (3), $20.50^{\Delta} \pm 3.98^{\Delta}$ and $4.12^{\Delta} \pm 2.78^{\Delta}$. Corrected vertical deviations were 19^{Δ}, 23^{Δ}, and 16^{Δ}, respectively. The pre- and postoperative limitation of elevations were -2.80 and -0.80 in group (1), -3.20 and -0.90 in group (2), and -2.37 and -1.12 in group (3). The pre- and postoperative vertical deviation improvements and limitations of elevation were statistically significant ($P<0.05$) in all groups. Success was achieved in 29 patients (74%). The limitation is the retrospective design of the study. In this study cohort, the results suggest all three procedures are reasonably effective in improving vertical deviations and limitation of elevation.

A Comparative Study of Prism Adaptation and the Augmented Surgery Formula in the Management of Acquired Comitant Esotropia
Kassem, Rehab R; Elhilali, Hala M; El-Sada, Mohammad A; El-Antably, Said A.
J Pediatr Ophthalmol Strabismus. 2020 Mar;57(2): 108-119.

Surgery for patients with partially accommodative esotropia based on the measured distance deviation when wearing full hyperopic correction not infrequently leads to under correction. To address this, both prism adaptation and augmented surgery formulas were created. This study compared these two approaches. Forty patients three years and older with acquired comitant non-accommodative or partially accommodative esotropia and normal AC/A ratios were included in this study. The augmented surgery formula used was the average of distance deviation with correction (smallest) and near deviation without correction (largest). The prims adapted group had surgery for the prism amount in the Fresnel plus and additional deviation found with alternate prism cover testing while wearing the Fresnel prism. The prism group was further subdivided into responders, who fused while wearing the prism and non-responders, who did not fuse. The study was prospective, randomization and blinding were not discussed. Three months after surgery the prism adaptation group had 90% success, whereas the augmented surgery formula group had 55% success. By 6 months the success rates were 95% and 80%, and not statistically different. Some of increased success in the augmented surgery group between 3 and 6 months was attributed to reducing or eliminating hyperopic correction to reduce exotropia. The subset of patients with acquired non-accommodative esotropia had higher success with the prism adaptation at 3 months and greater, though not statistically different, success at 6 months. The authors suggest that prism adaptation

and its associated financial and time costs are particularly useful in this group. The success rate among partially accommodative patients were fairly similar regardless of which strategy was used, though notably no consecutive exotropia occurred in the prism adaptation group.

Transposition of plicated horizontal muscles.
Shah PR, Pihlblad MS.
J AAPOS. 2020 Jul 17:S1091-8531(20)30146-4.

Multiple surgical approaches have been described to address strabismus with both vertical and horizontal components. This is a case series describing 4 patients who underwent unilateral horizontal rectus muscle plication combined with vertical transposition to treat combined vertical-horizontal strabismus. The surgical technique includes a plication using 6-0 polyglactin suture which is then secured to the sclera with partial thickness bites in the desired location, resulting in a triangular fold in the muscle (reference pictures are included). In this small case series, all 4 patients achieved target post-operative alignment. The authors conclude that this novel surgical technique has the advantage of sparing the ciliary artery circulation and should be considered in patients with combined vertical-horizontal strabismus.

Bilateral superior oblique temporal tenectomy for the treatment of A-pattern strabismus.
Debert I, Darcie AL, Polati M.
J AAPOS. 2020 Aug 27. In press.

Multiple surgical approaches have been described to address strabismus which displays vertical incomitance. The goal of this retrospective review was to describe outcomes for 102 patients with a history of A-pattern esotropia or exotropia in the setting of bilateral superior oblique overaction who underwent bilateral superior oblique tenectomy. The main outcome measure was change in A-pattern. Their technique included a previously described method of completing a temporal transection of the superior oblique 6 mm from its insertion and excising the temporal portion of the muscle. The A-pattern was corrected to <10 prism diopters in 76% of patients with a moderate A-pattern and 72% of patients with a large A-pattern (>25 prism diopters). The authors conclude that given the similarity of the results despite a heterogenous patient population, superior oblique tenectomy may be a “self-graded’ procedure and should be considered as a reliable surgical option for patients with A-pattern strabismus.

Efficacy of isolated inferior oblique anteriorization on large-angle hypertropia associated with unilateral superior oblique palsy.
Nabie R, Manouchehri V, Babaei A.
J AAPOS. 2020 Aug 31. In press.

The type of surgical intervention recommended for superior oblique palsy depends on many factors including pre-operative deviation and surgeon preference. This is a prospective study of 25 pediatric and adult patients evaluating inferior oblique anteriorization as the surgical approach for patients with a superior oblique palsy and large-angle hypertropia of at least 25 prism diopters in primary position. Their surgical approach included reattaching the inferior oblique parallel to the insertion of the inferior rectus. The primary endpoint was deviation in primary gaze, for which success was achieved in 72% of patients. 16% of patients developed a post-operative anti-elevation syndrome (though were clinically asymptomatic). Pre-operative extorsion was associated with lower rates of success. Overall, this represents a single muscle surgical option for patients with a superior oblique palsy and large pre-operative vertical deviation.

Single-stage superior oblique tendon recession with suture adjustment under topical anesthesia and sedation for A-pattern strabismus with superior oblique overaction.
Xie F, Guo X, Zhang W.
J AAPOS. 2020 Aug 14. In press.

A-pattern strabismus with superior oblique overaction can present a unique challenge to the strabismus surgeon. This is a retrospective study of 29 patients with A-pattern strabismus and superior oblique overaction who underwent superior oblique recession using an adjustable suture technique. The surgical technique consisted of translating and recession the superior oblique tenson insertion to a point 12 mm from the limbus and 4 mm medial to the nasal side of the superior rectus with the two arms tied together with a bow tie style slip knot. 79% of patients experienced a good 6-week post-operative result (A-pattern resolution or persistent <10 prism diopters). This paper is limited by the small number of patients and the very short-term post-operative follow up. The authors suggest that an adjustable superior oblique recession can be considered for patients with A-pattern strabismus and superior oblique overaction with a deviation of <15 prism diopters.

Enhanced adjustable nasal transposition of split lateral rectus muscle for surgical management of oculomotor nerve palsy.
Saxena R, Sethi A, Dhiman R, Sharma M, Sharma P.
J AAPOS. 2020 Jun 6;S1091-8531(20)30110-5.

Oculomotor palsy presents a surgical challenge. This case series describes 4 patients with a complete oculomotor nerve palsy who underwent adjustable nasal transposition of the split lateral rectus muscle. Their surgical technique includes creating four fornix incisions (one in each quadrant), detaching and splitting the lateral rectus muscle, performing a superior oblique tenectomy, and reattaching both halves of the lateral rectus to the superior and inferior poles of the medial rectus muscle crossing under the medial rectus. The authors describe an adjustable technique whereby the two poles of the lateral rectus are placed on sliding noose adjustable sutures. At 1 year post-operatively, mean exotropia had improved from 86 prism diopters to 1 prism diopter and all patients were within 10 prism diopters in primary gaze. This represents a unique and promising surgical treatment for oculomotor nerve palsy.

Surgical outcome of patients with unilateral exotropic Duane retraction syndrome.
Akbari MR, Masoumi A, Masoomian B, Mirmohammadsadeghi A, Mehrpour M.
J AAPOS. 2020 May 30:S1091-8531(20)30096-3.

This is a retrospective review of the clinical and surgical outcome from March 2015 to February 2018 in patients with unilateral exotropic Duane Retraction Syndrome (DRS) who underwent surgery at one institution. Results included 40 patients (21 males (53%) with unilateral exotropic DRS with 28 (70%) of 40 eyes with DRS being the left eye. Mean age at strabismus surgery was 18.75 years, SD 12.54 years (range 2-52 years). All 40 patients had an abnormal head turn toward the opposite side of the affected eye and globe retraction. Mean pre-operative angle of deviation in primary gaze was 24.37 PD, SD 12.34 PD (range 6 PD to 77 PD) for near and 19.67 PD, SD 10.76 PD (range 4 PD to 60 PD) for distance. In 2 patients, vertical angle deviations were noted pre-operatively: 14 PD hypertropia in one patient and 18 PD hypotropia in another patient. The initial strabismus surgeries completed were: ipsilateral LR recession with and without Y-splitting, ipsilateral LR recession and MR recession, bilateral LR recession, ipsilateral LR recession and IR recession, LR recession with vertical muscle nasal transposition. Of note, 24 patients (60%) had a successful surgery alignment with unilateral LR recession. Overall, mean post-operative angle deviation was 4.25 PD, SD 8.61 PD (range 0 PD to 50 PD) for near and 2.62 PD, SD 6.15 PD (range 0 PD to 35 PD) for distance. The authors reported statistical signficance with improved angle deviation from pre-to-post-operative measurement ($P < 0.001$). Of note, two patients needed a second strabismus surgery: SR recession and bilateral MR resection. Limitations of this study is that it is a retrospective review and that the authors analyze the outcomes when different surgeries were performed for different motility findings of the exotropic DRS. However, the authors do note that in this small study, the majority had the same successful surgery: unilateral LR recession with mean 7.45mm (range 6.0-8.5mm). In summary, the authors suggest from the small retrospective study of exotropic DRS patients that unilateral LR recession with or without Y-splitting can be a successful surgerical management.

Myectomy of the four horizontal rectus muscles with pulley fixation for the treatment of horizontal nystagmus in 10 adults: a pilot study.
Lingua RW, Gore C.
J AAPOS. 2020 Mar;24(2):80e1-6.

This was a small pilot cohort study of 10 adult patients with horizontal infantile nystagmus syndrome. Of the patients, they were in two groups: 5 presence of foveal hypoplasia (FH) or 5 absence of foveal hypoplasia (no-FH). The authors developed a surgical technique with a modified four-muscle myectomy with pulley-fixation, in which the myectomized muscles are attached to the pulley rather than released. This was a prospective study which recruited these 10 adults from July 2018 to October 2018 at one institution. Strabismus surgery was performed by only one of the authors with all four horizontal myectomized muscles sutured within the pulley or encircling fascia. In addition to the specific surgerical technique, the authors performed nystagmus-specific quality of life (QoL) questionnaire and nystagmographic video analysis before and after the surgery. Results indicated improved QoL for all 10 patients post-operatively, with no statistical difference between FH or no-FH groups. The authors also report a reduction in nystagmus amplitude and slow-phase velocities and improvement of binocularity and best corrected visual acuity in both groups. Although this was a prospective study, limitations of the study include the lack of statistical analysis, a very small cohort of patients, one surgeon. Another limitation is that the authors reported patients having additional strabismus surgeries, such as transposition muscle surgeries for horizontal or vertical deviations as well as prior strabismus surgeries. In summary, the small cohort of 10 patients with post-operative follow up of 6 months is a limited viewpoint to attribute the superiority of this surgerical technique for our patients with nystagmus, FH or no-FH.

Surgical treatment of strabismus in thyroid eye disease: characteristics, dose–response, and outcomes.
Honglertnapakul W, Cavuoto KM, McKeown CA, Capó H.
J AAPOS. 2020 Mar;24(2):72e1-7.

This is a retrospective study between 2014 and 2018 reviews the surgical management, dose–response, and postoperative outcomes of strabismus surgery in patients with thyroid eye disease (TED) at a single academic institution. Surgeries were performed by three surgeons at the institution and the type of surgery, including adjustable or non-adjustable, was at the disgression of the surgeon. Seventy patients with mean age of 62.2 years with SD 12.9 years with majority of 50 (71.4%) female patients. Of thes 70 patients, 87 strabismus surgeries were performed and the two most common surgeries were unilateral IR recession (48%) and BMR recession (23%). Motor sucess was achieved in 69% and sensory success in 58%. The dose-response for distance and for near for each of the surgery types. Unilateral IR recession dose-response at distance was 3.25 PD/mm ($P < 0.001$) and at near was 2.48 PD/mm ($P=0.002$). For BMR recession dose-response at distance was 3.93 PD/mm ($P=0.001$) and at near was 5.05 PD/mm ($P=0.002$). Mean post-operative drift was associated with overcorrection for both at distance and at near for both surgeries (unilateral IR recession, BMR recession). Of note, the authors did not find a statistical signifcance in age, sex, prior orbital decompression, duration of TED strabismus misalignment, concurrent vertical and horizontal procedures with dose-response or post-operative drift. Limitations of the study include the retrospective nature as well as that < 100 patients were analyzed without a standardized strabismus surgerical guideline pre-operatively. A second limitation is the post-operative follow up, with a median of 3 months (range of 6 weeks to 26 months) and analysis at post-operative days 1-3 does not help the longitudinal post-operative course analysis of these complex TED patients. In summary, the authors found that unilateral IR recession had a larger dose-response at distance, BMR recession had a larger dose-response at near, and overcorrection, rather than undercorrection, was noted post-operatively.

Superior oblique tendon advancement: its success as single or combined muscle treatment for selected cases of unilateral superior oblique palsy.
Yang S, Yue Y, Wang P, Chen G.
Strabismus. 2020 Mar;28(1):25-28.

The authors examined the outcome of unilateral superior oblique tendon advancement in patients with unilateral superior oblique palsy. They performed a retrospective chart review of 14 patients who underwent this procedure from May 2017-October 2018. The patients had a mean age of 16.7 years old (range 3-52) and followed for 5-12 months after surgery. Hypertropia changed from 6.25 PD pre-op to 0.86 PD post-op. Only one patient had an iatrogenic Brown syndrome that resolved spontaneously within two weeks. The authors conclude that this procedure is safe, however care should be taken in patients who had previously gone an inferior oblique weakening procedure. They recommended combining other vertical rectus muscle surgery with SO advancement instead of increasing the amount of advancement for large angles to avoid limitation of supraduction. One limitation is the size of the study did not allow a direct comparison of congenital versus acquired SO palsy. However this procedure may be consider in selected patients.

Unilateral recession and resection surgery with adjustable suture in adult sensory exotropia: long-term success and exotropic drift.
Pukrushpan P, Tharwaranan R, Praneeprachachon P, Honglertnapakul W.
Strabismus. 2020 Aug 3:1-7. doi: 10.1080/09273972.2020.1797125. Online ahead of print.

This retrospective chart review of 38 adults with sensory exotropia evaluated the correlation between the initial postoperative deviation and long-term outcome of unilateral recess-resect procedures that used adjustable sutures. The median preoperative deviation was 45 PD (range 25–70) and median initial postoperative deviation was esotropia 8 PD (range from exotropia 8 to esotropia 30). After a mean follow-up time was 5 ± 2.5 years, motor success (within 10 PD of ortho) was 50%. The authors found the initial postoperative deviation and amount of lateral rectus recession were significantly associated with long-term outcome ($p = .006$ and 0.029). The patients with initial moderate and minimal overcorrection had higher success rates (67% and 62%) than patients with initial orthotropia or undercorrection (10%) ($p = .002$). The median exotropic drift was 8 PD/year. Time to failure in the unsuccessful group was 24 months. The key point from this manuscript is that the surgical goal for patients with sensory exotropia should be toward overcorrection as they will tend to drift toward exotropia over time.

Extraocular muscle insertion shift after disinsertion during strabismus surgery.
Honglertnapakul W, Capo H, Cavuoto KM, McKeown CA.
Strabismus. 2020 Feb 21:1-6.

The position of the extraocular muscle insertion may shift after the muscle is detached, thus affecting the dose response of surgery. The authors performed a prospective study looking primarily at the amount of shift from the limbus of the insertion after the muscle was detached and secondarily to identify factors that influenced the amount of shift. Of the 110 muscles included, most were medial (53) or lateral (46) rectus muscles. 12 had paralytic strabismus, 9 had restrictive, and 21 had prior strabismus surgery on other rectus muscles. The limbus to insertion distance before and after disinsertion differed significantly in all rectus muscles with a median insertion shift for all EOMs of 1.0 mm (mean 1.0 ± 0.4, range 0.0–2.0) and did not significantly differ between the rectus muscles ($p = .158$). Factors that correlated with insertion shift were the forced duction test and limbus to insertion distance before insertion. Restrictive strabismus with moderate to severe limitation on forced ductions had greater shifts, as did muscles with greater limbus insertion distance. A conclusion from this study is that surgical measurement using the original insertion as a reference could lead to an undercorrection in recessions or overcorrection in resection when measuring from the anteriorly displaced insertion, which is particularly important in restrictive strabismus.

Surgical Outcomes of Exotropic Duane Retraction Syndrome From a Tertiary Eye Care Center.
Sheth J, Ezisi CN, Tibrewal S, Sachdeva V, Kekunnaya R.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):9-16.

This retrospective chart review identified 73 patients with exotropic Duane syndrome who underwent strabismus surgery. Patients with a prior history of strabismus surgery were excluded. Included patients had a deviation in primary position of 15 diopters or more, an abnormal head position of 15 degrees or more and/or overshoots in adduction. Bilateral lateral rectus recession was performed for exotropia of 20 PD or greater, whereas unilateral lateral rectus muscle recession in the affected eye was performed for less than 20 PD. In bilateral asymmetric lateral rectus recessions, a larger recession was performed in the unaffected fellow eye. Medial rectus muscle recession was performed in the affected eye when globe retraction was severe (> grade 3). The presence of overshoots in adduction was managed by Y-splitting the lateral rectus muscle with the two arms at least 10 to 14 mm apart. The Y split of the lateral rectus muscle was performed first and then the two arms of the lateral rectus muscle were fixed and/or sutured to the sclera at the desired measurement point for recession. Surgical success was defined as postoperative horizontal deviation within 8 PD of orthotropia, correction of AHP to less than 5 degrees, or two-step decrease in overshoot, and/or globe retraction at the final postoperative visit. This strategy achieved success in primary position in 74%, AHP in 82%, overshoots in 71%. No overcorrections occurred and 19% required reoperation for under correction. The article provides a framework to manage this relatively infrequently encountered surgical problem, with general prognostic information.

The Success of Unilateral Surgery for Constant and Intermittent Exotropia and Factors Affecting It in a Large Scandinavian Case Series.
Thorisdottir RL, Malmsjö M, Tenland K, Blohmé J, Hesgaard HB.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):34-41.

This retrospective chart review is the first large Scandinavian series to evaluate surgical results in exotropia. The study included 291 patients, with constant or intermittent exotropia undergoing initial surgical correction. Objective surgical success was defined as 5 PD or less of esodeviation to 10 PD or less of exodeviation. Unilateral recession and resection was performed. At short term 6 week follow up, 76% of patients achieved objective surgical success, and 94% were satisfied with the results. There was no difference between the constant and intermittent groups. Only 18% of patients had long term follow up, one year or more. Patients in the constant exotropia group followed long term had similar deviations to 6 week post operation, while patients in the intermittent group had increased deviations at long term follow up. The reoperation rate was 4.5% for the whole cohort and 20% of the patients in the long-term cohort. Preoperative angle of deviation predicted surgical success rate, with higher success in patients with lower angles of deviation. The other variables evaluated did not affect the success rate, including: age, gender, surgeon, amblyopia or spherical equivalent. Resection of the medial rectus of had a greater impact on near deviation while recession of the lateral rectus had a larger impact on distance deviation. The study's primary limitation is lack of long-term follow up, less than 20% of patients had examinations one year of more after surgery.

Initial Postoperative Alignment in Strabismus Related to Thyroid Eye Disease.
Ha SG, Kim SH.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):23-27.

In this retrospective chart review the authors sought to compare the day one post-operative alignment with the alignment 12 months after surgery in 78 patients with thyroid eye disease and strabismus. The patients were divided into two groups according to the type of strabismus: hypotropia and esotropia. The angle of deviation on postoperative day one was measured and classified into three groups: under correction (greater than 5 PD), full correction, and overcorrection (greater than 5 PD), compared with preoperative angle of deviation. The overall mean success rate was 65.4% at the final visit, and there was no significant difference in the success rate between the hypotropia and esotropia groups. Patients with combined strabismus and torsional diplopia were excluded. While under correction was not intended in the surgical plan in this study, the long term surgical success rates of under correction and full correction on postoperative day one were significantly higher than that of overcorrection. These results were observed in both patients with hypotropia and esotropia. This study adds to the literature that early under correction is preferable to overcorrection in this patient population.

Effects of the Gaze Fixation Position on AS-OCT Measurements of the Limbus and Extraocular Muscle Insertion Site Distance.
Inagaki R, Suzuki H, Haseoka T, Arai S, Takagi Y, Hikoya A, Komori M, Hotta Y, Sato M.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):28-33.

The prospective observational study evaluated horizontal EOM insertion location using AS-OCT and traditional caliper measurement in the OR. Patients undergoing strabismus surgery were enrolled for AS-OCT measurements prior to surgery, 82 muscles were evaluated. The authors had previously noted the degree of ocular rotation during the AS-OCT scan impacted image quality. In this study, they aimed to determine the optimal gaze fixation points for lateral rectus and medial rectus muscle insertions using AS-OCT compared with gold standard intraoperative measurements. Inner and outer fixation targets requiring 22 and 34 degrees of ocular rotation respectively were used. The medial rectus insertion from the limbus was most accurately measured using the inner target requiring approximately 22 degrees of ocular rotation (abduction). The lateral rectus muscle measurements performed best when using the outer fixation target, requiring approximately 34 degrees of adduction. AS-OCT machines come with standard fixation targets useful for evaluating structures like the angle. These targets may not be ideal for determining the insertion of EOMs. The study provides a useful protocol to measure the horizontal insertion sites.

Anterior Segment Optical Coherence Tomography in Locating the Insertion of Horizontal Extraocular Muscles After Strabismus Surgery.
Saffren BD, Yassin SH, Thau A, Nelson LB, Schnall B, Gunton KB.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):62-65.

In this prospective observational study, patients undergoing strabismus surgery had the distance from the insertion after resection or resection to the limbus measured intraoperatively with calipers and 1-2 weeks postoperatively using AS-OCT. Thirty-one eye muscles from 28 patients were included in the study. Intraclass correlation coefficients (ICCs) were used to calculate agreement between intraoperative and AS-OCT measurements. Good and excellent agreement was defined as 0.16 to 0.80 and less than 0.80, respectively. EOM insertion was identified in 45% of eye muscles. The identified muscles were located significantly closer to the limbus (as measured by caliper) compared with the muscles that could not be identified. The ICC between all AS-OCT and surgical measurements was 0.771. AS-OCT performed better when the insertion was closer to the limbus, all AS-OCT measurements that were within ±1 mm of caliper values had a caliper measurement less than 8 mm. This study, done in the immediate post-operative period, could have been impacted by tissue swelling that made identification of the muscle insertions more difficult. According to this study, AS-OCT can accurately determine the location of extraocular muscles when located close to the limbus, which could provide valuable, yet incomplete information prior to re-operation.

Inferior oblique belly transposition for V pattern strabismus.
Si M, Yang S, Tien DR, Yue Y, Shao X, Guo X.
Strabismus. 2020 Mar;28(1):29-33.

The goal of the manuscript was to evaluate the efficacy of inferior oblique belly transposition to address V pattern strabismus with an upshoot in adduction. The authors retrospectively reviewed the medical records of 13 patients who underwent the procedure over the course of two years. Post-operatively, all patients had resolution of the V pattern (mean 18.92 PD to 3.4 PD) and decreased upshoot in adduction (mean 1.92 to 0.12). No consecutive A pattern was noted. There was a selection bias of patients with a mild V pattern and lower grades of upshoots in adduction; however this procedure may be helpful to consider in patients with a V pattern strabismus and mild-moderate inferior oblique overaction.

Endophthalmitis after strabismus surgery: incidence and outcome in relation to age, operated eye muscle, surgical technique, scleral perforation and immune state.
Simonsz HJ, Rutar T, Kraft S, Thiadens AAHJ, Batstra MR, Verdijk RM, Loeffler KU, Kommerell G; Endophthalmitis-after-Strabismus-Surgery Reporting Group.
Acta Ophthalmol. 2020 Jun 13. doi: 10.1111/aos.14446. Online ahead of print.

A 71-question survey was administered to ophthalmologists internationally who had been involved in the care of a patient diagnosed with endophthalmitis after strabismus surgery (EASS). Overall, twenty-three ophthalmologists and one orthoptist reported on 26 patients (27 eyes). The overall rate of EASS in the 20-year period 1994–2013 was estimated at 1:11,000; however, the rate was higher in children ages 0-2 years (1:3000) and adults over age 65 years (1:800). There were no cases in patients 9-65 years of age, except for one patient with a retinal hemorrhage followed by EASS. In almost all children, EASS was associated with medial rectus recession; however, it varied in adults. There were no scleral perforations in children, although scleral perforation occurred in 2 of 7 elderly patients. In all 15 children aged 0–5 years, the 16 affected eyes were phthisical, eviscerated or enucleated. The authors conclude that age and perforation are key determinants that determine the occurrence of EASS. This study is useful in estimating the occurrence of a very rare event; however, it is difficult to generalize the findings given the lack of standardization of procedure regarding the prep, procedure, post-operative treatment regimen and study location. Future studies that standardize these factors would be helpful, although likely impractical.

Augmented vertical rectus transpositions: intraoperative measurement of torsion following sequential muscle detachment.
Serafino, M., Scaramuzzi, M., Magli, A., & Nucci, P.
Eur J Ophthalmol. 2020, E publication ahead of print. July 28.

Augmented vertical rectus transpositions for cranial nerve 6 palsies can be effective for correcting the subsequent esotropia. This technique can, however, cause new torsional vector forces. The authors seek to measure the intraoperative torsion using the Holmes' method for the augmented vertical rectus transposition. The authors had only 9 patients in their study with a cranial nerve 6 palsy for longer than 6 months and all patients had a -3 to -4 abduction deficit. Torsion was created after partial disinsertion of both the IR and SR muscle. This improved after the rectus was reattached to the sclera along the spiral of Tillaux. Augmentation of the surgery with posterior fixation sutures did not change the torsion.

Effect of unilateral vertical transposition of the horizontal rectus muscles on vertical strabismus
Rossel M, Bergholz R, Salchow DJ.
Eur J Ophthalmol. 2020, E publication ahead of print. June 19.

Combined horizontal and vertical strabismus can be treated by vertically transposing the horizontal muscles of an eye in the same direction during a combination recession-resection. Raising the insertion of the horizontal muscles will elevate an eye and also lowering the horizontal muscle insertion will depress the eye. The authors hypothesize that for every 1 mm of vertical shift is equivalent to 1 PD of change. They retrospectively reviewed records of patients who have undergone a combined unilateral muscle surgery for horizontal strabismus and simultaneous vertical transposition of these muscles over a 3 year period. Patients with restrictive or paretic strabismus were excluded.33 patients were included in the study (23 with exotropia and 10 esith esotropia). The mean peroperative vertical deviation was 7.8 (range 3-25) PD. The vertical transposition averaged 5.6 +/- 1.6mm. The mean effect on the vertical deviation at 3 months was 0.9+/-0.7 PD/mm at distance and 0.9+/- 0.9 PD/mm at near. No patient reported torsional diplopia post operatively. The degree of transposition correlateds with the surgical effect, but the effect is variable. A larger cohort study would be beneficial.

Surgical outcomes of plication versus resection in basic type of intermittent exotropia
Anand K, Baindur S, Dhiman S, Dutta P, Mishra M, et al.
Can J Ophthalmol. 2020 Aug;55(4):323-329

The authors of this study aimed to compare the functional and cosmetic outcomes and dose effects of plication versus resection in basic type intermittent exotropia. They performed a prospective interventional study of 60 patients (age 6 and older) equally divided into unilateral surgery: recession and plication (RP) group and a recession and resection (RR) group. Both groups received 8mm lateral rectus recessions. Mean ages were 20.67 years for RP group and 19.13 years for RR group. The mean preoperative and postoperative deviation was 44.67PD and 10.13PD respectively in group RP and 43.17PD and 9.40PD respectively in group RR (p = 0.423). At 12 months the exodeviation was 4.4PD in group RP and 4.67 in group RR. There was no statistical difference between the groups. The mean effect of plication was 5.91 PD/mm and for resection was 5.5 PD/mm (p=0.877). Cosmetic outcomes (injection, foreign body sensation, visible bump) were comparable between groups. There were no cases of slipped or lost muscle. The authors conclude both procedures are equally effective for achieving desired alignment with no cosmetic differences.

Comparison of Different Surgical Approaches to Inferior Oblique Overaction
Siek EG, MAdabhushi A, Patnaik JL, Jung JL, LynchAM, Singh JK.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):89-93

The purpose of this study is to compare surgical outcomes of recession, anteriorization, and myotomy for the treatment of inferior oblique overaction (IOOA). A retrospective chart review of all patients undergoing IOOA correction from July 2010 to March 2017 at the Children's Hospital of Colorado was performed. Preoperative grading of IOOA (+0.5 to +4.0) was compared to post-operative IOOA (0 to +4.0). The goal was reduction of IOOA to 0, but any decrease in IOOA was measured. There were a total of 260 patients with 357 eyes. Gender and age were similar across surgery types. Recession was the most common procedure and the amount of preoperative IOOA was greatest in patients who received anteriorization. A total of 94.6% of eyes had a decrease in IOOA with recession (n = 165) of the inferior oblique while 86.1% decreased to no IOOA. Anteriorization of the inferior oblique (n = 115) decreased overaction in 97.4% of eyes with 81.7% improving to zero degree of IOOA. Myotomy of the inferior oblique (n = 77) was found to decrease overaction in 98.7% of eyes and reduce IOOA to zero in 88.3%. The authors conclude that there was no significant difference among type of surgery and outcome. Of note there were patients in all groups that had no improvement in IOOA. All three surgical interventions were found to be equally successful in reducing the amount of IOOA.

One-Month Postoperative Horizontal Strabismus Surgery Outcomes Using Adjustable and Nonadjustable Sutures.
Kumar A, Shieh D, Bhargava S, Robal-Rather J, Simon JW.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):94-97

Previous series suggest adjustable sutures (AS) in adult strabismus surgery yield improved ocular alignment and better success rates compared to nonadjustable sutures (NAS). The authors questioned whether these differences are clinically significant and whether they justify the added time and discomfort required for AS. In this study, they reviewed all available records of adults undergoing horizontal strabismus surgery by the last two authors between 2000 and 2014. Independently, the two surgeons developed a preference for NAS midway through the study period, permitting comparisons between two treatment groups. Results were assessed at one to two months postoperatively. The primary outcome was alignment in primary position at one to two months postoperatively. The secondary outcome was success rate, defined as <10PD residual or consecutive deviation. The authors included 184 patients, 68 with AS and 116 with NAS. They round no significant difference in primary position alignment at 1–2 months was noted between AS and NAS for esotropia (P = .26) or for exotropia (P = .10). In addition, success rates were similar (P = .58 for esotropia and P = .34 for exotropia). These show a lower success rate of AS compared to other studies in the literature. One significant difference is that this paper looks at short term follow up (1-2 months) rather than long term follow up. Although the authors acknowledge limitations in this retrospective study, their results suggest that AS overall was not associated with improved alignment or success rates, compared to NAS, at 1- to 2- months postoperatively. Although

adjustable sutures represent a valuable surgical option at the discretion of individual surgeons and their patients, the authors no longer routinely use AS in all adult cases. A large prospective study involving more surgeons and techniques to evaluate long-term outcomes would be helpful.

The relationship of Age and Other Baseline Factors to Outcome of Initial Surgery for Intermittent Exotropia.
Repka MX, Chandler DL, Holmes JM et al on behalf of the pediatric eye disease investigator group.
Am J Ophthalmol. 2020 Apr; 212:153-161.

The purpose of this secondary analysis of a randomized trial was to determine if age at surgery for intermittent exotropia (IXT) is associated with outcome at 3 years. The authors studied 197 children aged 3 to <11 with the goal of understanding the difference in outcomes in patient who had a unilateral recession/resection or bilateral lateral rectus recessions. The outcome of that paper was that there was no significant difference in surgical outcomes between the two surgeries. This was a secondary paper looking at age at surgery as a factor predicting outcome. The authors defined a suboptimal surgical outcome at 3 years as a constant of intermittent exotropia greater than or equal to 10 prism diopters at distance or constant esotropia of 6 or more prism diopters at near. A decrease in near steroacuity or need for reoperation also was defined as suboptimal. The authors found that the children who had surgery between 3 and 5 years of age had a suboptimal result of 28% vs. 50% in the children 5-11 years old at the time of surgery. No other factors were found to be statistically significant between the two groups. This study suggests that in IXT, earlier surgery may have better outcomes. However the authors point out the main limitation, which is that this study was not designed to take in account if these were delayed vs early surgery. Nonetheless, this is a very interesting study based on prospective data and the first of its kind to answer an important question for the pediatric ophthalmologist.

The Effect of Horizontal Rectus Muscle Surgery on Distance-Near Incomitance.
Phillips PH, Fray KJ, Grigorian AP, et al.
Am J Ophthalmol. 2020 May; 213:97-108.

The goal of this prospective, comparative interventional case series was to determine the effect of horizontal rectus surgery on distance-near incomitance. This study included 45 patients over a 3-year period at two associated medical centers. Prism and alternative cover testing was performed at distance and near after one hour of occlusion at pre and post-operative exams within a week and closest to a year after surgery and the change in incomitance was calculated. Forty-two of the 44 patients had a change in incomitance within one week and all patients when examined 6-12 months post op had a change in incomitance. Interestingly, medial rectus surgery was not more likely to induce a greater effect at near and lateral rectus muscle surgery was not more likely to induce a greater effect at distance, contrary to pediatric ophthalmology dogma. The authors conclude that the surgeon does not need to consider distance-near incomitance when considering horizontal rectus muscle. The design of this paper was not randomized, which was a limitation, but the1 hour of patching to reduce or eliminate effect of fusion used in the methods makes this paper stronger than previous reports. This is the first prospective study of its nature and is of interest to any strabismus surgeon.

Strabismus Surgery for Esotropia, Down Syndrome and Developmental Delay; Is an Altered Surgical Dose Required? A Literature Review.
Harron A, Allen L, O'Connor A.
British and Irish Orthoptic Journal**.** Apr 2020;16(1).4–12.

There is a high rate of strabismus, in particular, esotropia, in children with Down syndrome or developmental delay, which frequently requires surgical correction. A paper in 1994 advocated that the surgical dose be adjusted due to an altered response in these children. The aim of this literature review was to evaluate the available evidence to establish whether an altered surgical approach is required in these populations. A literature review was conducted using PubMed and Web of Knowledge. Only

English language papers were eligible for inclusion. The papers were collated in chronological order for analysis, and their references searched for further relevant papers. Forward citation searches were also undertaken. A 2 × 2 comparison is made between publications on Down syndrome (in isolation) and developmental delay populations (including Down syndrome) with adjusted versus non-adjusted surgery. Published surgical success rates on esotropia from unaltered surgical doses range from 62.0%–85.7% (four papers) in the Down syndrome cohort, with none of the adjusted surgeries having a successful outcome. Surgical success rates from adjusted surgical doses in developmental delay cohort range from 37.5%–86.0% (seven papers), with one unadjusted surgical success rate of 76.0%. The results across the studies are summarised in a table and discussed in this paper. The results show an exaggerated surgical effect in individuals with developmental delay. The authors suggest that this population may benefit from a reduced surgical dose in surgery for esotropia. Published research does not, however, support giving a reduced surgical dose in individuals with Down syndrome for surgery in patients with esotropia although the number of studies available are limited. This study did not look at other types of deviations. The authors noted that more research needs to be done to make a definitive conclusion.

11. ANTERIOR SEGMENT

Lid-Related Keratopathy in Stevens-Johnson Syndrome: Natural Course and Impact of Therapeutic Interventions in Children and Adults.
Swapna S. Shanbhag, Sahil Shah, Madhu Singh, Chirag Bahuguna, Pragnya R. Donthineni and Sayan Basu.
American Journal of Ophthalmology, 2020 Nov; 219:357-365.

This retrospective comparative case series included 705 eyes of 401 patients (81 children) with SJS who presented with chronic lid-related keratopathy over a 25-year period. The goal of this study was to compare the long-term visual outcomes of different management strategies in this clinical scenario. The treatments were either conservative therapy (topical meds, n=363), or definitive management (n=342). The definitive management group included both those who had mucous membrane grafting (MMG) and those who had a prosthetic replacement of the ocular surface ecosystem (PROSE) contact lens, or both. The primary outcome in this study was best corrected acuity and secondary outcome was development of a corneal ulcer. The authors found that patients how had definitive treatment had a statistical benefit in acuity. And those who had conservative treatments had a risk 3x higher of developing a corneal ulcer. The combination of both treatments had the best results, though did not reach statistical significance. It is relevant to the pediatric ophthalmologist that the children did slightly better with the MMG group probably because many were less likely to tolerate the PROSE lens. The authors concluded that this is substantial evidence to change standard of care to a combination of MMG and PROSE for patients both pediatric and adult with lid related keratopathy in SJS. This is a large cohort of patients considering the rarity of this disease. Of note, 99% of the patients in this study were not treated acutely with amniotic membrane and might not be generalizable to the results that we see in this country.

Role of Microscope-Intraoperative Optical Coherence Tomography in Pediatric Keratoplasty: A Comparative Study
Namrata Sharma, K. Priyadarshini, Rinky Agarwal, Rahul Kumar Bafna, Ritu Nagpal, Rajesh Sinha, Tushar Agarwal, Prafulla Kumar Maharana and Jeewan Singh Titiyal.
American Journal of Ophthalmology, 2021 Jan; 221:190-198.

This prospective and retrospective comparative interventional study was done to evaluate the role of microscope integrated optical coherence tomography (i-OCT) in pediatric keratoplasty. There were 75 children from one institution aged 16 or younger included in this data set. The authors compared group 1 (prospective, n=56) in which i-OCT was used to group 2 (retrospective, n=19) where a conventional microscope was used during the surgery. The authors found that in cases where the i-OCT was used before and during keratoplasty, that the surgeons were more likely to perform synechiolysis, pupilloplasty, lens extraction and anterior vitrectomy. They concluded that the surgical planning was improved with i-OCT due to increased visualization of anterior structures. Additionally, guidance on the ability to perform anterior lamellar keratoplasty and placement of intraocular lens was also useful in some cases. The authors did mention that prohibitive cost of this microscope could be a barrier for most ophthalmologists. They could have discussed more why the Kaplan-Meier survival of the group 1 grafts was not as favorable as group 2. Overall this study supports intraoperative anterior segment OCT as a useful tool in these difficult cases. The data is not very strong but the reasoning is compelling and it makes sense that i-OCT is helpful in pediatric keratoplasty. It would be nice to compare this i-OCT to regular handheld supine OCT that is more accessible to the ophthalmologist.

Three-Dimensional Morphogeometric and Volumetric Characterization of Cornea in Pediatric Patients With Early Keratoconus.
Toprak I, Cavas F, Velazquez JS, Alio del Barrio JL, Alio JL.
Am J of Ophthalmol. 2021 Feb; 222:102-111.

This cross-sectional, single-center study conducted in Spain used 3-D corneal modeling to evaluate the morphogeometric and volumetric characteristics of the cornea and their diagnostic value in pediatric patients with keratoconus (KCN). The eyes of 49 pediatric patients (□16 yrs) with KCN and 31 controls were studied. Eyes of KCN patients were graded as early (n = 21) and mild KC (n = 28) based on the RETICS KC (Thematic Network for Co-Operative Research in Health) classification system. The 3-D corneal model was generated using raw topographic data. Deviation of anterior and posterior apex and minimum thickness points, total corneal volume, volumetric distribution, and percentage of relative volume increase between 2 consecutive radii centered to anterior/posterior apex and thinnest point were evaluated. The results showed that pediatric patients with early and mild KCN both have decreased corneal thickness and volume; however, posterior apex displacement, difference between anterior and posterior corneal apex deviation, and relative volume increase between 1.0- and 1.4-mm-diameter circles centered on the thinnest corneal point seem to be signs of early KCN.

Importance: This is the first study presenting morphogeometric and volumetric characterization of the cornea in pediatric patients with early and mild KCN using a 3-D corneal model. These morphogeometric and volumetric parameters can be integrated with ectasia-screening software of the topographer to assist the clinician in the early detection of KCN in the pediatric age group, when prompt treatment is critical.

Corneal collagen cross-linking in pediatric keratoconus with three protocols: a systematic review and meta-analysis.
Mahdavi Fard A, Reynolds A, Lilluis J, Nader D.
J AAPOS. 2020 Dec 3;S1091-8531(20)30302-5. doi: 10.1016/j.jaapos.2020.08.013.

Systematic review was performed to evaluate efficacy of corneal collagen cross-linking (CXL) protocols for treatment of pediatric patients with keratoconus. Keratoconus is a progressive degenerative disease that results in corneal thinning and distorsion that results in visual impairment not correctable with glasses. Presentation in childhood frequently has an aggressive course. Collagen cross-linking (CXL) is a technique using riboflavin photosensitization and ultraviolet wave A to stabilize the cornea slowing progression. Techniques are divided into: conventional and accelerated “epithelium-off” protocols vs. more recent “epithelium-on” technique.. Analysis of CXL with conventional and accererated “epithelium-off” techniques were effective in treating pediatric patients with keratoconus and the authors conclude that the accelerated “epithelium-off” protocol with its decreased operative time may be a preferred protocol. Further analysis suggests “epithelium-on” protocol is safe but not as efficient. CXL has become a frequently used technique for treatment of keratoconus. It is important for the pediatric ophthalmologist to be aware of different modalities and efficacies of treatment that will be offered to our patients that require surgical treatment.

Outcomes of Descemet's membrane endothelial keratoplasty for congenital hereditary endothelial dystrophy.
Saad A, Ghazzal W, Keaik M, Indumathy TR, Fogla R.
J AAPOS. 2020 Nov 27:S1091-8531(20)30297-4. doi: 10.1016/j.jaapos.2020.07.018. Epub ahead of print. PMID: 33253860.

Congenital hereditary endothelial dystrophy (CHED) is a rare disorder resulting in bilateral clouding secondary to dysfunction of corneal endothelium and thickened Descemet’s membrane (DM). Treatment with penetrating keratoplasty (PK) is challenging because of technical factors as well as increased postoperative complications. Descemet’s membrane endothelial keratoplasty may have advantages because of fast visual recovery and decreased risk of rejection. Descemet’s stripping may be technically difficult secondary to poor visibility and secure adhesion of DM. Donor detachment can occur requiring rebubbling surgical intervention .This series demonstrated 93% of cases demonstrated a clear cornea at final follow up. The lower risk of rejection could allow for less steroid use and the associated complications associated with it. DMEK can be a safe alternative to PK however longer term follow is necessary. This article provides an update for the pediatric ophthalmologist for the treatment of CHED.

Total corneal refractive power and shape in Down syndrome.
Asgari S, Mehravaran S, Fotouhi A, Makateb A, Hashemi H.
Eur J Ophthalmol. 2021 Jan;31(1):69-77.

It is suggested that patients with Down syndrome are more prone to developing keratoconus. The purpose of this paper is to examine the keratometric pattern and shape from the center to the periphery in a population of Down patients with normal corneas free from any clinical signs of keratoconus and compare them to age and gender matched controls. They examined patients between 10-30 years of age. Patients with Down syndrome had steeper Sim K steep, sim K flat, and front Kmax measurements compared to controls. Patients with Down syndrome also had higher total cornea refractive power in 1-8mm zones compared to normal. Overall, compared to control samples, patient with Down syndrome have a more prolate cornea which may not be indicative of keratoconus.

Three-year follow-up of accelerated transepithelial corneal cross-linking for progressive paediatric keratoconus
Tian M, Jian W, Zhang X, Sun L, Zhou X.
Br J Ophthalmol. 2020 Nov;104:1608-1612.

Previous studies have shown that conventional corneal collage cross-linking is effective and safe for adults and children with keratoconus. There are fewer studies examining accelerated transepithelial collage cross-linking in children. This reports provides 3 year follow-up data for children treated with this technique. 41 patients (53 eyes) were included in the study, with mean age 14.81 years. Best corrected distance visual acuity and manifest refraction were assessed pre-operatively and 36 months post-operatively. Pentacam, pachymetry and epithelial thickness were also measured. Best corrected distance visual acuity improved from 0.32 logMAR to 0.25 logMAR (p=0.025). Maximum keratometry values did not change significantly between pre-operative and post-operative time points over the 36 months of follow-up. There was also no significant difference over the period with central corneal thickness, apex thickness or thinnest corneal thickness. Posterior central corneal elevation and posterior highest elevation were stable at 12 months but did increase at 36 months. Epithelial thickness remained stable. Given these findings the authors conclude that this procedure is safe and effective in pediatric progressive keratoconus with stable keratometry and corneal thickness values at 36 months post-op. Overall corrected visual acuity also improved in the study. However, 20% of eyes did show a tendency for progression at 3 years (1.00 D increase in maximum keratometry), and the authors emphasize that there was not a control group in this study. It is also unclear how the progressive cases would react to retreatment.

Pediatric Corneal Structural Development During Childhood Characterized by Ultrasound Biomicroscopy
Snehaa Maripudi, Julia Byrd, Azam Qureshi, et al.
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):238-245.

The purpose of this prospective study was to quantitatively describe the structural corneal changes from infancy to early adulthood using ultrasound biomicroscopy. Participants younger than 18 years were imaged during examination under anesthesia, concurrent with the clinically indicated procedure (strabismus surgery, contralateral trauma repair, or oculoplastic procedure). Adult participants were imaged while awake with topical anesthesia. 168 ultrasound biomicroscopy images were obtained from 24 healthy eyes of 24 patients ranging in age from birth to 26 years. Twelve corneal structural parameters were measured. Means were compared between younger and older groups. Among the 12 measured structures, 5 demonstrated statistically significant differences ($P < .05$) between patients younger than 1 year and patients older than 1 year. The mean values for corneal cross-sectional width and length, central corneal thickness, and radii of curvature (anterior and posterior) were significantly different in patients younger than 1 year compared to older than 1 year. When comparing the youngest to oldest subgroups, anterior curvature flattened (6.14 to 7.55 radius), posterior curvature flattened (5.53 to 6.72 radius), angle-to-angle distance increased (8.93 to 11.40 mm), and endothelial cross-sectional distance increased

(10.63 to 13.61 mm). For 7 of the 12 parameters including angle-to-scleral spur distance, 3- and 6-mm peripheral thicknesses, epithelial thickness, endothelial thickness, and integrated density of the cornea and sclera, there was no significant difference between age groups. This study provides additional evidence that pediatric corneal structure changes with age, namely that the cornea flattens and increases in size over time. Additionally, the authors introduce a parameter that may be useful in future studies involving the biometry of the eye. Endothelial cross-sectional distance, or arc length of the cornea, incorporates both the vertical and horizontal dimensions of the cornea, and is easily measurable by ultrasound biomiscroscopy.

Corneal Biomechanical Properties in Childhood Obesity
Mehmet Erol Can; Kızıltoprak, Hasan; Buluş, Ayşe Derya; Özkoyuncu, Dilara; Koç, Mustafa; et al.
J Pediatr Ophthalmol Strabismus 2020 Mar;57(2):103-107.

In this cross sectional study exposure to the risk factor of childhood obesity was correlated with corneal biomechanical properties. Obesity is known to be related to glaucoma, though the underlying mechanism is unclear and both mechanical and vascular theories have been proposed. Corneal hysteresis is a measurement of the cornea's ability to absorb and dissipate energy and is a known glaucoma risk factor. The Ocular Response Analyzer (Reichert, buffalo, NY) was used to measure hysteresis in vivo. The hysteresis value depends on many factors including corneal thickness, hydration and rigidity. Lower hysteresis values are associated with glaucoma. This study found that obese children have lower corneal hysteresis and higher corneal compensated intraocular pressure than healthy controls. Given that corneal hysteresis is dependent on tissue characteristics, the authors propose that damaging factors related to obesity such as pro-inflammatory cytokines could be causative. This study adds additional information that could explain a causal link between obesity and glaucoma. The authors did not evaluate people with or without glaucoma and did not discuss the relationship between corneal hysteresis, obesity and glaucoma in adults.

Using IOLs for anterior segment photography in children.
Lagstein O, Huey D, Guyton DL, Davidson J, Kraus CL.
JAAPOS. 2020 Jul 17. In press.

Anterior segment photography can be challenging in children, who often are not cooperative enough to comply with positioning for conventional slit lamp photography. This short technique paper describes using an expired intraocular lens to supplement a smartphone camera and obtain clear, high-resolution images of the anterior segment in children. The authors use a single piece monofocal 13 diopter intraocular lens attached to an iPhone XR (the intraocular lens is inherently adherent, so does not require additional adhesive). They provide the optical formulas to explain the magnification and focus and also provide helpful images to replicate their technique.

Technique for pediatric corneal crosslinking under general anesthesia.
Fung SS, Mason M, Gore DM, Mireskandari K, Ali A.
J AAPOS. 2020 Jun 6. In press.

Corneal crosslinking is being done with increasing frequency in children to prevent the progression of keratoconus. This is a short report of 21 eyes of 13 patients describing the technique for performing corneal crosslinking in children under general anesthesia including bilateral simultaneous crosslinking. They include details regarding their protocol which includes removing the corneal epithelium, treating the corneal stroma with riboflavin 0.1% with 5% dextran in 2 minute intervals for 10 minutes then delivering pulsed (1.5 second on, 1.5 second off) 30 mW/cm^2 over 8 minutes. They also detail their protocol which calls to start treating the second eye in the middle of treatment of the first eye to shorten operative time. This is a small study with the main goal of sharing their surgical technique. The authors conclude that bilateral simultaneous corneal crosslinking under anesthesia reduces surgical time and may be preferred in patients with bilateral disease.

Keratoplasty in infancy: how early is early?.
Lyons CJ.
JAAPOS. 2020 Jun 8. In press.

There are many unanswered questions regarding optimal timing of keratoplasty in infants. These questions are generally divided into two categories centering on the technical aspects of the surgery and post-operative anatomic and visual outcomes. This is an editorial discussing optimal timing of penetrating keratoplasty in infants accompanying the previously discussed article on keratoplasty outcomes by Areaux et al. Regarding the first point, the author notes the technical challenges posed by early surgery in the pediatric eye including low scleral rigidity, a small eye, and positive vitreous pressure. Regarding the second point, he comments on the importance of removing a corneal opacity from an amblyopia treatment standpoint. He discusses the results of the paper and shows that two conclusions can be drawn: early surgery is better than later surgery; early surgery is no better than later surgery. A complex issue, he concludes by opining that future advances in surgical technique may improve outcomes in both situations.

Anatomic and visual outcomes of corneal transplantation during infancy.
Areaux Jr RG, Orlin SE, Zaidman GW, Kothari K, Wilson LB, Huang J, Ying GS, Binenbaum G.
J AAPOS. 2020 May 24. In press.

Corneal transplantation via penetrating keratoplasty in children is notoriously difficult with poor outcomes. This retrospective cohort study aims to describe the anatomic and visual outcomes of 62 eyes of 52 patients who underwent penetrating keratoplasty in the first year of life, the majority of which had congenital corneal opacities. These patients were divided into two groups: those that had surgery before 3 months of age (8 eyes) and those that had surgery at 3-12 months of age (12 eyes). Anatomically, the Kaplan-Meier graft survival estimate for all patients combined was 0.92 at 1 year and 0.61 at 5 years. There was a non-statistically significant tendency for earlier surgery to be associated with more complications. At final follow up, graft survival was actually higher in the early PKP group compared to the later group (74% compared to 65%). They defined favorable visual outcome as “good” or “good to fair” as mild to moderate impairment or severe impairment, respectively. In the early PKP group, 42% had good acuity and 74% had good to fair acuity compared to 56% and 81% respectively in the late PKP group. The assessment of visual outcomes is limited due to the retrospective nature of the study design and inability to further analyze factors such as amblyopia treatment and compliance. The authors conclude that their outcomes for penetrating keratoplasty performed in the first year of life are better than previously described and that surgery before 3 months had similar graft survival to later surgery and that early surgery was not correlated with better visual outcomes.

Keratoconus and corneal morphology in patients with Down syndrome at a pediatric hospital.
Imbornoni LM, Wise RE, Taravella MJ, Hickey F, McCourt EA.
J AAPOS. 2020 May 27. In press.

Down syndrome, a very common chromosomal disorder, is a risk factor for keratoconus, an ectatic disease associated with progressive thinning and steepening of the cornea. The introduction of Scheimpflug imaging has improved the ability to detect early keratoconus. This was a retrospective observational study evaluating 56 eyes of 31 patients with Down syndrome aged 4-24 who underwent Scheimpflug imaging with their main outcomes being keratometry, pachymetry, and presence of keratoconus or keratoconus suspect. They found that 32% of their cohort had definite or suspected keratoconus in one or both eyes. In general, the population had steeper and thinner corneas compared to previously reported normative data (mean Kmean 45.81, Kmax 48.20). Mean pachymetry was 519 microns at the thinnest point and 519 microns at the apex. The BAD-D value (from the Berlin/Ambrosio enhanced ectasia display) was over 1.88 in 34% of eyes, signifying an abnormal cornea. The heterogeneity of the cohort and the single image obtained from each patient are the main limitations of

the study design. The authors conclude that advances in corneal imaging may lead to previously unrecognized early keratoconus in patients with Down syndrome and may expedite early treatments such as corneal crosslinking. They recommend performing Scheimpflug imaging in all Down syndrome patients that are able to cooperate.

Partial-thickness scleral defect in a congenital scleral epithelial cyst.
Shakarchi AF, Woreta F, Stroh IG, Eberhart CG, Vizcaino MA, Collins ME.
J AAPOS. 2020 Apr 4. In press.

A congenital corneoscleral epithelial cyst is a relatively uncommon ocular developmental anomaly. This case report describes a 3 year old girl with a history of bluish scleral discoloration since birth and a 3 month history of increasing size, redness, and discoloration of the lesion. She was found to have a 10x7 mm cystic lesion along the inferonasal limbus and an underlying full thickness scleral defect on ultrasound biomicroscopy. This was repaired by slowly draining the cyst, removing part of the anterior cyst wall, placing a piece of tutoplast to cover the scleral defect, and closing the incisions with fibrin glue. Histopathology of the excised tissue showed epithelial lining typical of the ocular surface. The authors discuss possible mechanisms of scleral thinning in this condition including pressure atrophy versus a developmental scleral defect (more likely in this case). The authors conclude that congenital corneoscleral epithelial cysts can be associated with scleral defects and that this should be taken into account in surgical planning, including planning for the possibility of a fistula leading to aqueous egress and anterior chamber collapse.

Nanophthalmos in children: morphometric and clinical characterization.
Agarkar S, Koladiya N, Kumar M, Vijaya L, Raman R.
J AAPOS. 2020 Feb;24(1):27.e1–5.

Nanophthalmos is a rare congenital anomaly characterized by short axial length, smaller corneal diameter, high hyperopia, and reduced ocular volume and the possibility to develop angle closure glaucoma as a result through appositional or synechial closure. This is a descriptive retrospective review of 75 children under 18 years of age with nanophthalmos aimed to describe ocular biometric and clinic manifestations of the condition. As expected, the eyes they describe are short and hyperopic (mean axial length 16.88 mm, mean refraction +13.31 D). In their cohort, only 35% of children had a visual acuity of 20/40 or better and the main cause of visual impairment was ametropic amblyopia, followed by retinal abnormalities. 23% of eyes had occludable angles of which 88% underwent prophylactic laser peripheral iridotomy and 12% required glaucoma medications in addition to laser. The lens thickness to axial length ratio was statistically different between those with and without occludable angles. The authors conclude that increased lens thickness, with or without increasing age, is a risk factor for anterior chamber angle occlusion in children with nanophthalmos, though the most common cause of decreased vision is amblyopia.

Accelerated corneal crosslinking in children with keratoconus: 5-year results and comparison of 2 protocols.
Agca A, Tulu B, Yasa D, et al.
Journal of Cataract and Refractive Surgery. 2020 Apr;46(4):517-523.

Summary: This retrospective, case-control study study performed in a teaching hospital in Istanbul, Turkey, evaluated the long-term clinical results of 2 different accelerated corneal crosslinking (CXL) protocols in pediatric patients younger than 18 years old with keratoconus. Group 1 received 4 minutes of illumination at 30 mW/cm2, and Group 2 received 5 minutes of illumination at 18 mW/cm2. Uncorrected and corrected distance visual acuities, manifest refraction, corneal topographic parameters, and corneal higher-order aberrations (HOAs) were evaluated at baseline and during 1-, 3-, and 5-year follow-up visits.

A total of 143 eyes from 86 patients were included in the study. There were 30 eyes in Group 1 and 113 eyes in Group 2. The mean follow-up time was 4.15 ± 0.99 years. Mean keratometry (K) and/or maximum K progressed ≥1.00 diopter (D) in 7 eyes (23.3%) in Group 1 and 19 eyes (16.8%) in Group 2 (P = .411). Mean K and/or maximum K decreased ≥2.00 D in 2 eyes (6.7%) in Group 1 and 24 eyes (21.2%) in Group 2 (P = .06). In Group 1, there were no statistically significant differences in topographic parameters during follow-up. In Group 2, there was a statistically significant reduction in total HOA and coma during the 5-year visit when compared with the preoperative visit (P = .005 and P = .045, respectively). The authors conclude that accelerated CXL is beneficial in terms of halting the progression of keratoconus in pediatric patients over 5 years of follow-up. An increased irradiance with a reduced application time reduces the topographic effects of CXL.

Importance: The standard protocol of crosslinking (CXL) with an irradiance of 3 mW/cm2 for 30 minutes effectively halts the progression of keratoconus in the majority of pediatric patients. The long-term effectiveness of higher irradiances combined with lower application times (accelerated CXL) is not well established in pediatric patients. This work demonstrates that 2 different accelerated procedures, with parameters as presented above, effectively halted the progression of keratoconus in the majority of pediatric patients for up to 5 years. Both protocols have a lower potential to affect the corneal topographic indices, however, compared with 10 minutes of 10mW/cm2 or the standard protocol (3mW/cm2 for 30 minutes).

The prevalence of keratoconus in children with allergic eye disease in an Egyptian population
Ahmed AS, El-Agha MH, Khaled MO, Shousha SM.
Eur J Ophthalmol. 2020, E publication ahead of print. July 13.

Allergic eye disease, particularly vernal keratoconjunctivitis, is common in areas that are hot and humid and in the African population. Keratoconus has also been linked to diseases with frequent eye rubbing. The authors sought to find out the prevalence of keratoconus (KC) in children with allergic eye diseases in Egypt. This is a cross sectional study of all children seen for allergic ocular diseases including vernal keratoconjunctivitis (VKC), seasonal allergic conjunctivitis (SAC), perennial allergic conjunctivitis (PAC), and atopic keratoconjunctivitis (AKC). All of the study patients also had corneal topography done and topographic KC was determined by the criteria for manifest KC and keratoconus suspect. 101 patients were enrolled in the study. All patients had bilateral allergic eye disease. 79% of patients had VKC. The prevalence of KC in the population was 34% (7% with manifest KC and 27% with KC suspect). There was a significant difference between the KC and non KC groups in regards to age and mean duration of symptoms, signifying that duration is an important risk factor for the development of KC. These results are similar to those reported in other geographic regions

Twelve-Month Results of Cyclosporine A Cationic Emulsion in a Randomized Study in Patients With Pediatric Vernal Keratoconjunctivitis.
Bremond-Gignac D, Doan S, Amrane M, et al for the Vektis study group
Am J Ophthalmol. 2020 Apr; 212:116-126.

Vernal keratoconjunctivitis (VKC) is most common in boys under 10 and is a severe ocular allergic conjunctivitis found globally and can cause vision loss and can adversely affect quality of life. Topical Cyclosporine A has been shown to help in cases of VKC, however it is lipophilic. A cationic emulsion of cyclosporine A (CsA CE) was developed to help increase surface time and bioavailability of the same medication. The goal of this study was to assess the safety and efficacy of the CsA CE drops in severe VKC in children. The authors performed a multicenter, double-masked, randomized controlled trial of 169 patients, aged 4-17 over 8 months. The main outcomes were safety, efficacy, and fluorescein staining scores. The authors found that the higher dose regimen (qid) had more benefit than the lower dose (bid) and that both groups showed improvement in staining, decrease rescue medication use, improved quality of life, and fewer VKC symptoms. Both groups had site instillation pain. The authors concluded that CsA CE has a favorable safety profile in children. This is a very well designed and powered study and when available will be another tool in our toolkit for treating this sometimes difficult disease.

VanderVeen DK, Drews-Botsch, CD, Nizam A, Bothun ED, et al. Outcomes of secondary intraocular lens implantation in the Infant Aphakia Treatment Study. Journal of Cataract & Refractive Surgery. 2021;47(2):172-177.

Summary: The purpose of this report was to describe outcomes for eyes that received secondary IOL implantation, including a comparison of outcomes with aphakic eyes that did not undergo secondary IOL implantation, and eyes that had primary intraocular lens implantation in early infancy. The stud was a secondary analysis of patients enrolled in the Infant Aphakia Treatment Study (IATS), a randomized clinical trial conducted at multiple clinical centers throughout the United States, that involved review of the details of all secondary intraocular lens surgeries performed. Visual outcomes, refractive outcomes, and adverse events at age 10.5 years were evaluated. Comparisons were made with eyes that remained aphakic and with eyes randomized to primary IOL placement. The IATS included 114 infants with unilateral cataracts, 57 in the aphakic group and 57 in the primary IOL group. Of those randomized to the aphakia with contact lens correction group, 55/57 were evaluated at a 10.5 year study visit and 44% (24/55) of these patients had had a secondary IOL implanted. The median age at the time of surgery was 5.4 years (range 1.7-10.3 years). For secondary IOL surgery, biometry and surgical technique were by surgeon preference. Mean absolute prediction error was 1.00 +/- 0.70 D. At age 10.5 years, the median logarithm of the minimum angle of resolution visual acuity was 0.9 (range 0.2-1.7), similar to Va in the 31 eyes still aphakic (0.8, range 0.1-2.9). The number of eyes with stable or improved Va scores between the 4.5 year and 10.5 year study visits was also similar (78% secondary IOL eyes; 84% aphakic eyes). For eyes undergoing IOL implantation after the 4.5 year study visit (n=22), the mean refraction at age 10.5 years was -3.20 +/- 2.70 D (range -9.90 to 1.10D), compared with -5.50 +/- 6.60 D (n=53, range -26.50 to 3.00 D) in eyes with primary IOL (p=0.03).

Importance: While most patients with infantile cataracts are anticipated to receive an IOL at some point, the timing of implantation has been controversial. For one thing, prediction error after pediatric cataract surgery is more variable than after adult cataract surgery. Secondly, significant axial elongation occurs in early childhood, so large degrees of myopic shift can occur in pseudophakic eyes. It has been thought that postoperative myopic shift might be minimized by performing IOL implantation after 5 years of age. This study shows that even with delayed IOL implantation, myopic shift was greater than that anticipated in many eyes. Also, while delayed IOL implantation allows a more predictable refractive outcome range at 10.5 years, the range of refractive error is still large. Finally, the results show that it is important to counsel families that the Va after IOL implantation is not expected to be significantly different than the Va obtained with contact lens or spectacle use. The authors provide a detailed explanation of the limitations of the study, but despite these limitations, the report suggests that there are refractive advantages to delaying secondary IOL surgery until school age. When the elective surgery is performed by an experienced surgeon after age 5 years, the complication rate is low and there are far fewer adverse effects than when IOL implantation is performed in infancy.

Binocular reading in children following extraction of a dense congenital or infantile unilateral cataract. Kelly KR, Jost RM, Wang SX, Stager Jr DR, Birch EE.
J AAPOS. 2020 Aug 10. In press.

Reading relies on ocular motor function which is affected by the disruption of binocularity. This is a cross-sectional study evaluating the reading rate for 20 children aged 7-13 with a history of treated unilateral or congenital cataract and 49 age-similar controls. Overall, the study shows no significant difference in reading rate between children with or without a history of unilateral congenital cataract. Additionally, reading rate with not associated with visual acuity or sensory fusion. There was no difference in reading rate between those with good and poor vision. There was a tendency toward slower reading in the cataract group, but this was not statistically significant. The one significant difference they identified was a

higher number of forward saccades in those with a history of cataract, particularly in those with fusion at near. The study is limited by its sample size and the lack of fusion in nearly all cataract patients. The authors conclude that while binocular reading rate did not differ between children with and without a unilateral congenital cataract, but that increased forward saccades in those with a history of cataract may be a result of fixation instability.

Aphakic contact lens use for improved handheld optical coherence tomography imaging in pediatric aphakic patients.
Quist MS, Brodie FL, Cai CX, Toth CA.
J AAPOS. 2020 Jul 4. In press.

Handheld optical coherence tomography serves as the only cross-sectional retinal imaging option available in some children who are unable to comply with standard in office optical coherence tomography. Many of these children have had prior surgery which may affect image quality or ease of image acquisition. This is a short report describing significant improvement in handheld optical coherence tomography image quality secondary to aphakic contact lens use. They describe a 15 year old girl with developmental delay, microphthalmia, optic nerve and retinal coloboma, and choroidal neovascularization status post lensectomy and vitrectomy for lens subluxation. Despite clear media, the image was still poor. After placing a +20 diopter aphakic contact lens on the eye, image quality improved significantly. The authors discuss that images obtained using handheld optical coherence tomography in aphakic patients may benefit from aphakic contact lens placement to overcome focal length limitations.

13. CATARACT SURGERY

Secondary intraocular lens implantation using the flanged intrascleral fixation technique in pediatric aphakia: case series and review of literature.
Sternfeld A, Taranum Basith SS, Kurup SP, Basti S.
J AAPOS. 2020 Oct;24(5):286.e1-286.e6.

This is a retrospective review of medical records of patients who underwent secondary flanged intraocular lens (IOL) implantation by a single surgeon from May 2018 to January 2020 using a fixation technique (Yamane Technique) to correct aphakia. A total of 12 eyes of 10 consecutive patients were included. Mean age at surgery was 10 $\pm$ 6 years. Indications for scleral fixation were ectopia lentis (secondary to Marfan syndrome [n = 3] or idiopathic [n = 1]), lens subluxation with intermittent pupillary block secondary to Weill- Marchesani syndrome (n = 2), early childhood lensectomy with insufficient residual capsular support (n = 5), and traumatic aphakia after an open globe (n = 1). Mean follow-up was 8 $\pm$ 5 months. No major intraoperative complications occurred. Postoperatively 1 patient required IOL repositioning 1 week after surgery. The location of one haptic was noted to be intrascleral but superficial in another patient, who did not require surgical intervention. The mean postoperative astigmatism was 2 $\pm$ 2 D. Good visual results were achieved in all eyes. The limitations of this study include the small sample size, short follow up period, and the inability to measure visual acuity in some patients due to age. This study suggests the Yamane technique can be adapted for use in pediatric aphakic eyes and provide good visual outcomes with minimal adverse events

A sustained-release intracanalicular dexamethasone insert (Dextenza) for pediatric cataract surgery.
Trivedi RH, Wilson ME.
Journal of AAPOS (2021), doi: https://doi.org/10.1016/j.jaapos.2020.10.001.

Studies of the use of a sustained-release intracanalicular dexamethasone insert in adults show efficacy in controlling intraocular inflammation after cataract extraction. The authors looked at efficacy in pediatric patients after cataract surgery. Children often have increased postoperative inflammation when compared to adults and often have limited cooperation for the instillation of eye drops by caretakers after surgery. This modality could be effective in overcoming these challenges. The authors placed the insert in 21 eyes of 18 patients and reported on 17 eyes of 17 children. One patient was eliminated because of age over 18 years old. In this study, the anterior chamber was quiet in 18% of eyes at 1-2 weeks after surgery consistent with a study looking at same metric using steroid eye drops. The authors found an intraocular pressure spike requiring intervention in 18% of eyes Additional steroid in the form of topical eye drops was needed to control inflammation in 29% of eyes. Limitations in this study included small sample size and lack of control group. The sustained-release intracanalicular dexamethasone insert may provide a useful method to improve the control of intraocular inflammation in pediatric patients. Additional studies are necessary to determine if this technique is safe and effective for pediatric ophthalmologists to use in pediatric patients.

Outcomes of sutureless and sutured scleral fixated intraocular lens in paediatric population.
Sindal MD, M A.
Eur J Ophthalmol. 2020 Oct 18

The options for intraocular lens implantation (IOL) in the absence of capsular support are anterior chamber intraocular lens (ACIOL), iris fixated IOL, and scleral fixated intraocular lens (SFIOL); however, ACIOL and iris fixated IOL may not be considered appropriate for a pediatric patient. This study was to analyze the outcomes of SFIOLs using the XNIT technique in a pediatric population. This was a retrospective case series at Aravind Eye Hospital. The mean age of a patient resulting in aphakia was 8.8

years of age mostly secondary to trauma, open globe injury, and complicated cataract surgery. The mean age for undergoing a SFIOL was 10.1 years. Patients had the most improvement in their vision in the following 1 month post SFIOL. Complications included transient hypotony, vitreous hemorrhage, haptic exposure, or disinsertion of the haptic. The authors indicated that many of their patients did not receive any refractive correction or amblyopia treatment prior to the SFIOL. However, the interval between aphakia and SFIOL was short which may be an indication to the improvement in vision. They recommend strict adherence to refractive rehabilitation with glasses or contact lenses with patching, however considering SFIOL as a secondary situation. The age of the patient and scleral rigidity should be considered in the surgical planning of SFIOL. This provides some outcomes regarding this procedure that is not typically done in a pediatric population.

Secondary glaucoma and visual axis opacification in aphakic and pseudophakic patients following congenital cataract surgery: A 28-year longitudinal case series.
Murphy M, Murtagh P, McAnena L, Eldouri A, Kirwan C, O'Keefe M.
Eur J Ophthalmol. 2020 Nov;30(6):1370-1380

Secondary glaucoma and posterior capsular opacification are well-recognized complications of congenital cataracts. In this prospective case series, the authors aim to determine the incidence, characteristics, and outcomes of secondary glaucoma. The secondary aim was to analyze the rates of posterior capsular opacification (PCO). 135 eyes were included in this single center analysis. The average length of follow up was 13.3 years. The mean time to glaucoma diagnosis post-surgery in the pseudophakic group was 3.14 years and 6.56 years in the aphakic group. For those who were operated on less than 6 weeks of age, the incidence of glaucoma was 35.60%. There was no difference between pseudophakia and aphakia. The overall results were similar to the IATS study. Overall, over half the children in this series developed a PCO. These rates were higher in the pseudophakia group. The poorest final BCVA was in the unilateral aphakia group. The bilateral pseudophakia group had the best BCVA. This study provides good outcomes similar to the IATS study.

Effect of Age at Primary Intraocular Lens Implantation on Refractive Growth in Young Children
Adrianna E. Eder, MD; Kyle F. Cox, MD; T. Amerson Pegram, MD; Scott M. Barb, MD; Mary Ellen Hoehn, MD; Natalie C. Kerr, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):264-2.

Understanding refractive growth of the pseudophakic eye during childhood is important for selecting the best intraocular lens (IOL) power at the time of implantation in children. This study evaluated the effect of age at primary intraocular lens (IOL) implantation on rate of refractive growth during childhood. A retrospective chart review was performed for children undergoing primary IOL implantation during cataract surgery. Rate of refractive growth was calculated for one eye from each patient using the first postoperative refraction, the last stable refraction, and the corresponding ages. Rate of refractive growth was compared among pseudophakic patients operated on from ages 0 to 5 months, 6 to 23 months, and 24 to 72 months.
Of 296 eyes identified from 219 patients, 46 eyes met the inclusion criteria. There was a statistically significant difference in rate of refractive growth between the two youngest and the oldest age groups. The mean value was -19.82 ± 5.23 D for the 0 to 5 months group, -22.32 ± 7.45 D for the 6 to 23 months group (0 to 5 months vs 6 to 23 months, P = 0.43), and -9.64 ± 11.95 D for the 24 to 72 months group (0 to 5 months vs 24 to 72 months, P =0.01, and 60 to 23 months vs 24 to 72 months, P =0.01). The higher negative numbers mean higher rates of refractive growth.
The authors conclude that younger age at time of IOL implantation affects the rate of refractive growth. Surgeons performing primary IOL implantation in infants may want to use age-adjusted assumptions, because faster refractive growth rates can be expected in young children. The primary critique of this study is that the majority (84%) of eyes of children having primary intraocular lens implantation were excluded from the study for a myriad of exclusion criteria, limiting the generalizability of the study. If a formula for expected refractive change is developed using only ideal situations, does it apply to the typical pediatric patient presenting for intraocular lens implantation?

Practice Patterns in the Surgical Management of Pediatric Traumatic Cataracts
Angela Y Zhu, Courtney L Kraus
J Pediatr Ophthalmol Strabismus 2020 May 1;57(3):190-198.

The authors surveyed pediatric ophthalmologists to report practice patterns regarding management of traumatic pediatric cataracts emphasizing areas of potential difference. Fifty six respondents completed the survey and were predominantly academic ophthalmologists. In cases of corneal laceration, sutures were removed 4-6 weeks after surgery most commonly. Keratometry from the uninvolved eye was used most frequently and the refractive target was based on patient age. Forty one percent of respondents preferred simultaneous cataract extraction and open globe repair when the anterior capsule was obviously violated, while only 4% would undertake simultaneous cataract surgery with an intact anterior capsule. In cases of zonular weakness >180 degrees most surgeons intentionally left the patient aphakic. When less than 180 degrees of zonular weakness was present most surgeons inserted a three piece lens in the sulcus. Greater than 90% of respondent's performed primary posterior capsulotomy in patents less than 7 years old or when they felt the patient would be unable to cooperate for YAG capsulotomy. Amblyopia therapy was typically initiated at one week after surgery. Regarding most management questions a plurality of surgeons chose the same response, while a substantial minority preferred various alternatives. For example when greater than 180 degrees of zonular weakness is present, 18% of surgeons place a three piece in the sulcus while 66% intentionally leave the patient aphakic. The authors emphasize the importance of clarifying best practices and establishing evidence based protocols to guide important management decisions such as the timing of cataract surgery, IOL related issues, and amblyopia therapy.

Proliferative Status in the Aqueous Humor of Eyes With Congenital Cataract
Zhang, Yinglei; Li, Dan; Lu, Qiang; Du, Yu; Lu, Yi; et al.
J Pediatr Ophthalmol Strabismus 2020 May 1;57(3):159-168.

The authors prospectively investigate the aqueous microenvironment's impact on lens epithelial cell growth to better understand visual axis opacification (VAO) after pediatric cataract surgery. VAO remains a persistent problem after pediatric cataract surgery, despite primary posterior capsulotomy and anterior vitrectomy. Various inflammatory cytokines in the aqueous have been studied, but less is known about how growth hormones in the aqueous are involved. Aqueous samples from 55 pediatric patients undergoing cataract surgery were screening for 40 growth factors and compared with adults undergoing cataract surgery for age related cataract. The authors found significantly elevated levels of fibroblast growth factor 4 [FGF4] in the pediatric patients. Furthermore, the levels declined as age of the children increased, indicating that its levels are highest in the youngest patients who are also most at risk for VAO. To study the impact of FGF4 on lens epithelial cells (LEC), a population of LECs cultured from the capsulorhexis was exposed to FGF4. These cells demonstrated proliferation and migration after this exposure that was both time and concentration dependent. In contrast to previous studies, overexpression of TGF-β1 was not identified in the pediatric cataract population relative to the control population. This study is important because despite advances in surgical technique VAO remains the most common problem after pediatric cataract surgery, especially in our younger patients.

Safety of piggyback intraocular lenses (polypseudophakia) in children: long-term outcomes of a 15-year, single-surgeon study.
Wilson ME, Trivedi RH.
J AAPOS. 2020 Aug 19. In press.

Piggyback intraocular lens implantation, also called polypseudophakia, is a technique in which multiple intraocular lenses are placed in the eye with the goal of utilizing the optical power of both lenses to minimize residual post-operative ametropia, particularly in eyes that require very high power lenses. This is a retrospective review including 48 eyes of 38 children aged 6 months to 2.5 years at time of surgery

who underwent piggyback intraocular lens implantation from 1998-2013 by one surgeon with a median follow up on 12.5 years (range 3-20). The technique described includes placing one intraocular lens (usually 1 piece) in the capsular bag and then a second (usually 3 piece) in the ciliary sulcus with the goal of “temporary polypseudophakia” and plan to remove the sulcus lens at a later point when the eye grows. The target refraction was plano to slightly myopic and the power of the sulcus lens was based on the anticipated growth-related refractive change. The median duration between cataract surgery and sulcus lens explantation was 3.2 years, performed when biometry predicted minimal refractive error accounting only for the posterior lens. 8% of eyes required re-operative for an early adverse event related to piggyback lens including lens tilt, pupillary capture, pupillary block glaucoma, and pupillary membrane. 21% required topical IOP-lowering therapy and 17% were diagnosed with glaucoma or glaucoma suspect. All explantations were without complication. Median final visual acuity was 20/200 in the unilateral group and 20/40 in the bilateral group. This study is limited by its lack of a control group and the disclosed negative selection bias that the authors generally reserved this technique for patients with existing dense amblyopia. Overall, the authors conclude that given their experience, piggyback intraocular lens implantation is relatively safe in children and may be a good choice particular in infant or toddlers with unilateral cataracts who may not comply with contact lens or high hyperopic spectacle correction.

Outcomes and complications of immediate versus delayed sequential bilateral cataract surgery in children.
Bhambhwani V, Khalili S, Tehrani N, Ali A, Mireskandari K.
J AAPOS. 2020 Jun 1. In press.

Cataract surgery in children, in contrast to adults, is performed under general anesthesia. Given concerns regarding repeated anesthetic events on the developing brain and resource allocation, some surgeons advocate for performing bilateral cataract surgery on the same day. Similar trends are happening in the adult cataract domain. Others advocate for a delayed sequential approach given concerns for rare events such as endophthalmitis or toxic anterior segment syndrome. This is a retrospective study of 53 children who underwent surgery at <2 years of age with either of those treatment paradigms (37 same day, 16 delayed sequential). The groups had similar baseline characteristics with the exception of more systemic and ocular associations in the same day group. The incidence of post-operative complications was 7% in same the day group versus 25% in the delayed sequential group. Mean operating room time was 3.61 hours in the same day group compared to 4.09 hours in the delayed sequential group. Neither group had any intraoperative complications. Anesthesia related adverse events were minor and uncommon but occurred more in the delayed sequential group (13% compared to 6%). Patients with same say surgery required a statistically significant fewer number of follow ups. There were no cases of endophthalmitis or toxic anterior segment syndrome, though given the size of the cohort, no evidence-based comment can be made on that. The authors conclude that same day bilateral cataract surgery in infants may be a preferred approach because it is associated with decreased operating room time, less post-operative complications, and a decreased number of follow up visits.

Comparison of visual acuity and complications between primary IOL implantation and aphakia in patients with congenital cataract younger than 2 years: a meta-analysis.
Chen J, Chen Y, Zhong Y, et al.
Journal of Cataract and Refractive Surgery. 2020 Mar;46(3):465-473.

Summary: This review/ update article consisted of a literature search performed in March 2019 and subsequent meta-analysis to locate and review data for patients with congenital cataract having surgery at younger than 2 years of age. The authors were interested in analyzing the visual acuity outcomes and complications between patients receiving primary intraocular lens (IOL) implantation and contact lens wear. Seven identified studies enrolling 675 eyes were selected for analysis. Patients with primary IOL implantation had better visual acuity than those with aphakia corrected by a contact lens (weighted mean difference = 0.161; 95% CI, 0.108-0.214). Primary IOL implantation increases the incidence of visual axis opacification compared with contact lens wear (relative risk =0.23; 95% CI, 0.13-0.42). No statistically

significant difference was found between the 2 groups regarding the prevalence of glaucoma and strabismus. Primary IOL implantation achieved better visual outcomes after cataract extraction in patients younger than 2 years. In addition, no higher risk for complications among primary IOL implantation compared with contact lens wearing was noted. The authors conclude that implanting a primary IOL during congenital cataract surgery is a better therapy for children younger than 2 years than wearing a contact lens.

Importance: The superiority of primary intraocular lens implantation vs. aphakia with contact lens wear for children having surgery under 2 years of age for congenital cataract has been debated. A significant potential limitation of this study is selection bias in the studies that were selected and the heterogeneous approaches utilized in the studies selected for inclusion.

Femtosecond laser-assisted anterior and posterior capsulotomies in children with persistent hyperplastic primary vitreous.
Tereshchenko, Aleksandr V.; Trifanenkova, Irina G.; Vladimirovich, Vlasov M.
Journal of Cataract and Refractive Surgery. 2020 Apr;46(4):497-502.

Summary: This technique-focused article describes anterior and posterior capsulotomies performed in 12 eyes of 12 patients (age range 3 months to 6 years) with congenital cataracts and primary persistent hyperplastic primary vitreous (PHPV) syndrome using a femtosecond laser. The procedure was performed in 8 eyes with PHPV severity level 1 and 4 eyes with severity level 2 (Sudovsky classification). Surgeries were performed at the Kaluga branch of the S. Fyodorov Eye MicrosurgeryFederal State Institution, Russia. Postoperative follow-up was between 8 months and 36 months. The authors report that the use of a low-energy femtosecond laser–assisted posterior capsulotomy in this pediatric population provided safe and predictable results with a reduced number of intraocular manipulations and reduced the risk for complications.

Importance: The authors argue that manual surgical manipulation of the posterior capsule is technically complicated in cases of persistent fetal vasculature and that it is “therefore difficult to achieve optimal anatomical results regarding the required diameter, shape, and localization.” They report that “an ideally round and smooth posterior capsulotomy of the required diameter was obtained in all cases” using the femtosecond laser. While this may be true, they also note that “performing a femtosecond laser–assisted posterior capsulotomy does not cause serious difficulties for a surgeon who is confident with the technology of femtosecond laser–assisted cataract surgery in adults” but do not discuss the difficulties inherent in use of the femtosecond laser by pediatric ophthalmologists, who are generally performing these procedures.

Loteprednol etabonate gel 0.5% vs. prednisolone acetate suspension 1% for the treatment of inflammation after cataract surgery in children.
Vittitow, JL, Williams JI.
Journal of Cataract & Refractive Surgery. 2020 Aug;46(8):1092-1101.

Summary: This randomized, double-masked, parallel-group, noninferiority study was conducted at 11 sites in the United States to compare loteprednol etabonate (LE) gel 0.5% with prednisolone acetate suspension (PA) 1% for the treatment of inflammation after cataract surgery in children. Eligible patients were aged 11 years or younger and candidates for routine, uncomplicated cataract surgery. Patients were randomized to a 4-week postsurgical regimen with LE gel 0.5% or PA 1%, twice on the day of surgery, 4 times daily for 2 weeks, twice daily for 1 week, and once daily for 1 week. Assessments included anterior chamber (AC) cells/flare, anterior chamber inflammation (ACI), synechiae, precipitates on the intraocular lens/cornea, visual acuity, and intraocular pressure. The intent-to-treat population comprised 105 patients (LE gel, n = 53; PA 1%, n = 52) including 52 patients aged 3 years or younger. Patients achieved a similar mean ACI grade on postoperative day 14 (primary efficacy endpoint) whether treated with LE gel 0.5% or PA 1% (difference = 0.006, 2-sided 95% CI, -0.281 to 0.292). Similar ACI outcomes additionally were observed in patients aged 3 years or younger. LE gel 0.5% and PA 1% also

appeared equally effective in resolving inflammation at all visits (days 7, 14, and 28 postsurgery), based on categorical distributions of ACI, AC cells, and AC flare scores/grades (P ≥.06). Synechiae and corneal/IOL precipitates occurred infrequently with no significant differences between groups. No safety or tolerability concerns were identified, including no treatment-related IOP increases. LE gel 0.5% was safe and effective in treating pediatric postcataract surgical inflammation, with similar outcomes as PA 1%.

Importance: Until this study was performed, there had been no published data on the use of LE gel 0.5% in the pediatric population after cataract surgery.

Visual outcomes after toric intraocular lens implantation in pediatric eyes undergoing cataract surgery.
Vasavada V, Shastri L, Vasavada AR, et al.
Journal of Cataract & Refractive Surgery. 2020 Aug;46(8):1102-1107.

Summary: This was a prospective, interventional case series performed in Ahmedabad, India, aimed at evaluating the long-term visual outcomes and complications after toric intraocular lens (IOL) implantation in children with preexisting corneal astigmatism undergoing cataract surgery. Children with regular corneal astigmatism of at least 1.5 diopters (D) were included. A standardized surgical technique with in-the-bag implantation of a toric IOL was performed. All children were followed up on postoperative day 1 and periodically thereafter, until 36 months postoperatively. The uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), and residual refractive astigmatism were documented 36 months postoperatively. Rotational stability of toric IOL was also evaluated through the follow-up duration. Complications, particularly visual axis obscuration (VAO) and glaucoma, were documented. In total, 76 eyes (51 children) were included in the study. Mean age at surgery was 7.41 ± 2.82 years (SD) and mean preoperative keratometric astigmatism was 1.56 ± 2.13 D. The CDVA (logarithm of the minimum angle of resolution [logMAR]) improved significantly from 0.59± 0.43 preoperatively to 0.23 ± 0.27 36 months postoperatively (P = .03).Mean postoperative UDVA was 0.32 ± 0.26 logMAR. Mean refractive astigmatism at final follow-up was -0.55 ±0.40 D, with 74% patients having a UDVA of at least 20/40; 5% of eyes needed VAO treatment and none developed glaucoma. No eye required repositioning of toric IOL until final follow-up. The authors conclude that toric IOL implantation reduced postoperative refractive astigmatism and gave excellent UDVA at 36 months follow-up in pediatric eyes undergoing nontraumatic cataract surgery.

Importance: Not much information is available in the literature about the long-term outcomes and efficacy of toric IOLs in addressing corneal astigmatism in older children. Of note, these toric IOLs were placed even when primary posterior capsuorhexis was performed as part of the surgery. The authors noted that surgeons attempting toric IOL placement should be confident of good biometry and perioperative measurements (not always easy to obtain in the pediatric population).

Longitudinal changes of the macular structure after lens removal combined with anterior vitrectomy after pediatric cataract surgery.
Wang D, Tian T, Wang J, et al.
Journal of Cataract & Refractive Surgery. 2020 Aug;46(8):1108-1113.

Summary: This prospective study conducted at Wenzhou Medical University, Zhejiang, China, evaluated macular thickness changes after lens removal combined with anterior vitrectomy for pediatric cataract surgery. Forty eyes of 30 children between 3 years and 9 years with pediatric cataracts, including 20 children (20 eyes) with unilateral cataracts and 10 children (20 eyes) with bilateral cataracts, were enrolled. Spectral-domain optical coherence tomography was used to obtain macular images. Central subfield thickness (CST) and retinal thickness in the Early Treatment Diabetic Retinopathy Study subfields (inner 1.0 to 3.0 mm annulus and outer 3.0 to 6.0 mm annulus) were recorded preoperatively as well as at 1, 3, 6, and 12 months postoperatively. The study found that retinal thickness in every subfield significantly thickened at 3 months postoperatively (all P < .05). CST significantly thickened compared with preoperative levels (228.03 ± 18.58 vs 240.35 ± 17.41, P = .005) at 3 months postoperatively.

Macular thickness gradually decreased in the following months. At 6 months postoperatively, retinal thickness in inner nasal, inferior, temporal, and outer nasal subfields remained significantly thicker compared with preoperative levels (P = .048, P = .036, P = .029, and P = .017, respectively). At 12 months, the retinal thickness in all subfields reached the preoperative level. The authors conclude that the influence of pediatric cataract surgery on macular thickness lasts for 12 months. The inner macular thickness increased for a longer time than the outer macular thickness postoperatively.

Importance: This study is important because the incidence of CME after pediatric cataract surgery is still not well known. This paper looked at postoperative changes in the macular structures of all ETDRS sections, not just changes in CST.

Visual Axis Opacity after Intraocular Lens Implantation in Children in the First 2 Years of Life
Ameenat Lola Solebo, Jugnoo Sangeeta Rahi, on behalf of the British Congenital Cataract Interest Group
Ophthalmology. 2020 Sep;127(9):1220-1226.

Data for this study was from the IoLunder2 cohort study which followed children in the United Kingdom and Ireland who underwent cataract surgery with or without intraocular lens (IOL) implantation for infantile cataracts in the first two years of life between January 2009 and December 2010. Of the 254 children who underwent either unilateral or bilateral cataract surgery, 110 had an IOL implanted at the time of surgery. After 5 years, 105 had completed follow up. All IOLs were acrylic monofocal lenses with square-edged optics. This study reported that 45% of the eyes that underwent IOL implantation with primary posterior capsulotomy and anterior vitrectomy developed visual axis opacity during the follow up period and were removed within the first year of surgery in 64/67 of these eyes. The majority (11/13 eyes) of those that did not undergo primary capsulotomy and anterior vitrectomy developed visual axis opacity which necessitated surgical intervention. Increasing age at surgery (OR 0.98, CI 0.96-0.99; p=0.03) and those with 3-piece IOL (OR 0.27, CI 0.07-1.00, P<0.05) were less likely to develop visual axis opacity in those with bilateral cataracts. Increasing age at surgery (OR 0.96, CI 0.92-0.99; P=0.02) and intensive postoperative topical steroids (OR 0.13, CI 0.02-0.93; P=0.04) were associated with less risk of development of visual axis opacity in children with unilateral cataracts. Limitations of this observation study include the heterogenous cohort and lack of standardization of surgical technique, but modifiable risks were identified in this study which could potentially be applied in practice to decrease the risk of visual axis opacification in this young population.

Long-term Effect of Intraocular Lens vs Contact Lens Correction on Visual Acuity After Cataract Surgery During Infancy. A Randomized Clinical Trial.
Lambert SR, Cotsonis G, DuBois L, Nizam A et al for the Infant Aphakia Study Group.
JAMA Ophthalmol. 2020 Apr;138(4): 365-372.

This study presents the long-term best corrected visual acuity (BCVA) outcome collected from the Infant Aphakia Study (IATS) in 110 of the 114 (96%) children who were initially randomized to aphakic contact lens (CL) versus intraocular lens (IOL) implantation during infancy. These children were enrolled in the multicenter randomized clinical trial with the diagnosis of unilateral congenital cataract and who underwent cataract surgery with or without a primary IOL implantation between 1 and 6 months old and now had mean age of 10.5 years (data collected from July 14, 2015 to July 12, 2019). The authors wanted to compare long-term BCVA from the two main treatment modalities after having unilateral cataract surgery during infancy. Participants in this study included 58 girls (53%) and 52 boys (47%). BCVA for 27 (25%) children had 20/40 (Snellen equivalent, logMAR 0.30) or better in the treated eye (12 (22%) in the IOL group and 15 (27%) in the aphakic CL group). However, BCVA for 50 (44%) children had 20/200 (Snellen equivalent, logMAR 1.00) or worse in the treated eye (25 (44%) in IOL group and 25 (44%) in the aphakic CL group). Of note, results in the treated eye, after a decade, indicate that the median logMAR acuity was similar in children randomized for the IOL implantation group versus aphakic CL group. The difference in median BCVA between the two groups was small and non-statistically significant; the authors address that the estimate was imprecise: 99% CI for the difference in medians was -0.54 to 0.47. In summary, the results of the BCVA at 10.5 years old in IATS participants were highly

variable; only 27 (25%) children achieving excellent BCVA in the treated eye and 50 (44%) children having poor vision in the treated eye. While the two treatment groups had non-statistically significant VA outcomes, the implantation of IOL at the time of unilateral cataract surgery during infancy was neither beneficial nor detrimental to the BCVA with longitudinal evaluation.

Outcomes of Bilateral Cataracts Removed in Infants 1 to 7 Months of Age Using the Toddler Aphakia and Pseudophakia Treatment Study Registry
Erick D. Bothun, M. Edward Wilson, Deborah K. Vanderveen, David A. Plager, Sharon F. Freedman, Rupal H. Trivedi, Elias I. Traboulsi, Jill S. Anderson, Allison R. Loh, Kimberly G. Yen, Natalie C. Weil, David Morrison, Scott R. Lambert
Ophthalmology. 2020 Apr(4);127:501-510

This retrospective study analyzed the outcomes of infants 1 to 7 months of age who underwent cataract extraction with or without intraocular lens placement. The participants were not randomized to receive intraocular lenses and intraoperative and post-operative care was not standardized. The visual acuity closest to age 5 and adverse events and findings were recorded and correlated with structural abnormalities like microcornea (<9.5mm) and microphthalmia (<17.5mm). Of the 164 children with bilateral cataract surgery, 96 were eligible for inclusion based on age at time of surgery and sufficient follow up. An intraocular lens was placed into 42 eyes, most after 2 months of age at time of surgery. Anterior vitrectomy was performed in all eyes at the time of initial surgery. At the final visit, the average logMar was 0.35 (20/45) in the better seeing eye and 0.48 (20/60) in the worse seeing eye. About 1% had 20/200 vision or worse. Microcornea was associated with poorer visual outcomes. Adverse events were identified in 47% of eyes, primarily glaucoma or glaucoma suspect in 30% of eyes. Visual axis opacification was more common in pseudophakic eyes (32%) versus aphakic eyes (14%). Fewer patients developed strabismus compared with unilateral cataract surgery patients (44% versus 81%). Each month of age correlated with a 40% reduction in glaucoma postoperatively. The authors conclude that the bilateral cataract surgery in infants results in good visual outcomes with better binocular function than unilatearal catarfact surgery.

Simultaneous Bilateral Pediatric and Juvenile Cataract Surgery Under General Anesthesia: Outcomes and Safety.
Eibenberger K, Stifter E, Pusch F, et al.
Am J Ophthalmol. 2020 Jun;214: 63-71.

The authors of this retrospective interventional case series aimed to evaluate the outcome, safety, and surgical approach of bilateral simultaneous cataract surgery (BS-Cat) compared with unilateral cataract surgery (US-Cat) and bilateral 2-timed cataract surgery (BT-Cat) in children. This study included children under 19 who had cataract surgery over a 15-year period at one institution. There were 220 eyes of 147 patients and the mean age of surgery was about 16 months. An accidental oxygen decrease below 93% was rare in all groups. Intraoperative and post-operative complications and interventions were rare and similar in all groups. The patients with bilateral surgery had longer surgical times and did spend more time in the recovery area. Simultaneous removal of bilateral cataracts in children had no statistically significant differences in intraoperative or post-operative complications compared to unilateral and 2-times surgery. The anesthesia time was longer but only by the time of the surgery in the second eye and was not associated with higher risk of decreased oxygen saturation levels. Of note the visual axis obscuration rates were seemingly high in all groups (did not differ between the study groups) but the surgical techniques have changed over the time course of the study. Importantly there was no increase in complications and no cases of bilateral TASS or endophthalmitis. The authors concluded that bilateral simultaneous cataract surgery is safe in pediatric patients. This paper is helpful to the pediatric ophthalmologist counseling parents, especially those nervous about multiple anesthetics, about the different approaches to the patient with bilateral cataracts.

Globe Axial Length Growth at Age 10.5 Years in the Infant Aphakia Treatment Study.
Wilson ME, Trivedi RH, Weakley DR, et al for the Infant Aphakia Treatment Study Group.
Am J Ophthalmol. Aug 2020; 216:147-155.

This is a comparative case series performed with the goal of reporting the change in globe axial length (AL) from the time of unilateral cataract surgery (at age 1-7 months) to age 10.5 years for infants enrolled in the Infant Aphakia Treatment Study. This study also compared AL growth of operated eyes to their unoperated fellow eyes. For the primary analysis, eyes with glaucoma or who had glaucoma suspect were excluded. Fifty-seven patients had reliable axial length data at both time points. AL growth was similar in the contact lens and IOL groups. Eyes with acuity of 20/200 or worse grew more than eyes with better acuity. Interestingly, the eyes that needed surgery to clear the visual axis grew more than eyes not requiring surgery despite being monitored every 3 months with prompt return to OR when needed. Glaucomatous eyes also grew more, as expected. The authors concluded that eyes with glaucoma and poor acuity grew longer than the fellow eyes and eyes in the CL and IOL groups grew similarly to their fellow eyes and kept pace with their fellow eye. This is the first paper to look at axial length growth after a decade of cataract surgery. It's strength lies in its prospective nature and robust data collection and is an important read for the pediatric cataract surgeon.

Predicting future axial length in patients with paedriatric cataract and primary intraocular lens
Lottelli, AC
Eur J Ophthalmol. 2020, E publication ahead of print. August 5.

There are challenges when predicting the dioptric power of an intraocular lens in a pediatric patient such as the myopic shift that can occur. As a way to minimize this effect, the strategy of aiming for hyperopia at the time of surgery has been used but how much hyperopia is the main question of this study. The goal of this author is to create a model to predict the axial length (AL) of children with unilateral and bilateral cataracts using serial AL to guide future IOL power choice. The author conducted a prospective analysis from children with unilateral and bilateral cataracts who received a hydrophobic acrylic IOL. AL was measured by immersion under anesthesia or by optical biometry in a cooperative child in clinic. Eyes with glaucoma were excluded. The results showed that the rate of axial length growth (RALG) for all eyes was 4.51 +/-3.06mm without a difference based on unilaterality, gender, and age at surgery. The model that was developed was Al=initial AL+slope x Log 10 ((age +0.6(initial age+0.6))

Cataract surgery in treated retinoblastoma eyes: A study of 29 eyes
Kaliki S, Maniar A, Kekunnaya R.
Eur J Ophthalmol. 2020, E publication ahead of print. July 25.

Patients with a history of retinoblastoma (RB) can also have simultaneous cataract for many reasons such as lens trauma, biochemical changes, exposure to radiotherapy, etc. A cataract can make the view difficult in assessing the retina and monitoring the tumor. Cataract extraction in an eye with RB can be associated with the risk of extraocular tumor extension. The authors analyze their experience in cataract surgery with treated RB in this retrospective study at the LV Prasad Eye Institute of all eyes up to 1 year after cataract surgery. 29 eyes were included in this study. The mean time between tumor regression and cataract surgery as 51 mo (range 6-245 mo). Post operatively the visual acuity was 20/200 or better in 12 eyes. 55% of eyes had improvement in vision. Complications of surgery included visual axis opacification, pupillary membrane, and hyphema. Extraocular tumor extension occurred in 1 patient. This patient had a total cataract and the RB was monitored and stable by ultrasonography alone. Cytology was suspicious and an enucleation was recommended, however this patient was lost to follow-up for almost a year and extrascleral extension was observed. Overall the authors report that cataract surgery with prior history of treated RB is safe although with a rare occurrence of extraocular tumor extension in 3%.

Safety of intracameral moxifloxacin in the pediatric population: an equivalence study.
Khalili S, Imtirat A, Williams S, et al.
Journal of Cataract and Refractive Surgery. 2020 Feb;46(2):228-234.

Summary: This retrospective consecutive cohort study performed at the Hospital for Sick Children in Toronto, Canada, investigated whether the safety of intracameral moxifloxacin (IC-Mox) was equivalent to subconjunctival antibiotics (SC-Abs) in pediatric cataract surgery. It was an equivalence study that compared 95% CI in the difference between the preoperative and postoperative safety variables of best corrected visual acuity (BCVA), intraocular pressure (IOP), central corneal thickness (CCT), endothelial cell density (ECD), corneal edema, and anterior chamber (AC) inflammation in IC-Mox with SC-Abs. The zone of clinical equivalence for BCVA was set at ±0.2 logarithm of the minimum angle of resolution, IOP at ±3 mm Hg, CCT at ±30 µm, and ECD at ±400 cells/mm2. The charts of 358 patients undergoing lens-related surgeries were reviewed. Of 317 eyes (215 patients) included, 170 eyes received IC-Mox and 147 eyes had SC-Abs. The mean age was 4.9 and 5.1 years with a mean follow-up of 19 and 34.4 months ($P < .001$) in IC-Mox and SC-Ab groups, respectively. The 95% CIs for the change from preoperative to postoperative safety parameters between IC-Mox and SC-Abs were all in the zones of clinical equivalence. During the first 6 weeks postoperatively, there was no difference in corneal edema ($P = .69$) and ACflare ($P = .4$) between IC-Mox and SC-Ab groups, whereas AC cellular activity was significantly higher in the SC-Ab group ($P = .028$). IC-Mox prophylaxis in pediatric patients showed equivalent postoperative safety outcomes when compared with SC-Abs. The authors conclude that use of IC-Mox (250 µg) for endophthalmitis prophylaxis appears to be safe in the pediatric population.

Importance: While the efficacy and safety of intracameral moxifloxacin has been established in adult populations, its safety profile in children requires further investigation for many reasons unique to the pediatric eye and the nature of pediatric cataract surgery (for example, primary posterior capsulotomy resulting in unicameral eye).

14. GLAUCOMA

Failure of Goniosurgery for Glaucoma Associated With Sturge-Weber Syndrome. Yeung HH, Kane SA, Turlapati N, Nzuna JS, Walton DS.
J Pediatr Ophthalmol Strabismus. 2020 Nov 1;57(6):384-387.

This retrospective chart review of 46 eyes (42 patients) with Sturge-Weber associated glaucoma reviewed the results of goniosurgery. Goniosurgery included both goniotomy (n=51) and trabeculotomy (n=11). Complete success, defined as IOP 22 mmHg or less without medications, was achieved in zero patients. Qualified success, IOP 22 mmHg of less with medications, was achieved in 2%. The remaining 98% failed to achieve control of IOP, defined by persistent IOP elevation or need for non-goniosurgery. IOP measurements were included from the final two follow up visits and 6 months minimum of follow up was required for inclusion. The average postoperative interval to failure was 4 months. These results suggest that while goniosurgery is unlikely to achieve complete success, it can be useful along with medications to provide short-medium term IOP control.

From Conventional Angle Surgery to 360-Degree Trabeculotomy in Pediatric Glaucoma
Osvaldo Berger, Jibran Mohamed-Noriega, Sancy Low, Moritz C. Daniel, Sakaorat Petchyim, Maria Papadopoulos and John Brookes.
American Journal of Ophthalmology, 2020 Nov; 219: 77-86.

This retrospective comparative interventional case series was designed with the purpose of describing the transition from conventional angle surgery (CAS) to 360-degree trabeculotomy with microcatheter (MCT). The authors reviewed 106 consecutive cases (77 patients) in a 6-year period at one institution. The authors included patients with previous angle surgery. Fifty-four of these eyes had MCT and 52 CAS. After a single surgery and at last visit (year 1 or longer) the authors found a 69% complete success rate and a 85% qualified success rate in the patients with MCT. There was a 23% complete success rate and 37% qualified success rate in patients who had CAS. The MCT surgical time was 18 min longer on average. The authors concluded that MCT had better results, lower reoperation rates and that this transition from CAS to MCT is quite achievable. This article is a really important for the pediatric ophthalmologist treating glaucoma because it really encourages the transition away from CAS toward MCT. For those of us comfortable with a success of a well -known intervention, it is tempting to continue the same surgery we have always done. However decreased return to OR rates balance out the cost and longer surgical learning curve over time. This paper strongly supports the transition away from conventional angle surgier and to 360-degree surgery especially for primary congenital glaucoma.

Facial Port-Wine Stain Phenotypes Associated with Glaucoma Risk in Neonates.
Ahnul Ha, Jin-Soo Kim, Sung Uk Baek, Young Joo Park, Jin Wook Jeoung, Ki Ho Park and Young Kook Kim.
American Journal of Ophthalmology, 2020 Dec; 220:183-190.

This is a retrospective cohort study of 34 patients with port wine stains (PWS) (7 of these with bilateral PWS), over 15 years. The authors' aim was to determine if the size and location of the PWS can predict glaucoma risk in neonates. Infants were included if they had an ophthalmology exam by the age of 4 weeks and had facial photographs, intraocular pressure, corneal diameters, cup to disc ratio, SWS diagnosis, and distribution of the facial vasculature. Over half (53%) of the patients had a diagnosis of glaucoma and those tended to be patients with both S1 and S1 involvement. Additionally, patients with lower eyelid involvement were more likely to have glaucoma. This paper is very important to the pediatric ophthalmologist who is counseling parents of newborns with port wine stain on their baby's risk of glaucoma. However this study only looks at risk at one month, so more longitudinal studies will be more meaningful in the future.

Follow-up Adherence and Barriers to Care for Pediatric Glaucomas at a Tertiary Care Center
Brian Mikolajczyk, Ethan R. Greenberg, Hannah Fuher, Michael Berres, Laura L. May and Raymond G. Areaux.
American Journal of Ophthalmology, 2021 Jan; 221: 48-54.

The authors of this retrospective cohort study aimed to determine the adherence to follow for patients with pediatric glaucoma with the goal of better understanding risk factors for non compliance. The authors studied patients with pediatric glaucoma at one institution over an 8.5-year period and they defined adherence as following up between 0-30 days from recommended follow up period, non-adherence as 31-180 days of follow up, and lost to tertiary follow up if latera than 180 days or never. Surprisingly, only 54% of patients were adherent and 43% were lost to follow up. The authors concluded that this adherence rate was extremely low. Patients with better vision were more likely to have had good adherence. They found that non-white race and distance to the clinic were risk factors for non-compliance. This is important information for the pediatric ophthalmologist treating glaucoma when assessing risk factors for lack of adherence. Additionally, the authors were careful not to draw causation, but the improved vision in the patients who had compliance with follow up suggests that patients who come to their visits may have better visual outcomes. These numbers are surprisingly high and a great reminder to those who treat glaucoma to train their staff about the importance of reaching out to patients who miss their appointments.

Common and rare complications following filtering surgery for children with congenital glaucoma; a 5 year study.
Sayed KM.
Eur J Ophthalmol. 2021 Jan 9

Patients with congenital glaucoma (CG) in this single center retrospective observational study in Egypt require more aggressive initial management of their disease compared to other parts of the world. For this reason, patients are assigned to a combined procedure as initial treatment of their CG. The purpose of this study is to identify and determine early and late post-operative complications following a combined trabeculectomy-trabeculotomy with MMC. The study included 190 eyes who underwent this surgery. Intraoperative complications included difficult trabeculotomy, premature penetration into the AC, hyphema, and vitreous pocket herniation after a PI. Early postoperaetive complications developed in 40% of the eyes and included hypotony with shallow AC (16.3% of eyes) and hyphema (10.5%). Late postoperative complications included elevated IOP requiring another surgery in 16.5% of eyes, thin cystic blebs (13.1%), and rarely blebitis. This study describes potential complications following this specific intervention.

Vision-related quality of life in patients with a history of congenital glaucoma.
Miraftabi A, Coleman AL, Nilforushan N, Parsamanesh M, Nguyen AH, Karimi N, Chibaksh S.
Eur J Ophthalmol. 2020 Dec 21

Patients who have primary congenital glaucoma can have varying degrees of visual impairment that can affect their quality of life as adults. The authors used the NEI-VFQ 25 survey which assesses vision, driving, role difficulties, and social functioning due to vision in adult patients with a history of congenital glaucoma. A total of 23 patients were included in those study. The lowest score belonged to mental health and the highest score was for color vision. The authors found that a significant impact of visual field loss and cornea clarity with lower self-reported survey subscales. This is an important consideration in counselling families of a patient with congenital glaucoma as they age into adulthood.

Clinical characteristics and treatment of secondary glaucoma, glaucoma suspects and ocular hypertension after congenital cataract surgery. Eibenberger K, Kiss B, Schmidt-Erfurth U, Stifter E.
Eur J Ophthalmol. 2021 Feb 1

Secondary glaucoma is a main risk of children who have cataract surgery. The purpose of this study was to evaluate changes in IOP after congenital cataract surgery. This is a retrospective case series of children who had cataract extraction from ages 0-2. Patients were categorized into 3 groups: secondary glaucoma (IOP measurements above 21 mmHg with either myopic shift, cornea edema or enlargement, or optic nerve cupping) , glaucoma suspect (C/D >0.4 with temporary or without increase in IOP and use of topical IOP drops), and ocular hypertension (increase in IOP measured on 2 visits without anatomical changes but prescription of topical IOP drops). 161 eyes of 110 patients were included. 29 eyes of 17 children had secondary glaucoma, 3 eyes of 3 patients with glaucoma suspect, and 15 eyes of 10 patients with ocular hypertension. There was no difference in surgical procedure. A younger age of cataracts surgery was more significant in secondary glaucoma group, especially in the first 2-3 months of life. The development of secondary glaucoma was associated with a significant increase in surgical re-treatments. This is an important consideration when counselling families of patients with congenital glaucoma.

Incidence and outcome of suprachoroidal hemorrhage associated with pediatric glaucoma surgery.
Al-Abeeri A, Ahmad S, Al-Gaeed A, Ahmad A, Malik R.
J AAPOS. 2020 Feb;24(1):25.e1-25.e6.

The authors report on the incidence and outcomes of suprachoroidal hemorrhage (SCH) associated with pediatric glaucoma surgery. This retrospective study from King Khaled Eye Specialist Hospital involved reviewing records of pediatric patients (<18 years of age) who had undergone glaucoma surgery and developed SCH from June 2014 to September 2017. In all cases, the SCH was suspected clinically and was confirmed by B-scan ultrasound. Of 2,656 glaucoma surgeries during the study period, there were 31 cases of suspected SCH. 17 were confirmed (11 girls), for an overall incidence of 0.64%; the remaining 14 were cases of choroidal effusion. 16 of the 17 SCH cases occurred postoperatively, and 1 was noted intraoperatively. The incidence of SCH was highest for trabeculectomy (4/121 = 3.3%), followed by glaucoma drainage device surgery (6/463 = 1.3%), deep sclerectomy (6/ 851 = 0.7%), and transcleral cyclophotocoagulation (1/542 = 0.2%). Of note, however, the difference between trabeculectomy and glaucoma drainage device did not reach statistical significance. At a mean final follow-up of 1.7 +/- 1.1 years), visual acuity in the affected eye was 20/50 or better in 3 children, between 20/50 and 20/200 in 5 children, and counting fingers or worse in 9 children. The strength of this study is including a very large number of pediatric glaucoma surgeries to find an overall estimated incidence of subprachoroidal hemorrhage of 0.64%, similar to a retrospective literature search of case series estimating it at 0.36%.

The Relationship Between Optic Nerve Cup-to-Disc Ratio and Retinal Nerve Fiber Layer Thickness in Suspected Pediatric Glaucoma
Mocan, Mehmet C; Machen, Lindsay; Jang, Inae; Cao, Dingcai.
J Pediatr Ophthalmol Strabismus 2020 Mar;57(2):90-96.

In this retrospective study, 43 pediatric glaucoma suspects due soley to increased cup-to-disc ratio (CDR) were included for review of OCT findings. Included patients had CDR of >0.5, normal IOP and no predisposing risk factors (Sturge-Weber, etc). The authors found that global peripapillary RNFL did correlate with refractive error and Bruch's membrane opening (BMO) and did not correlate with CDR or patient age. Enlarged BMO and greater hyperopia were both associated with higher RNFL measurements. BMO and digitally derived CDR were also correlated supporting the notion that a large disc can have a large cup due to the normal number of axons distributed over a larger area. The results suggest that OCT RNLF measurements are expected to be essentially normal in patients with enlarged CDR who do not have glaucoma. This is especially usefully information when IOP is difficult to obtain or unreliable. The authors mentioned taking into account refractive error and BMO when evaluating OCT RNFL results, but did not provide specific adjustments or corrections for clinicians.

Distribution of intraocular pressure in healthy Iranian children: the Shiraz Pediatric Eye Study.

Masoumpour MB, Nowroozzadeh MH, Talebnejad MR, Mahdaviazad H, Khalili MR, Keshtkar M, Mohammadi E, Tajbakhsh Z.
J AAPOS. 2020 Jun 6. In press.

Given variability with age and with different tonometers, there is an interest in obtaining normative values for ocular biometrics in children. To that end, this is a cross-sectional study assessing ocular characteristics of 1,901 Iranian school children aged 6-12 as part of the Shiraz Pediatric Eye Study. Demographic and medical characteristics were collected. Eyes were examined using non-contact air-puff tonometry (CT-80), an auto-refractor, and biometry (IOL Master 500). Intraocular pressure data histograms showed Gaussian distribution curves skewed to the right and only 3% of the cohort had intraocular pressure higher than 20 mmHg. They perform a regression analysis showing slightly lower intraocular pressure in children with asthma. One limitation of this study is the unreliability of non-contact tonometry. This is recognized in the study design, where the authors referred children with IOP >21 mmHg using non-contact tonometry to see a specialist to perform Goldmann applanation tonometry (Goldmann tonometry values were included in analysis). Overall, the authors provide a normative database for non-contact tonometry in Iranian children aged 6-12.

The shrinking eye: dimensional changes in the young child's eye after glaucoma drainage device implantation for refractory childhood glaucoma.
Le H, Shue A, Freedman SF.
J AAPOS. 2020 Feb;24(2):84e1-4.

Due to the elasticity of the sclera in children compared to adults, fluctuations in axial length occur in the setting of large changes in intraocular pressure. This paper is a retrospective review describing 16 eyes of 10 children who underwent glaucoma drainage device implantation at <3 years of age with available data regarding pre- and post-operative axial length, intraocular pressure, corneal diameter, and optic nerve cup:disc ratio. They found a mean post-operative decrease in axial length of 0.8 mm, corneal diameter of 0.3 mm, and intraocular pressure of 15.0 mmHg, all of which were statistically significant. Intraocular pressure and corneal diameter reduction were both significantly correlated with axial length reduction. The authors also describe the previously reported post-operative optic nerve cupping reversal in 50% of patients, though many patients did not have an initial optic nerve exam due to media opacity. This study addresses the immediate 6 month post-operative axial length change and is limited in its ability to assess longer term axial length changes The authors conclude that post-operative axial length shortening should be taken into account when considering glaucoma drainage device placement to prevent optic nerve impingement.

Choroidal neovascular membrane associated with primary congenital glaucoma and buphthalmos.
Wang YE, Ramirez DA, Hussain RM, Berrocal AM, Chang TC.
J AAPOS. 2020 Feb;24(1):53-6.

Choroidal neovascular membranes can cause significant visual morbidity and are most commonly seen in conditions such as age-related macular degeneration and pathologic myopia. This is a case report of a choroidal neovascular membrane in an 18 year old man with a history of primary congenital glaucoma diagnosed at age 4 who had undergone angle surgery (ab externo trabeculotomy) and subsequent incisional surgery (Baerveldt glaucoma drainage device implantation). The patient presented with acutely decreased vision and was found to have an intraretinal hemorrhage temporal to the optic disc. Further investigations revealed a neovascular membrane with subtle subretinal fluid associated with a break in Bruch’s membrane. He received 3 monthly injections of intravitreal bevacizumab and his vision returned to baseline. The authors conclude that this is the first report of a choroidal neovascular membrane secondary to buphthalmos and that this can be successfully treated with intravitreal bevacizumab.

Contemporary management of refractory pediatric glaucoma.
Malik R, AlDarrab A, Edward DP.

Curr Opin Ophthalmol. 2020 Mar;31(2):123-131.

The authors review the management of refractory pediatric glaucoma with discussion of different treatment modalities. Of note, circumferential trabeculotomy may have a significant role in pediatric patients who failed prior goniotomy or trabeculotomy, as well as patients with uveitis or who are aphakic. The procedure, however, may not be successful in those patients with glaucoma drainage devices (GDD). Trabeculectomy is more likely to be successful (60-70%) in patients with primary congenital glaucoma vs those with secondary causes and who have failed prior goniotomy and trabeculotomy. In addition, it has a good success rate in children who are phakic. GDDs with valves have good short term success rates as high as 80% at 1 year but late encapsulation or fibrous ingrowth into the valve can cause significant 5 year failure rate. Revision of the plate with excision of the capsule, use of a non-valved device exchange can have good short term solutions but may ultimately fail as well. GDDs are good options for patients with prior four quadrant surgery. Deep sclerectomy has been reported to have an 80% success rate in Middle Eastern populations and requires less use of postoperative steroids and EUAs compared with trabeculectomy. Lastly, the authors discuss cyclodestructive procedures which are generally a last resort. However, newer modalities such as micropulse cyclophotocoagulation may be as efficacious as trans-scleral procedure with a safer post-op course. Endocyclophotocoagulation is associated with a medium success rate (50%) and has a significant risk of retinal detachment. The authors provide a review of surgical options for refractory glaucoma however it is limited by the retrospective nature of most of the papers cited, small case reports, and the authors include recommendations from their own experience as well.

Glaucoma in pregnancy: an update.
Strelow B, Fleischman D.
Curr Opin Ophthalmol. 2020 Mar;31(2):114-122.

The authors review the approach to patients with glaucoma in relation to pregnancy. They discuss preconception counseling with discussion of the increased risk of progressive visual field loss and IOP spike seen in pregnant patients. A consideration of early surgical intervention in advanced or high-risk glaucoma patients who seek to become pregnant, should be undertaken to minimize the possible exposure to potentially harmful medications during pregnancy. Patients who become pregnant should likely undergo increased frequency of monitoring, at least once every trimester. In the first 8 weeks all medications should be discontinued, and if therapy is required brimonidine should be used. Timolol may also be used alone or in combination with brimondine. Prostoglandin analogues (PA) are not recommended due to the theoretical risk of affecting uterine tone which could lead to miscarriage. Topical CAIs should not be precluded however should not be used as first or second line agents, however, if a patient is on multidrug therapy it could be continued. Systemic CAI's should be limited in the first trimester. In the second trimester, brimonidine remains safe as a first line agent, however beta blockers can cause IUGR when administered systemically and therefore should be used with caution. If continued, the patient may require increased fetal growth monitoring. PAs and CAIs could be used as third-line treatments if necessary and systemic CAIs could be employed in refractory cases. In the third trimester brimonidine must be discontinued due to CNS depression in neonates. Fetal heart rate and growth should be monitored with the use of beta-blockers, into the peripartum period. Caution in the use of topical and systemic CAIs should be used in the peripartum period as well, and PAs should be restricted due to the possible tocolytic effect of latanaprostene which may impair labor progression. Post-partum, brimonidine should not be used in nursing mothers, and beta blockers are safe except in mothers with infants who have heart disease. PAs have a short half-life and therefore it is suggested that they be administered just after breastfeeding so that they can dissipate and limit exposure. CAIs have no reported complications in either systemic or topical forms. SLT and endocyclophotocoagulation can both be considered in pregnancy as well as PI, and surgery can be used with caution with careful consideration of surgical positioning. MIGs may be a good choice as they can be done quickly and with topical anesthesia. MMC and 5-FU should not be used as they are Category X in pregnancy. The authors undertake a fairly comprehensive discussion of the management and considerations in patients with a history of glaucoma who are considering pregnancy, or are already pregnant.

Association of Ambient Particulate Matter Exposure with the Incidence of glaucoma in Childhood.
Min KB and Min JY
Am J Ophthalmol. 2020 Mar;211:176-182.

This was a retrospective cohort study of 9,004 infants born in 2002 and followed over 11 years conducted with the purpose of investigating if exposure to air pollution is associated with the diagnosis of congenital glaucoma. The authors specifically looked at exposure levels of particles with a mass median aerodynamic diameter $\leq$ 10um (PM10). The authors collected data on patients from the National health Insurance Service-National Sample Cohort and they extrapolated exposure levels to PM10 using geographic information systems. Over this 11-year period, 85 (0.94%) patients developed glaucoma and the authors found that the probability of having glaucoma increased with quartile increases in PM10 exposure. The hazard ratio for developing glaucoma in the 4th PM10 quartile was 6.61. The authors concluded that both short- and long-term exposure to PM10 was associated with an increased incidence of glaucoma. This is the first paper to show a connection between air pollution and childhood glaucoma risk. The authors point out the limitations being mostly that other socioeconomic factors were not controlled for and also that individual household PM10 measurements were not made, but rather grouped by national air pollution monitoring system and thus could not be generalized to other settings. This paper raises an interesting new concern about air pollution and childhood glaucoma, though done in a very specific geographic setting.

Rate of Complete Catherization of Schlemm's Canal and Trabeculotomy Success in Primary and Secondary Childhood Glaucomas.
Rojas C and Bohnsack BL.
Am J Ophthalmol. 2020 Apr; 212:69-78.

The retrospective observational case series at one institution was performed to describe the rate of complete canalization in pediatric glaucomas. Eighty-five eyes of 60 pediatric patients underwent trabeculotomy over a 6-year period and surgical success was described as an IOP between 5-20 without additional glaucoma surgery. In bilateral cases the authors used the first eye in the analysis. Most pateints in this series had primary congenital glaucoma, next most common was juvenile open angle glaucoma, glaucoma following cataract surgery, and other forms. Microcatheter canalization was attempted in 52 of the 60 eyes and was achieved a full 360 degree in 21 eyes (40%). This success for 360-degree catheterization was higher in patients in JOAG (69%). The 5-year survival rates in eyes with the 360-degree catherterization was higher than those who could not be successfully cannulated. The surgeries were all performed by one surgeon at one institution in an external fashion suing the iTRACK device.

The authors concluded that the 360-degree catheter trabeculotomy is highly effective when it's completed, but congenital anomalies often prevent full canalization. The authors discuss an important point – was the high success of the 360 catheter trabeculotomy in pediatric glaucomas due to the large cleft formation or a bias toward the more intact angle structures? Additionally, many of the congenital glaucoma cases had already had a prior surgery before this technique was attempted. Nonetheless this is an important paper for the pediatric ophthalmologist to council their patients on success of this surgical approach in different forms of pediatric glaucoma.

Aurolab Aqueous Drainage Implant With and Without Scleral Patch Graft in Refractory Adult and Pediatric Glaucomas: A Comparative Study.
Puthuran GV, Palmberg P, Kaushalya H, et al.
Am J Ophthalmol. 2020 Aug;216:226-236.

The Aurolab aqueous drainage implant (AADI) glaucoma drainage device (GDD) is a low cost, non-valved device as an alternative to the Ahmed or Baerveldt implants. While scleral patch grafts are

considered standard with GDDs, they require access to an eye bank, limiting the ability to place these in some parts of the world. Instead, in this technique, the surgeons used a needle generated scleral tunnel without a patch graft. This retrospective comparative interventional case series included 215 adult eyes and 111 pediatric eyes. The goal was to compare the 2-year outcomes of eyes with the AADI with and without scleral patch graft. Failure was defined as IOP over 18 or not reduced by 30% below baseline on 2 follow up visits after 3 months. They found that in the pediatric eyes, there was no difference in success with or without the scleral patch graft and there were no eyes with exposure of the tube. The authors concluded that the AADI without a patch graft was as successful as the AADI with the patch graft. The limitations of this study are due to its retrospective nature. Additionally the low numbers of tube erosions makes it underpowered to determine a difference between the two groups.

15. REFRACTIVE SURGERY

There are no articles in this section.

16. GENETICS

Silencing of the Long Noncoding RNA MYCNOS1 Suppresses Activity of MYCN-Amplified Retinoblastoma Without RB1 Mutation.
Saengwimol D, Chittavanich P, Laosillapacharoen N, Srimongkol A, Chaitankar V, Rojanaporn D, Aroonroch R, Suktitipat B, Saisawang C, Svasti S, Hongeng S, Kaewkhaw R.
Invest Ophthalmol Vis Sci. 2020 Dec 1;61(14):8.

In a novel subtype of retinoblastoma carrying wild-type RB1 gene, high focal amplification of the oncogene MYCN has been identified as the primary driver of tumorigenesis. In these patients, MYCNOS (opposite strand of MYCN) is co-amplified with MYCN. MYCNOS encodes several RNA variants. In this study, the authors examined profiles of MYCNOS variants and MYCN status in 17 retinoblastoma tissues, cell lines, retinas, and retinal organoids. Functional studies showed that expression of MYCNOS1 variant was associated with the expression and copy number of MYCN. Knockdown of MYCNOS1 caused instability of the MYCN protein, leading to cell cycle arrest and impaired proliferation and chemotaxis-directed migration in MYCN amplified retinoblastoma cells with wild-type RB1. MYCNOS1 expression was associated with gene signatures of photoreceptor cells and epithelial–mesenchymal transition. MYCNOS1 silencing enhanced the response of retinoblastoma cells to topotecan but not carboplatin. The findings in this study suggest that inhibition of MYCNOS1 may be important in treatment of MYCN- driven retinoblastoma.

PDE6C: Novel Mutations, Atypical Phenotype, and Differences Among Children and Adults.
Daich Varela M, Ullah E, Yousaf S, Brooks BP, Hufnagel RB, Huryn LA.
Invest Ophthalmol Vis Sci. 2020 Oct 1;61(12):1.

Genetic variation in PDE6C is associated with achromatopsia and cone dystrophy, with rare reports of cone–rod dystrophy in the literature. PDE6C-related cone–rod dystrophy consists of a severe phenotype characterized by early-onset nystagmus, decreased best-corrected visual acuity, poor color discrimination, progressive constriction of the visual field, and night blindness. This case series describes four patients (two pediatric and two adult) with PDE6C related cone and cone–rod dystrophy, including longitudinal data of a pediatric patient with PDE6C-related cone dystrophy. All patients in this series have decreased best-corrected visual acuity (ranging from 20/125 to 20/250) and poor color discrimination. Three of the four patients had a cone–rod dystrophy, who have ERG showing decreased amplitude on both photopic and scotopic waveforms and a mild to moderately constricted visual field. One of the pediatric patients was diagnosed with cone dystrophy with a preserved peripheral field. The children had none to minor structural retinal changes, whereas the adults had clear macular dystrophy. This study provides important findings on phenotypic variation of novel PDE6C mutations, including evidence of rod involvement. Gene therapy for achromoatopsia is currently in the clinical trial phase; therefore, knowing when clinical findings appear could narrow the therapeutic window and guide treatment.

SVEP1 as a Genetic Modifier of TEK-Related Primary Congenital Glaucoma.
Young TL, Whisenhunt KN, Jin J, LaMartina SM, Martin SM, Souma T, Limviphuvadh V, Suri F, Souzeau E, Zhang X, Dan Y, Anagnos E, Carmona S, Jody NM, Stangel N, Higuchi EC, Huang SJ, Siggs OM, Simões MJ, Lawson BM, Martin JS, Elahi E, Narooie-Nejad M, Motlagh BF, Quaggin SE, Potter HD, Silva ED, Craig JE, Egas C, Maroofian R, Maurer-Stroh S, Bradfield YS, Tompson SW.
Invest Ophthalmol Vis Sci. 2020 Oct 1;61(12):6.

Primary congenital glaucoma (PCG) is an early childhood disease that can cause debilitating vision loss. TEK haploinsufficiency accounts for 5% of PCG in diverse populations with low penetrance explained by variable dysgenesis of Schlemm's canal in mouse models. In this retrospective cohort study of eight families with TEK-related PCG, the authors identified heterozygous TEK loss-of-function alleles, with parent–child disease transmission observed in two pedigrees. Family 8 exhibited greater disease

penetrance and severity, histology of an enucleated eye from this family revealed absence of Schlemm's canal, and SVEP1:p.R997C was identified in four of the five affected individuals. Mouse model tissue studies showed that during Schlemm's canal development, SVEP1 is secreted by surrounding tissues. Additionally, the authors found that in human umbilical vascular endothelial cells, extracellular wild type SVEP1 protein was able to stimulate expression of TEK expression, while p.R997C SVEP1 failed to promote TEK expression. This study affirms the role of TEK haploinsufficiency in PCG, in an autosomal pedigree pattern. Additionally, the authors identified SVEP1 as a modifier of TEK expression, which can potentially serve as a new therapeutic target.

Candidate Genetic Modifiers for RPGR Retinal Degeneration.
Appelbaum T, Murgiano L, Becker D, Santana E, Aguirre GD.
Invest Ophthalmol Vis Sci. 2020 Dec 1;61(14):20.

X-linked Retinitis pigmentosa (XLRP) accounts for 10-20% of all RP cases, and comprise of some of the most severe diseases. Approximately 75% of XLRP cases map to the RP3 locus that encodes the disease causative gene retinitis pigmentosa GTPase regulator (RPGR). This study is conducted in naturally occurring canine models of X-linked progressive retinal atrophy (XLPRA), with the aim to examine the genetic basis of phenotypic variation caused by a five-nucleotide deletion in canine RPGR exon ORF15. A genome-wide association study (GWAS) was performed in XLPRA1 phenotype informative pedigree, and identified 4.6Mb candidate genomic interval on CFA31 containing seven protein-coding genes expressed in retina (ROBO1, ROBO2, RBM11, NRIP1, HSPA13, SAMSN1, and USP25), as well as two novel lncRNAs (ROBO1-AS and ROBO2-AS), that display overlapping gene organization with axon guidance pathway genes (ROBO1 and ROBO2). The authors also evaluated the gene variants and their association with disease phenotype. This study provides insight into the genetic basis of phenotypic variation in severity of RPGRorf15-associated retinal degeneration, and suggests an important role for ROBO pathways in disease progression. These results provide opportunities to explore genetic variants in corresponding human orthologous genes and their prognostic value in RPGR-XLRP.

Clinical Phenotype and Course of PDE6A-Associated Retinitis Pigmentosa Disease, Characterized in Preparation for a Gene Supplementation Trial.
Kuehlewein L, Zobor D, Andreasson SO, Ayuso C, Banfi S, Bocquet B, Bernd AS, Biskup S, Boon CJF, Downes SM, Fischer MD, Holz FG, Kellner U, Leroy BP, Meunier I, Nasser F, Rosenberg T, Rudolph G, Stingl K, Thiadens AAHJ, Wilhelm B, Wissinger B, Zrenner E, Kohl S, Weisschuh N; RD-CURE Consortium.
JAMA Ophthalmol. 2020 Oct 15;138(12):1241–50.

This is a prospective, longitudinal, observational cohort study conducted at a single center in Germany of retinitis pigmentosa patients with variants in PED6A. 57 patients from 44 families were included in the study. The results showed that the most frequently observed alleles were c.304C>A;p.(R102S), c.998 + 1G>A;p.?, and c.2053G>A;p.(V685M). Clinical features including best corrected visual acuity, visual field, electroretinography, and optical coherence tomography imaging were evaluated. The authors found that the variant c.998 + 1G>A;p.? led to a more severe phenotype when compared with the variant c.304C>A;p.(R102S). The results of this study provides more information on genotype-phenotype correlation of PDE6A variants in retinitis pigmentosa, and provides further potential treatment targets for gene therapy.

Association of a Novel Intronic Variant in RPGR With Hypomorphic Phenotype of X-Linked Retinitis Pigmentosa.
Cehajic-Kapetanovic J, McClements ME, Whitfield J, Shanks M, Clouston P, MacLaren RE.
JAMA Ophthalmol. 2020 Sep 24;138(11):1151–8.

This is a case series of 3 members of an X-linked retinal degeneration family with atypical preservation

of visual acuity in the presence of a novel deep intronic splice site RPGR c.779-5T>G variant. Clinical evaluation was performed to evaluate phenotype. The pathogenicity of this variant was assessed by in silico splice prediction tools and purpose- designed in vitro splicing assay, and showed this variant to have reduced efficiency of intron splicing compared with wild type, leading to a population of mutant and normal transcripts. The predicted consequences of the pathogenic variant are potential use of an alternative splice acceptor site, resulting in premature truncation, or complete skipping of exon 8, resulting in a protein with some normal function, which would explain preserved visual acuity. This study demonstrates the important value of a molecular splice assay in confirming new pathogenic variants in noncoding regions.

Association of Sex With Frequent and Mild ABCA4 Alleles in Stargardt Disease.
Runhart EH, Khan M, Cornelis SS, Roosing S, Del Pozo-Valero M, Lamey TM, Liskova P, Roberts L, Stöhr H, Klaver CCW, Hoyng CB, Cremers FPM, Dhaenens CM; ABCA4 Disease Consortium Study Group.
JAMA Ophthalmol. 2020 Oct 1;138(10):1035-1042.

This is a cross-sectional study of autosomal recessive Stargardt disease (STGD1) patients from multicenter genetic studies. 550 unrelated patients with genetically confirmed STGD1 with variants in ABCA4 were included in the study to evaluate the mechanisms behind phenotypic variability and reduced penetrance. All 5 of the mild ABCA4 alleles were calculated to have incomplete penetrance. In those carrying one of the two most frequent and mild alleles, c.5603A>T and c.5882G>A, the women to men ratios were 1.7 to 1, and 2.1 to 1, respectively. These ratios were higher compared to subgroups not carrying a mild allele. This study adds to the evidence of reduced penetrance for some ABCA4 genotypes, and introduces an association of sex and disease penetrance.

An ophthalmic rating scale to assess ocular involvement in juvenile CLN3 disease.
Dulz S, Atiskova Y, Wibbeler E, Wildner J, Wagenfeld L, Schwering C, Nickel M, Bartsch U, Spitzer MS, Schulz A.
American Journal of Ophthalmology. 2020 Dec 1;220:64-71.

Juvenile CLN3 disease, the most prevalent form of Batten disease, is a progressive neurodegenerative disorder resulting from mutations in the CLN3 gene. This retrospective, cross-sectional study aimed to design an ophthalmic rating scale for CLN3 disease in order to quantify disease progression. Forty-two eyes of 21 patients were included. The mean age at the time of examination was 13.2 years (range, 5.3-21.9 years). The mean ophthalmic severity grade was 2.4 (range, 0-3). The mean neurological severity score was 9.9 (range, 4-14). Ophthalmic manifestations increased in severity with increasing age of the patients ($r = -0.84$; $P < .001$), and a strong correlation was found between the CLN3 ophthalmic rating scale score and the Hamburg JNCL score ($r = 0.83$; $P < .001$). The newly established Hamburg CLN3 ophthalmic rating scale may serve as an objective marker of ocular disease severity and progression and may be valuable tool for the evaluation of novel therapeutic strategies for CLN3 disease.

Genotype–Phenotype Correlations in a Spanish Cohort of 506 Families With Biallelic ABCA4 Pathogenic Variants.
Del Pozo-Valero M, Riveiro-Alvarez R, Blanco-Kelly F, Aguirre-Lamban J, Martin-Merida I, Iancu IF, Swafiri S, Lorda-Sanchez I, Rodriguez-Pinilla E, Trujillo-Tiebas MJ, Jimenez-Rolando B.
American Journal of Ophthalmology. 2020 Nov 1;219:195-204.

506 patients with ABCA4 variants were characterized in this cohort study, using conventional genetic tools and next-generation sequencing technologies. A total of 228 different pathogenic variants were identified in 506 ABCA4 patients, 50 of which were novel. Genotype–phenotype correlations showed that most of the patients with biallelic truncating variants presented with CRD and that these cases had a significantly earlier AO than patients with STGD1. Three missense variants are associated with CRD for the first time (c.1804C>T; p.[Arg602Trp], c.3056C>T; p.[Thr1019Met], and c.6320G>C; p.[Arg2107Pro]).

Analysis of the most prevalent ABCA4 variant in Spain, c.3386G>T; p.(Arg1129Leu), revealed that is correlated to STGD1, later AO, and foveal sparing. Patients with ABCA4 presenting with 2 truncating variants may first present features of STGD1 but eventually develop rod dysfunction, and specific missense variants may be associated with a different phenotype, underscoring the importance of an accurate genetic diagnosis.

Sector Retinitis Pigmentosa: Extending the Molecular Genetics Basis and Elucidating the Natural History.
Georgiou M, Grewal PS, Narayan A, Alser M, Ali N, Fujinami K, Webster AR, Michaelides M.
American Journal of Ophthalmology. 2021 Jan;221:299-310.

This retrospective case series aims to determine the genetic background of sector retinitis pigmentosa (RP) natural history to better inform patient counseling. Twenty-six molecularly confirmed patients from 23 different families were identified harboring likely disease-causing variants in 9 genes. The modes of inheritance were autosomal recessive (AR, n=6: USH1C, n=2; MYO7A, n=2; CDH3, n=1; EYS, n=1), X-linked (XL, n=4: PRPS1, n=1; RPGR, n=3), and autosomal dominant (AD, n=16: IMPDH1, n=3; RP1, n=3; RHO, n=10), with a mean age of disease onset of 38.5, 30.5, and 39.0 years old, respectively. Five of these genes have not previously been reported to cause sector RP (PRPS1, MYO7A, EYS, IMPDH1, and RP1). Inferior and nasal predilection was common across the different genotypes, and patients tended to maintain good central vision. Progression on serial FAF was observed in RPGR, MYO7A, CDH23, EYS, IMPDH1, RP1, and RHO-associated sector RP. The longitudinal data provided will help to make accurate patient prognoses and counseling as well as inform patients' potential participation in the increasing numbers of trials of novel therapeutics and access to future treatments.

Whole-exome sequencing of patients with posterior segment uveitis.
Li AS, Velez G, Darbro B, Toral MA, Yang J, Tsang SH, Ferguson PJ, Folk JC, Bassuk AG, Mahajan VB.
American Journal of Ophthalmology. 2021 Jan 1;221:246-59.

The goal of this genetic association cohort study was to elucidate molecular risk factors for posterior segment uveitis using a functional genomics approach. 164 patients with clinically diagnosed uveitis of the posterior segment were included and whole exome sequencing was used to detect variants. A phenotype-driven analysis, protein structural modeling, and in silico calculations were then used to rank and predict the functional consequences of key variants. Both known and novel variants were identified in genes previously implicated in specific types of syndromic uveitis- such as NOD2 (Blau syndrome) and CAPN5 NIV (neovascular inflammatory vitreoretinopathy)- as well as variants in genes not previously linked to posterior segment uveitis. Based on a ranked list and protein-protein-interaction network, missense variants in NOD-like receptor family genes (NOD2, NLRC4, NLRP3, and NLRP1), CAPN5, and TYK2 were characterized via structural modeling and in silico calculations to predict how specific variants might alter protein structure and function. This study implicates new pathways and immune signaling proteins that may be associated with posterior segment uveitis susceptibility. In specific cases, whole-exome sequencing can help diagnose nonsyndromic uveitis in patients harboring known variants for syndromic inflammatory diseases.

Incidence and Natural History of Retinochoroidal Neovascularization in Enhanced S-Cone Syndrome.
Nowilaty SR, Alsalamah AK, Magliyah MS, Alabdullah AA, Ahmad K, Semidey VA, Mura M, Schatz P.
American Journal of Ophthalmology. 2021 Feb 1;222:174-84.

This single-center, retrospective case series aimed to examine the incidence and natural history of macular retinochoroidal neovascularization (RCN) in enhanced S-cone syndrome (ESCS). 14 of 93 patients with ESCS who had signs of active or inactive RCN in ≥1 eye. Fourteen (15.1%) of 93 patients with ESCS had RCN in ≥1 eye at 2 to 27 years of age. All 22 RCNs (21 eyes of 14 patients) were macular. Twelve of the RCNs were active with exudates/hemorrhages. Of these, 5 appeared de novo in a subretinal location, with photographic evidence of no pre-existing lesions. The latter were compatible with type 3 neovascularization or retinal angiomatous proliferation and subsequently evolved into unifocal

fibrotic nodules. The remaining active lesions all had some degree of pre-existing fibrosis and remained stable. Ten inactive fibrotic nodules, identical to end-stage de novo lesions, were found and were presumed to represent healed RCNs. RCN, a treatable condition, may occur as early as 2 years of age and may be much more common in patients with ESCS than previously estimated. It may be the primary cause of the unifocal submacular fibrosis that is commonly observed in this condition.

Inherited cataracts: molecular genetics, clinical features, disease mechanisms and novel therapeutic approaches.
Berry V, Georgiou M, Fujinami K, Quinlan R, Moore A, Michaelides M.
British Journal of Ophthalmology. 2020 Oct 1;104(10):1331-7.

Cataract is the most common cause of blindness in the world; during infancy and early childhood, it frequently results in visual impairment. Congenital cataracts are present in 1–6/10 000 live-births in developed countries and 5–15/10 000 births in developing countries. Congenital cataracts are phenotypically and genotypically heterogeneous and can occur in isolation or in association with other systemic disorders. Over the last 10 years, enormous progress has been made in elucidating the molecular basis of congenital cataract, with causative mutations identified in genes encoding many different proteins including intracellular lens proteins (crystallins), membrane gap junction proteins (connexins), water channel proteins (aquaporins), cytoskeletal proteins (eg, BFSP1 (filensin), BFSP2 (phakinin) and vimentin) and transcription factors (TFs) (eg, FOXE3, PAX6, PITX3 and MAFA). 115 genes to date have been found to be associated with syndromic and non-syndromic cataract and 38 disease-causing genes have been identified to date to be associated with isolated cataract. Recent advances in molecular genetics, particularly next-generation sequencing, has improved molecular diagnosis in the clinic.

Clinical and genetical features of probands and affected family members with familial exudative vitreoretinopathy in a large Chinese cohort.
Wang S, Zhang X, Hu Y, Fei P, Xu Y, Peng J, Zhao P.
British Journal of Ophthalmology. 2021 Jan 1;105(1):83-6.

This retrospective chart review aims to explore the clinical and genetical features of families with strictly confirmed familial exudative vitreoretinopathy (FEVR) in a large Chinese cohort. 105 FEVR families (223 FEVR affected subjects with 434 eyes); 105 probands with mean age of 3.8 years old and 118 affected family members of 32.7 years old averagely. Mutations in FZD4 were most prevalent (33.33%), followed by LRP5 (29.52%), TSPAN12 (22.86%), NDP (5.71%), KIF11 (1.9%) and ZNF408 (0.95%). 81% of the probands were classified as stage 4 or worse which most prevalently contributed to FZD4 mutations. All of the three affected family members with stage 4 or worse carried FZD4 variants. More than half (51.43%) of the probands in FZD4 group showed asymmetry. Unilateral FEVR was detected in 11 (10.5%) families consisting of six probands and six affected relatives, and FZD4 mutations accounted for 63.64% of all the cases with variant (c.1282_1285del, p. D428fs) identified in three families. Genotype-phenotype correlation in FEVR was complex with family dependent; mutations in FZD4 might initiate the most diverse and asymmetric phenotypes.

Prevalence and genetic–phenotypic characteristics of patients with USH2A mutations in a large cohort of Chinese patients with inherited retinal disease.
Gao FJ, Wang DD, Chen F, Sun HX, Hu FY, Xu P, Li J, Liu W, Qi YH, Li W, Wang M.
British Journal of Ophthalmology. 2021 Jan 1;105(1):87-92.

This study investigates the frequency of USH2A mutation and the clinical and genetic differences between Usher syndrome type II (USH2) and retinitis pigmentosa (RP) in a large cohort of Chinese patients. 1381 patients with inherited retinal disease (IRD) were recruited. The prevalence of patients with USH2A mutations was 15.75%; hotspot of USH2A mutations was c.8559-2A >G and c.2802T >G. Patients with USH2 had an earlier and more serious decline of visual function and damage to retina

structure than did patients with RP in the first 10 years ($p<0.05$), but there was no difference in the visual prognosis between the two groups when the course of disease exceeded 10 years ($p>0.05$). Missense variants had less severe consequences and were found more commonly in RP, whereas more deleterious genotypes were associated with an earlier onset of disease and were found more commonly in USH2. Although the rate of disease progression was not directly related to genotype, no difference in visual prognosis among patients with USH2A mutations when the course of disease exceeded 10 years.

Long-term natural history of visual acuity in eyes with choroideremia: A systematic review and meta-analysis of data from 1004 individual eyes.
Shen LL, Ahluwalia A, Sun M, Young BK, Nardini HK, Del Priore LV.
British Journal of Ophthalmology. 2021 Feb 1;105(2):271-8.

Choroideremia (CHM) is a progressive X-linked recessive disease due to mutations in the CHM gene. The prevalence of CHM is approximately 1 in 50 000 individuals. Currently, there are no approved treatment options for CHM, however, phase I/II human clinical trials of gene therapy showed promising results. This study searched 7 databases to identify studies that reported BCVA of untreated eyes with CHM. 1004 eyes from 23 studies were included. BCVA of the right and left eyes was moderately correlated (r=0.60). BCVA as a function of age followed a 2-phase decline (slow followed by rapid decline), with an estimated transition age of 39.1 years (95% CI 33.5 to 44.7). After the introduction of horizontal translation factors to longitudinal datasets, BCVA followed a 2-phase decline until it reached 0 letters (r2=0.90). The BCVA decline rate was 0.33 letters/year (95% CI −0.38 to 1.05) before 39 years, and 1.23 letters/year (95% CI 0.55 to 1.92) after 39 years (p=0.004). BCVA in eyes with CHM follows a 2-phase linear decline with a transition age of approximately 39 years. Future trials enrolling young patients may not be able to use BCVA as a primary or sole endpoint, but rather, may need to employ additional disease biomarkers that change before age 39.

Handheld spectral domain optical coherence tomography findings of X-linked retinoschisis in early childhood.
Ling KP, Mangalesh S, Tran-Viet D, Gunther R, Toth CA, Vajzovic L.
Retina. 2020 Oct 1;40(10):1996-2003.

X-linked retinoschisis (XLRS) is an inherited retinal degenerative disease caused by mutations in the retinoschisin 1 (RS1) gene on chromosome Xp22.1. This is a retrospective analysis of handheld SD OCT images in children who had established XLRS diagnosis based on genetic testing or clinical history. Spectral domain OCT images were available of both eyes in 8 pediatric patients with ages 7 months to 10 years. The schisis cavities involved inner nuclear layer in over 90% (15/16) of eyes in all 3 regions. Retinal nerve fiber and ganglion cell layer involvement was present only in the extrafoveal region in 63% (10/16) eyes and outer nuclear and plexiform layer in few others. In 7 children followed over 2 months to 15 months, the location of schisis remained consistent. Central foveal thickness decreased from the baseline to final available visit in 4/6 eyes. Ellipsoid zone disruption seemed to accompany lower visual acuity in 1/4 eyes. Early in life, the SD OCT findings in XLRS demonstrate differences in schisis location in fovea–parafoveal versus extrafoveal region, possible association between poor visual acuity and degree of ellipsoid zone disruption and decrease in central foveal thickness over time in this group. The pattern of XLRS in adults is already present in very young children, and unlike in older children and adults, those presenting with earlier disease may have a more aggressive course.

Progression of ABCA4-related retinopathy: Prognostic value of demographic, functional, genetic, and imaging parameters.
Müller PL, Pfau M, Treis T, Pascual-Camps I, Birtel J, Lindner M, Herrmann P, Holz FG.
Retina. 2020 Dec 1;40(12):2343-56.

ABCA4-related retinopathy is the most common single-gene retinal dystrophy. Sixty-eight eyes of 37 patients (age range, 14–78 years) with a follow-up time of 10 to 100 months with ABCA4 retinopathy were

included. The mean annual progression of retinal pigment epithelium atrophy was 0.89 mm2. The number of atrophic areas, the retina-wide functional impairment, and the age-of-onset category constituted significant predictors for future retinal pigment epithelium atrophy growth, explaining 25.7% of the variability. By extension of a simulated study length and/or specific patient preselection based on these baseline characteristics, the required sample size could significantly be reduced. Trial design based on specific shape-descriptive factors and patients' baseline characteristics and the adaption of the trial duration may provide potential benefits in required cohort size and absolute number of visits.

Variable expressivity in patients with autosomal recessive retinitis pigmentosa associated with the gene CNGB1.
Radojevic B, Jones K, Klein M, Mauro-Herrera M, Kingsley R, Birch DG, Bennett LD. Ophthalmic Genetics. 2020 Oct 15:1-8.

Retinitis Pigmentosa (RP) is a group of inherited disorders involving progressive degeneration of the retina that leads to severe visual impairment. A cohort of 8 families (11 patients) with autosomal recessive retinitis pigmentosa (arRP) disease associated with mutations in CNGB1 was characterized. Age of onset ranged from 4 to 49 years; age at visit was 27–54 years. The range of visual acuity was Snellen 20/16 to 20/400 in the right eye and Snellen 20/16 to 20/160 in the left eye. Electrophysiological testing in 5 patients showed an absence of the rod response; cone responses ranged from normal to severely reduced. Funduscopic images showed widespread retinal degeneration with pigment clumping, optic disk pallor, arteriole attenuation, and a peri-foveal ring of hyper autofluorescence. Three families were tested for olfactory dysfunction and results indicated mild to complete anosmia in individuals with mutations in CNGB1. Genetic analysis revealed 6 novel variants, c.2127 C > G, p.Phe709Leu; c.1431 C > A, p.Cys477*; c.2034 G > A, p.Trp678*; c.2092 T > C, p.Cys698Arg; and c.583 + 2 T > C, c.2305–34 G > A and 3 variants that have been previously described, c.2957A>T, p.Asn986Ile; c.2544dup, p.Leu849Alafs*3; and c.2492 + 1 G > A. This is the first report for six novel CNGB1 variants associated with arRP. Two families had olfactory dysfunction in patients with arRP and family members who were heterozygous for a CNGB1 mutation. Additionally, findings demonstrated variable penetrance and expressivity of disease in these patients.

The mutational spectrum of Myocilin gene among familial versus sporadic cases of Juvenile onset open angle glaucoma.
Gupta V, Somarajan BI, Gupta S, Walia GK, Singh A, Sofi R, Chaudhary RS, Sharma A.
Eye (Lond). 2021 Feb;35(2):400-408.

This study focused on the relative prevalence of Myocilin (*MYOC*) mutations in familial versus sporadic cases of Juvenile onset primary open angle glaucoma (JOAG). The study authors screened 92 unrelated (sporadic) JOAG patients, and 22 affected families (70 affected members and 36 unaffected) for variations in the *MYOC* gene and analyzed the clinical features associated with these variations.
Three coding sequence variants were identified as mutations causing JOAG. The frequency of MYOC mutations in familial cases (27%) was significantly higher than in sporadic JOAG cases (2%); p = 0.001. A 90% penetrance for the Gly367Arg variant was seen by the age of 40 years.
The study authors suggest that genetic screening for *MYOC* mutations should be focused toward cases with familial rather than sporadically occurring JOAG.

Efficacy and Safety of Intravitreal Gene Therapy for Leber Hereditary Optic Neuropathy Treated within 6 Months of Disease Onset.
Newman NJ, Yu-Wai-Man P, Carelli V, Moster ML, Biousse V, Vignal-Clermont C, Sergott RC, Klopstock T, Sadun AA, Barboni P, DeBusk AA, Girmens JF, Rudolph G, Karanjia R, Taiel M, Blouin L, Smits G, Katz B, Sahel JA; LHON Study Group.
Ophthalmology. 2021 Jan 12:S0161-6420(20)31187-8.

RESCUE is a multicenter, randomized, double-masked, sham-controlled, phase 3 clinical trial to evaluate the efficacy of a single intravitreal injection of rAAV2/2-ND4 in Leber hereditary optic neuropathy (LHON). Subjects with the m.11778G>A mitochondrial DNA mutation and vision loss ≤6 months from onset in 1 or both eyes were included. The right eye was randomly assigned (1:1) to treatment with rAAV2/2-ND4 (single injection of 9 × 1010 viral genomes in 90 µl) or to sham injection. The left eye received the treatment not allocated to the right eye. The primary end point was the difference of the change from baseline in best-corrected visual acuity (BCVA) between rAAV2/2-ND4-treated and sham-treated eyes at week 48. Follow-up extended to week 96.

Efficacy analysis included 38 subjects. Mean age was 36.8 years, and 82% were male. Mean duration of vision loss at time of treatment was 3.6 months and 3.9 months in the rAAV2/2-ND4-treated eyes and sham-treated eyes, respectively. Mean baseline logarithm of the minimum angle of resolution (logMAR) BCVA (standard deviation) was 1.31 (0.52) in rAAV2/2-ND4-treated eyes and 1.26 (0.62) in sham-treated eyes, with a range from -0.20 to 2.51. At week 48, the difference of the change in BCVA from baseline between rAAV2/2-ND4-treated and sham-treated eyes was -0.01 logMAR (P = 0.89); the primary end point of a -0.3 logMAR (15-letter) difference was not met. The mean BCVA for both groups deteriorated over the initial weeks, reaching the worst levels at week 24, followed by a plateau phase until week 48, and then an improvement of +10 and +9 Early Treatment Diabetic Retinopathy Study letters equivalent from the plateau level in the rAAV2/2-ND4-treated and sham-treated eyes, respectively.

At 96 weeks after unilateral injection of rAAV2/2-ND4, comparable visual outcomes were present in the injected and uninjected eyes.

Genome-Wide Association Study in Asians Identifies Novel Loci for High Myopia and Highlights a Nervous System Role in Its Pathogenesis.
Meguro A, Yamane T, Takeuchi M, Miyake M, Fan Q, Zhao W, Wang IJ, Mizuki Y, Yamada N, Nomura N, Tsujikawa A, Matsuda F, Hosoda Y, Saw SM, Cheng CY, Tsai TH, Yoshida M, Iijima Y, Teshigawara T, Okada E, Ota M, Inoko H, Mizuki N.
Ophthalmology. 2020 Dec;127(12):1612-1624.

Genome-wide association study (GWAS) was performed in 3269 Japanese individuals (1668 with high myopia), followed by replication analysis in a total of 10 827 additional samples (881 with high myopia and 9946 control participants) from Japan, Singapore, and Taiwan. Functional annotation and Gene Ontology (GO) analyses was done to confirm the biological role of the identified loci in the pathogenesis of high myopia.
Six novel loci with genome-wide significance were identified (HIVEP3 on 1p34.2, NFASC/CNTN2 on 1q32.1, CNTN4/CNTN6 on 3p26.3, FRMD4B on 3p14.1, LINC02418 on 12q24.33, and AKAP13 on 15q25.3). The GO analysis revealed a significant role of the nervous system related to synaptic signaling, neuronal development, and Ras/Rho signaling in the pathogenesis of high myopia.

Autosomal Recessive Bestrophinopathy: Clinical Features, Natural History, and Genetic Findings in Preparation for Clinical Trials.
Casalino G, Khan KN, Armengol M, Wright G, Pontikos N, Georgiou M, Webster AR, Robson AG, Grewal PS, Michaelides M.
Ophthalmology. 2020 Oct 8:S0161-6420(20)30978-7.

Fifty-six eyes of 28 unrelated patients with a clinical phenotype consistent with autosomal recessive bestrophinopathy (ARB) or with biallelic likely disease-causing BEST1 variants were included in this retrospective study. Compound heterozygous variants were detected in most patients (19/27), with 6 alleles recurring in apparently unrelated individuals, the most common of which was c.422G→A, p.(Arg141His; n = 4 patients). Mean presenting visual acuity (VA) was 0.52 ± 0.36 logarithm of the minimum angle of resolution (logMAR), and final VA was 0.81 ± 0.75 logMAR (P = 0.06). The mean rate of change in VA was 0.05 ± 0.13 logMAR/year. A significant change in VA was detected in patients with a follow-up of 5 years or more (n = 18) compared with patients with a follow-up of 5 years or less (n = 10; P

= 0.001). Presence of subretinal fluid and vitelliform material were early findings in most patients, and this did not change substantially over time. A reduction in central retinal thickness was detected in most eyes (80.4%) over the course of follow-up. Many patients (10/26) showed evidence of generalized rod and cone system dysfunction. These patients were older (P < 0.001) and had worse VA (P = 0.02) than those with normal full-field electroretinography results. Although patients with ARB are presumed to have no functioning bestrophin channels, significant phenotypic heterogeneity is evident.

Genetic Basis of Inherited Retinal Disease in a Molecularly Characterized Cohort of More Than 3000 Families from the United Kingdom.
Pontikos N, Arno G, Jurkute N, Schiff E, Ba-Abbad R, Malka S, Gimenez A, Georgiou M, Wright G, Armengol M, Knight H, Katz M, Moosajee M, Yu-Wai-Man P, Moore AT, Michaelides M, Webster AR, Mahroo OA.
Ophthalmology. 2020 Oct;127(10):1384-1394.

This is a retrospective study of electronic patient records from the Genetics Service of Moorfields Eye Hospital in whom a molecular diagnosis was identified. The authors identified 3195 families with a molecular diagnosis (variants in 135 genes), including 4236 affected individuals. The pediatric cohort comprised 452 individuals from 411 families (66 genes). The current cohort comprised 2614 families (131 genes; 3130 affected individuals). The 20 most frequently implicated genes overall (with prevalence rates per families) were as follows: *ABCA4* (20.8%), *USH2A* (9.1%), *RPGR* (5.1%), *PRPH2* (4.6%), *BEST1* (3.9%), *RS1* (3.5%), *RP1* (3.3%), *RHO* (3.3%), *CHM* (2.7%), *CRB1* (2.1%), *PRPF31* (1.8%), *MY07A* (1.7%), *OPA1* (1.6%), *CNGB3* (1.4%), *RPE65* (1.2%), *EYS* (1.2%), *GUCY2D* (1.2%), *PROM1* (1.2%), *CNGA3* (1.1%), and *RDH12* (1.1%). These accounted for 71.8% of all molecularly diagnosed families. Spearman coefficients for correlation between numbers of families and transcript length were 0.20 (P = 0.025) overall and 0.27 (P = 0.017), -0.17 (P = 0.46), and 0.71 (P = 0.047) for genes in which variants exclusively cause recessive, dominant, or X-linked disease, respectively.
The findings help to quantify the burden of IRD attributable to each gene. More than 70% of families showed pathogenic variants in 1 of 20 genes.

Dopachrome tautomerase variants in patients with oculocutaneous albinism.
Pennamen P, Tingaud-Sequeira A, Gazova I, Keighren M, McKie L, Marlin S, Gherbi Halem S, Kaplan J, Delevoye C, Lacombe D, Plaisant C, Michaud V, Lasseaux E, Javerzat S, Jackson I, Arveiler B.
Genet Med. 2020 Oct 26.

Albinism is a clinically and genetically heterogeneous condition. Despite analysis of the 20 known genes, ~30% patients remain unsolved. This study proposes biallelic mutations in the gene Dopachrome tautomerase (*DCT*) as a new cause of oculocutaneous albinism named OCA8. Variants in *DCT* were identified in two patients. One was compound heterozygous for a 14-bp deletion in exon 9 and c.118T>A p.(Cys40Ser). The second was homozygous for c.183C>G p.(Cys61Trp). Both patients had mild hair and skin hypopigmentation, and classical ocular features. CRISPR-Cas9 was used in C57BL/6J mice to create mutations identical to the missense variants carried by the patients, along with one loss-of-function indel. When bred to homozygosity the three mutations revealed hypopigmentation of the coat, milder for Cys40Ser compared with Cys61Trp or the frameshift mutation. Histological analysis identified significant hypopigmentation of the retinal pigmented epithelium (RPE) indicating that defective RPE melanogenesis could be associated with eye and vision defects. DCT loss of function in zebrafish embryos elicited hypopigmentation both in melanophores and RPE cells.

Revealing hidden genetic diagnoses in the ocular anterior segment disorders.
Ma A, Yousoof S, Grigg JR, Flaherty M, Minoche AE, Cowley MJ, Nash BM, Ho G, Gayagay T, Lai T, Farnsworth E, Hackett EL, Fisk K, Wong K, Holman KJ, Jenkins G, Cheng A, Martin F, Karaconji T, Elder JE, Enriquez A, Wilson M, Amor DJ, Stutterd CA, Kamien B, Nelson J, Dinger ME, Bennetts B, Jamieson RV.
Genet Med. 2020 Oct;22(10):1623-1632.

Ocular anterior segment disorders (ASDs) are clinically and genetically heterogeneous, and genetic diagnosis often remains elusive. The authors utilized a combination of chromosome microarray, exome sequencing, and genome sequencing with structural variant and trio analysis to investigate a cohort of 41 predominantly sporadic cases.
Likely causative variants were identified in 54% (22/41) of cases, including 51% (19/37) of sporadic cases and 75% (3/4) of cases initially referred as familial ASD. Two-thirds of sporadic cases were found to have heterozygous variants, which in most cases were de novo. Approximately one-third (7/22) of genetic diagnoses were found in rarely reported or recently identified ASD genes including *PXDN, GJA8, COL4A1, ITPR1, CPAMD8*, as well as the new phenotypic association of Axenfeld-Rieger anomaly with a homozygous *ADAMTS17* variant. The remainder of the variants were in key ASD genes including *FOXC1, PITX2, CYP1B1, FOXE3*, and *PAX6*.

Bilateral visual improvement with unilateral gene therapy injection for Leber hereditary optic neuropathy.
Yu-Wai-Man P, Newman NJ, Carelli V, Moster ML, Biousse V, Sadun AA, Klopstock T, Vignal-Clermont C, Sergott RC, Rudolph G, La Morgia C, Karanjia R, Taiel M, Blouin L, Burguière P, Smits G, Chevalier C, Masonson H, Salermo Y, Katz B, Picaud S, Calkins DJ, Sahel JA.
Sci Transl Med. 2020 Dec 9;12(573).

REVERSE is a randomized, double-masked, sham-controlled, multicenter, phase 3 clinical trial that evaluated the efficacy of a single intravitreal injection of rAAV2/2-ND4 in subjects with visual loss from Leber hereditary optic neuropathy (LHON). A total of 37 subjects carrying the m.11778G>A (MT-ND4) mutation and with duration of vision loss between 6 to 12 months were treated. Each subject's right eye was randomly assigned in a 1:1 ratio to treatment with rAAV2/2-ND4 (GS010) or sham injection. The left eye received the treatment not allocated to the right eye. Unexpectedly, sustained visual improvement was observed in both eyes over the 96-week follow-up period. At week 96, rAAV2/2-ND4-treated eyes showed a mean improvement in best-corrected visual acuity (BCVA) of -0.308 LogMAR (+15 ETDRS letters). A mean improvement of -0.259 LogMAR (+13 ETDRS letters) was observed in the sham-treated eyes. Consequently, the primary end point, defined as the difference in the change in BCVA from baseline to week 48 between the two treatment groups, was not met (P = 0.894). At week 96, 25 subjects (68%) had a clinically relevant recovery in BCVA from baseline in at least one eye, and 29 subjects (78%) had an improvement in vision in both eyes. A nonhuman primate study was conducted to investigate this bilateral improvement. Evidence of transfer of viral vector DNA from the injected eye to the anterior segment, retina, and optic nerve of the contralateral noninjected eye supports a plausible mechanistic explanation for the unexpected bilateral improvement in visual function after unilateral injection.

Senior- Løken Syndrome: A Case Series and Review of The Reno-Retinal Phenotype and Advances of Molecular Diagnosis
Yahalom C, Volovelsky O, Macarov M, Altalbishi A, Alsweiti Y, Schneider N, Hanany M, Khan MI, Cremers FPM, Anteby I, Banin E, Sharon D, Khateb S.
Retina. 2021 Jan 27. Epub ahead of print.

The goal of this retrospective study was to report genetic and clinical findings in a case series of 10 patients from eight unrelated families diagnosed with Senior-Løken syndrome (SLS). Data collected included clinical findings electroretinography and ocular imaging. Genetic analysis was based on molecular inversion probes (MIPs), whole-exome (WES) and Sanger sequencing. All patients who underwent electrophysiology (8/10) had widespread photoreceptor degeneration. Genetic analysis revealed two mutations in NPHP1, two mutations in NPHP4 and two mutations in IQCB1 (NPHP5). Five of the six mutations identified in the current study were found in a single family each in our cohort. The IQCB1- p.R461* mutation has been identified in three families. Patients harboring mutations in IQCB1 were diagnosed with Leber congenital amaurosis (LCA), while patients with NPHP4 and NPHP1 mutations showed early and sector retinitis pigmentosa (RP), respectively. ffERG was extinct for 6 out of 10 patients, moderately decreased for two and unavailable for another two subjects. Renal involvement was evident in 7/10 patients at the time of diagnosis. Kidney function was normal (based on serum

creatinine) in patients younger than 10 years. Mutations in IQCB1 were associated with high hypermetropia whereas mutations in NPHP4 were associated with high myopia. Patients presenting with infantile inherited retinal degeneration are not universally screened for renal dysfunction. Modern genetic tests can provide molecular diagnosis at an early age and therefore facilitate early diagnosis of renal disease with recommended periodic screening beyond childhood and family planning.

Concomitant mutations in inherited retinal dystrophies: why the reproductive and therapeutic counselling should be addressed cautiously
Rodríguez-Muñoz A, García-Bohórquez B, Udaondo P, Hervás-Ontiveros A, Salom D, Aller E, Jaijo T, García-García G, Millán JM. Concomitant mutations in inherited retinal dystrophies: why the reproductive and therapeutic counselling should be addressed cautiously.
Retina. 2021 Jan 4. Epub ahead of print.

Up to 4% of the families with inherited retinal dystrophies display the co-existence of mutations in multiple disease-causing genes. This fact supposes a drawback for genetic counselors to provide a correct reproductive and therapeutic counselling.
The goal of the paper was to highlight the challenge of correct reproductive and therapeutic counselling in complex pedigrees with different inherited retinal dystrophies. 208 patients diagnosed with non-syndromic inherited retinal dystrophies underwent full ophthalmologic examination and molecular analysis using targeted next-generation sequencing. Results: Five families (4%) carried mutations in more than one gene that contribute to different inherited retinal dystrophies. Family fRPN-NB had a dominant mutation in SNRNP200, which was present in nine affected individuals and four unaffected, and a mutation in RP2 among 11 family members. Family fRPN-142 carried a mutation in RPGR that cosegregated with the disease in all affected individuals. Additionally, the proband also harbored two disease causingmutations in the genes BEST1 and SNRNP200. Family fRPN-169 beared compound heterozygous mutations in USH2A and a dominant mutation in RP1. Genetic testing of fRPN- 194 determined compound heterozygous mutations in CNGB3 and a dominant mutation in PRPF8 only in the proband. Finally, fRPN-219 carried compound heterozygous mutations in the genes ABCA4 and TYR. These findings reinforce the complexity of IRD and underscore the need for the combination of high-throughput genetic testing and clinical characterization. Because of these features, the reproductive and therapeutic counselling for IRD must be approached with caution.

CLINICAL CHARACTERISTICS AND MOLECULAR GENETIC ANALYSIS OF A COHORT OF CHINESE PATIENTS WITH CHOROIDEREMIA
Han X, Wu S, Li H, Zhu T, Wei X, Zhou Q, Sui R.
Retina. 2020 Nov;40(11):2240-2253.

The study aimed to describe the clinical and molecular genetic characteristics of a large cohort of Chinese patients with choroideremia (CHM). Forty-eight Chinese participants from 35 families with a clinical diagnosis of CHM who harbored sequence variants in the CHM gene were enrolled. Comprehensive clinical evaluations and molecular genetic analysis of the CHM gene were performed. The median age of the 48 patients was 31.5 years (range, 5–78 years). There were 30 different sequence variants detected in 35 families; of which, 13 sequence variants were novel. The mean (±SD) best-corrected visual acuity best in logarithm of the minimum angle of resolution equivalents was 0.71 (±0.87) (range, 0.00–2.80) or approximately 20/100 in Snellen visual acuity. A significant correlation was revealed between best-corrected visual acuity best and age (P , 0.001). The trend in the change in the best-corrected visual acuity over age showed that relatively good vision remained until 20 years old. The patterns of fundus photography and fundus autofluorescence finding demonstrated that residual retinal pigment epithelium areas significantly declined in patients at the age of 20 years or older. The results of visual field and full-field electroretinography showed that these measures might be of limited value for evaluating the condition of the late stage of CHM in Chinese patients. This study described for the first time the clinical and molecular genetic characteristics of a large cohort of Chinese patients with CHM. The findings from bestcorrected visual acuity best and visual field showed that the impairment of visual function in CHM might be more severe in Chinese patients than in western patients. The study provides

interesting information in helping classify subsets of CHM.

PROGRESSION OF ABCA4-RELATED RETINOPATHY: Prognostic value of demographic, functional, genetic, and imaging parameters
Müller PL, Pfau M, Treis T, Pascual-Camps I, Birtel J, Lindner M, Herrmann P, Holz FG.
Retina. 2020 Dec;40(12):2343-2356.

The study aimed to investigate the prognostic value of demographic, functional, genetic, and imaging parameters on retinal pigment epithelium atrophy progression secondary to ABCA4-related retinopathy. Patients with retinal pigment epithelium atrophy secondary to ABCA4-related retinopathy were examined longitudinally with fundus autofluorescence imaging. Lesion area, perimeter, circularity, caliper diameters, and focality of areas with definitely decreased autofluorescence were determined. A model was used to predict the lesion enlargement rate based on baseline variables. Sample size calculations were performed to model the power in a simulated interventional study. Sixty-eight eyes of 37 patients (age range, 14–78 years) with a follow-up time of 10 to 100 months were included. The mean annual progression of retinal pigment epithelium atrophy was 0.89 mm2. The number of atrophic areas, the retina-wide functional impairment, and the age-of-onset category constituted significant predictors for future retinal pigment epithelium atrophy growth, explaining 25.7% of the variability. By extension of a simulated study length and/or specific patient preselection based on these baseline characteristics, the required sample size could significantly be reduced. Trial design based on specific shape-descriptive factors and patients' baseline characteristics and the adaption of the trial duration may provide potential benefits in required cohort size and absolute number of visits. Information is provided in the study to help physicians counsel patients about the prognosis of the inherited condition.

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, Claveria MA, Coll-Alsina N, Bonnet C, Petit C, Caminal JM, Prat J.
Eye (Lond). 2020 Mar;34(3):499-506.

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 analysed 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 the 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 oedema (CMO) 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 CMO-in the inner retinal layers.

CEP290 mutation spectrum and delineation of the associated phenotype in a large German cohort: a monocentric study.
Feldhaus B, Weisschuh N, Nasser F, Den Hollander AI, Cremers FP, Zrenner E, Kohl S, Zobor D.
American Journal of Ophthalmology. 2020 Mar 1;211:142-50.

Gene therapy for Leber congenital amaurosis (LCA) is becoming available, and therefore it is crucial to identify eligible candidates. Twenty-three patients with mutations in CEP290 were included. The most frequent mutation was c.2991+1655A>G, found in 87% of patients (20/23). Thirty percent of patients

(7/23) carried the mutation in an apparent homozygous state and 57% (13/23) in a likely compound heterozygous state. The most common clinical diagnosis was LCA and/or early onset severe retinal dystrophy in 82% (19/23), followed by retinitis pigmentosa in 14% (3/23) and cone-rod dystrophy (4%, 1/23). Best-corrected visual acuity was severely reduced to residual light perception and hand motion vision, with the exception of 3 patients with best-corrected visual acuity of 0.8 (Snellen). The visual field was severely decreased and electroretinogram was undetectable in most cases; however, retinal layers at the fovea appeared to be relatively well preserved. Systemic disorders were not noticed. c.2991+1655A>G is by far the most important CEP290 mutation, contributing to 87% of patients with the CEP290 mutation in Germany. A homozygous c.2991+1655A>G genotype presented with a more severe phenotype in this cohort.

A novel missense mutation in LIM2 causing isolated autosomal dominant congenital cataract.
Berry V, Pontikos N, Dudakova L, Moore AT, Quinlan R, Liskova P, Michaelides M.
Ophthalmic Genetics. 2020 Mar 3;41(2):131-4.

Congenital cataract is the most common cause of blindness in the world. Congenital cataracts are clinically and genetically heterogeneous and are mostly inherited in an autosomal dominant fashion. We identified the genetic cause of isolated autosomal dominant cataract in a four-generation British family and a Czech family. Whole exome sequencing (WES) was performed on one affected member in the British family and two affected members in the Czech family. A novel missense variant c.388C > T; p.(R130C) was identified in the Lens integral membrane protein (LIM2) and found to co-segregate with disease in both families. This report of the first autosomal dominant congenital cataract variant p.(R130C) in LIM2, causing a non-syndromic pulverulent and nuclear phenotype in European families.

Is it Usher syndrome? Collaborative diagnosis and molecular genetics of patients with visual impairment and hearing loss.
Stiff HA, Sloan-Heggen CM, Ko A, Pfeifer WL, Kolbe DL, Nishimura CJ, Frees KL, Booth KT, Wang D, Weaver AE, Azaiez H.
Ophthalmic Genetics. 2020 Mar 3;41(2):151-8.

Usher syndrome is the most common hereditary syndrome combining deafness and blindness. From 2012 to 2019, 21 families (25 patients) were referred to the collaborative Genetic Eye-Ear Clinic (GEEC) at the University of Iowa. Overall molecular diagnostic rate in this cohort was 14/21 (67%). Evaluation resulted in a change of diagnosis in 11/21 (52%) families. Ultimately, there were eleven unique diagnoses including hereditary, non-hereditary, and independent causes of combined visual impairment and hearing loss. The most common diagnosis was Usher syndrome, which represented 6/21 (29%) families. Providing a correct diagnosis for patients with visual impairment and hearing loss can be challenging for clinicians and their patients, but it can greatly improve clinical care and outcomes. We recommend an algorithm that includes multidisciplinary collaboration, careful clinical evaluation, strategic molecular testing, and consideration of a broad differential diagnosis.

Congenital monocular elevation deficiency associated with a novel TUBB3 gene variant.
Thomas MG, Maconachie GD, Constantinescu CS, Chan WM, Barry B, Hisaund M, Sheth V, Kuht HJ, Dineen RA, Harieaswar S, Engle EC.
British Journal of Ophthalmology. 2020 Apr 1;104(4):547-50.

The genetic basis of monocular elevation deficiency (MED) is unclear. Two brothers with MED (aged 7 and 12 years) were unable to elevate the right eye. Their father had bilateral ptosis, left esotropia and bilateral limitation of elevation. Chin up head posture was present in the older sibling and the father. Bell's phenomenon and vertical rotational vestibulo-ocular reflex were absent in the right eye for both children. Mild bilateral facial nerve palsy was present in the older sibling and the father. Both siblings had slight difficulty with tandem gait. MRI revealed hypoplastic oculomotor nerve. Left anterior insular focal cortical dysplasia was seen in the older sibling. Sequencing of TUBB3 revealed a novel heterozygous variant

(c.1263G>C, p.E421D) segregating with the phenotype. This residue is in the C-terminal H12 α-helix of β-tubulin and is one of three putative kinesin binding sites. Familial MED can arise from a TUBB3 variant and could be considered a limited form of CFEOM. Neurological features such as mild facial palsy and cortical malformations can be present in patients with MED. Thus, in individuals with congenital MED, consideration may be made for TUBB3 mutation screening.

Clinical utility of genetic testing in 201 preschool children with inherited eye disorders.
Lenassi E, Clayton-Smith J, Douzgou S, Ramsden SC, Ingram S, Hall G, Hardcastle CL, Fletcher TA, Taylor RL, Ellingford JM, Newman WD, Fenerty C, Sharma V, Lloyd IC, Biswas S, Ashworth JL, Black GC, Sergouniotis PI.
Genet Med. 2020 Apr;22(4):745-751.

This study assesses the current clinical utility of genetic testing in diverse pediatric inherited eye disorders (IEDs). Two hundred one unrelated children (0-5 years old) with IEDs were ascertained through the database of the North West Genomic Laboratory Hub, Manchester, UK. The cohort was collected over a 7-year period (2011-2018) and included 74 children with bilateral cataracts, 8 with bilateral ectopia lentis, 28 with bilateral anterior segment dysgenesis, 32 with albinism, and 59 with inherited retinal disorders. All participants underwent panel-based genetic testing.

The diagnostic yield of genetic testing for the cohort was 64% (ranging from 39% to 91% depending on the condition). The test result led to altered management (including preventing additional investigations or resulting in the introduction of personalized surveillance measures) in 33% of probands (75% for ectopia lentis, 50% for cataracts, 33% for inherited retinal disorders, 7% for anterior segment dysgenesis, 3% for albinism).

Recurrent Rare Copy Number Variants Increase Risk for Esotropia
Mary C Whitman, Silvio Alessandro Di Gioia, Wai-Man Chan, Alon Gelber, et al
Invest Ophthalmol Vis Sci. 2020 Aug;61:22.

Large genetic study looked at the prevalence of rare copy number variants in patients with comitant esotropia. They were able to find three rare copy number variants that had a higher frequency in patients with esotropia compared to the controls, though there was no overlap with one patient having more than one rare copy number variant. This study opens the doors to a better understanding of underlying causes of comitant strabismus. Even though the study did not have the power to effectively determine which rare copy number variants have a causative relationship with comitant esotropia, it leaves the door open for future studies to gain a better understanding of the pathophysiology and possible gene therapies for treatment.

The mutational spectrum of Myocilin gene among familial versus sporadic cases of Juvenile onset open angle glaucoma.
Gupta V, Somarajan BI, Gupta S, Walia GK, Singh A, Sofi R, Chaudhary RS, Sharma A.
Eye (Lond). 2020 Apr 16. Epub ahead of print.

Juvenile onset primary open angle glaucoma (JOAG) is a rare disorder associated with high IOP and progressive optic neuropathy in patients diagnosed before the age of 40 years. Pattern of inheritance is reported as primarily autosomal dominant in some populations and primarily sporadic in others. This study screened 92 unrelated (sporadic) JOAG patients, and 22 affected families (70 affected members and 36 unaffected) for variations in the *MYOC* gene.
Three coding sequence variants were identified as mutations causing JOAG. The frequency of *MYOC* mutations in familial cases (27%) was significantly higher than in sporadic JOAG cases (2%); p = 0.001. A 90% penetrance for the Gly367Arg variant was seen by the age of 40 years in this cohort.

Ocular complications and prophylactic strategies in Stickler syndrome: a systematic literature review.

Boysen KB, La Cour M, Kessel L.
Ophthalmic Genetics. 2020 Apr 23:1-2.

Stickler syndrome is a collagenopathy caused by mutations in the genes COL2A1 (STL1) or COL11A1 (STL2). Affected patients manifest ocular, auditory, articular, and craniofacial manifestations in varying degrees. 37 articles with 2324 individual patients were included. Myopia was found in 83% of patients, mostly of a moderate to severe degree. Retinal detachments occurred in 45% of patients. Generally, the first detachment occurred in the second decade of life in STL1 patients and later in STL2. Cataracts were more common in STL2 patients, 59% versus 36% in STL1. Glaucoma (10%) and visual impairment (blind: 6%; vision loss in one eye: 10%) were rare. Three studies reported on the effect of prophylactic treatment being protective.

Rates of diagnostic genetic testing in a tertiary ocular genetics clinic.
Lowery RS, Dehnel JR, Schaefer GB, Uwaydat SH.
Ophthalmic Genetics. 2020 May 3;41(3):271-4.

Clinical genetics has evolved significantly to become an efficient and effective means of diagnosing disease. This paper explores the patient experience at the Ocular Genetics Clinic (OGC) at the University of Arkansas for Medical Sciences (UAMS) Jones Eye Institute and discusses reasons why patients continue to not pursue genetic testing. Patients mainly did not undergo testing due to the cost of testing. However, patient availability, patient interest, and diagnostic workup also drove a significant amount of this lack of testing. Ocular genetic testing is becoming an increasingly beneficial tool for diagnosing ocular disease. However, to date, patients do not utilize this service fully. At the OGC, there are several main drivers for this lack of testing, namely finances, interest/availability, and diagnostic workup. As more ocular genetics clinics are established, it will be imperative to address reasons for forgoing genetic testing and to develop strategies to encourage patients to pursue this testing.

Living with type I Usher syndrome: insights from patients and their parents.
Roborel de Climens A, Tugaut B, Piscopo A, Arnould B, Buggage R, Brun-Strang C.
Ophthalmic Genetics. 2020 May 1:1-2.

Type 1 Usher syndrome (USH1) is a rare disease and major cause of genetic deaf-blindness. Deafness is present from birth while retinitis pigmentosa (RP) which typically presents during childhood is progressive leading to blindness. A total of 18 patients (7 in the US; 11 in France)– 9 adults, 4 adolescents, and 5 children– and 9 mothers were interviewed. The most cited ocular symptoms were difficulty seeing at night and loss of peripheral vision. Interviewees reported limitations on Physical (e.g. difficulty moving), Mental (e.g. fear about falling), Social (e.g. difficulty discussing disease with others) and Role (e.g. difficulties at school/work) functioning. These impacts were, when possible, mitigated by coping strategies and support (e.g. using electronic devices, having a positive/proactive attitude). This research provides an overview of symptoms experienced by patients with USH1 and highlights the dramatic impact these have on patients' lives, allowing the identification of concepts of importance when evaluating therapeutic treatments in development for RP.

KCNV2 retinopathy: clinical features, molecular genetics and directions for future therapy.
Guimaraes TA, Georgiou M, Robson AG, Michaelides M.
Ophthalmic Genetics. 2020 May 23:1-8.

KCNV2-associated retinopathy or "cone dystrophy with supernormal rod responses" is an autosomal recessive cone-rod dystrophy with pathognomonic ERG findings. This gene encodes Kv8.2, a voltage-gated potassium channel subunit that acts as a modulator by shifting the activation range of the K+ channels in photoreceptor inner segments. Currently, no treatment is available for the condition. However, there is a lack of prospective long-term data in large molecularly confirmed cohorts, which is a prerequisite for accurate patient counselling/prognostication, to identify an optimal window for intervention

and outcome measures, and ultimately to design future therapy trials. Herein we provide a detailed review of the clinical features, retinal imaging, electrophysiology and psychophysical studies, molecular genetics, and briefly discuss future prospects for therapy trials.

Whole Exome Sequencing Reveals Novel and Recurrent Disease-Causing Variants in Lens Specific Gap Junctional Protein Encoding Genes Causing Congenital Cataract.
Berry V, Ionides A, Pontikos N, Moghul I, Moore AT, Quinlan RA, Michaelides M.
Genes (Basel). 2020 May 6;11(5):512.

Pediatric cataract is clinically and genetically heterogeneous. This study aimed to identify disease-causing variants in three large British families and one isolated case with autosomal dominant congenital cataract, using whole exome sequencing. Heterozygous variants in the genes *GJA8* and *GJA3* were associated with the disease phenotype (either lamellar or nuclear cataract). The study extends the mutation spectrum of these genes and further facilitates clinical diagnosis.

Loss of Function of *RIMS2* Causes a Syndromic Congenital Cone-Rod Synaptic Disease with Neurodevelopmental and Pancreatic Involvement.
Mechaussier S, Almoallem B, Zeitz C, Van Schil K, Jeddawi L, Van Dorpe J, Dueñas Rey A, Condroyer C, Pelle O, Polak M, Boddaert N, Bahi-Buisson N, Cavallin M, Bacquet JL, Mouallem-Bézière A, Zambrowski O, Sahel JA, Audo I, Kaplan J, Rozet JM, De Baere E, Perrault I.
Am J Hum Genet. 2020 Jun 4;106(6):859-871.

Congenital cone-rod synaptic disorder (CRSD), also known as incomplete congenital stationary night blindness (iCSNB), is a non-progressive inherited retinal disease (IRD) characterized by night blindness, photophobia, and nystagmus, and distinctive electroretinographic features. In this report, bi-allelic *RIMS2* variants are identified in seven CRSD-affected individuals from four unrelated families. Apart from CRSD, neurodevelopmental disease was observed in all affected individuals, and abnormal glucose homeostasis was observed in the eldest affected individual. This is the first report of a syndromic stationary congenital IRD.

Copy-number variation contributes 9% of pathogenicity in the inherited retinal degenerations.
Zampaglione E, Kinde B, Place EM, Navarro-Gomez D, Maher M, Jamshidi F, Nassiri S, Mazzone JA, Finn C, Schlegel D, Comander J, Pierce EA, Bujakowska KM.
Genet Med. 2020 Jun;22(6):1079-1087.

Current sequencing strategies can genetically solve 55-60% of inherited retinal degeneration (IRD) cases, despite recent progress in sequencing. This can partially be attributed to elusive pathogenic variants (PVs) in known IRD genes, including copy-number variations (CNVs), which have been shown as major contributors to unsolved IRD cases. In this study, five hundred IRD patients were analyzed with targeted next-generation sequencing (NGS). The NGS data were used to detect CNVs with ExomeDepth and gCNV and the results were compared with CNV detection with a single-nucleotide polymorphism (SNP) array. Likely causal CNV predictions were validated by quantitative polymerase chain reaction (qPCR). Likely disease-causing single-nucleotide variants (SNVs) and small indels were found in 55.6% of subjects. PVs in *USH2A* (11.6%), *RPGR* (4%), and *EYS* (4%) were the most common. Likely causal CNVs were found in an additional 8.8% of patients. Of the three CNV detection methods, gCNV showed the highest accuracy. Approximately 30% of unsolved subjects had a single likely PV in a recessive IRD gene.

Next generation sequencing using phenotype-based panels for genetic testing in inherited retinal diseases.
Shah M, Shanks M, Packham E, Williams J, Haysmoore J, MacLaren RE, Németh AH, Clouston P, Downes SM.

Ophthalmic Genetics. 2020 Jul 3;41(4):331-7.

Diagnostic next generation sequencing (NGS) services for patients with inherited retinal diseases (IRD) traditionally use gene panel based approaches, which have cost and resource implications. Results of 655 consecutive patients referred for phenotype-based panel testing over 54 months were analysed to assess diagnostic yield. Variants were identified in 450 patients (68.7%). The overall diagnostic yield from phenotype-based panels was 42.8%. The diagnostic yield was highest from panels representing distinct clinical phenotypes: Usher panel 90.9% and congenital stationary night blindness panel 75.0%. Retinitis pigmentosa/rod-cone dystrophy was the commonest presenting phenotype (n = 243) and Usher syndrome was the commonest presenting syndromic disease (n = 39). Patients presenting with late-onset (≥50 years) macular disease had a lower diagnostic yield (18.0%) compared with patients <50 years (24.2%). Additionally, a diagnostic yield of 1.8% was attributable to copy number variants. The overall diagnostic yield achieved in this study reflects the wide range of phenotypes that were referred. This pragmatic approach provides a high yield for early-onset and clearly defined genetically determined disorders but clinical utility is not as clear for late-onset macular disorders. This phenotype-based panel approach is clinician-referrer orientated, and can be used as a front-end virtual panel, when whole genome sequencing is introduced into diagnostic services for IRD.

Homozygosity for a novel double mutant allele (G1961E/L857P) underlies childhood-onset ABCA4-related retinopathy in the United Arab Emirates.
Khan AO.
Retina. 2020 Jul 1;40(7):1429-33.

22 identified patients (19 families; 11 males, 11 females; first visual symptoms 5–33 years old) were found to harbor biallelic ABCA4 pathologic variants. There were 14 childhood-onset cases, all were homozygous, 11 for the same novel double mutant allele G1961E/L857P. Those who underwent electroretinography (8) had cone-rod rather than isolated macular dystrophy. There were 8 adult-onset cases—all were compound heterozygous, seven harboring the common G1961E mutant allele. The molecular yield for clinically diagnosed ABCA4-related retinopathy in Emiratis was 100% in this case series (22 patients, 19 families). Many cases were childhood-onset cone-rod dystrophy related to a novel double mutant allele (G1961E/L857P) that likely represents a founder effect for the region.

Preferentially Paternal Origin of De Novo 11p13 Chromosome Deletions Revealed in Patients with Congenital Aniridia and WAGR Syndrome.
Vasilyeva TA, Marakhonov AV, Sukhanova NV, Kutsev SI, Zinchenko RA.
Genes (Basel). 2020 Jul 17;11(7):812.

Congenital *PAX6*-associated aniridia is a hereditary eye disorder caused by mutations or chromosome rearrangements involving the PAX6 gene. 11p13 chromosome deletions were identified in 30 out of 91 probands with congenital aniridia or WAGR syndrome (characterized by Wilms' tumor, Aniridia, and Genitourinary abnormalities as well as mental Retardation). The loss of heterozygosity analysis (LOH) was performed in 10 families with de novo chromosome deletion in proband. In 7 out of 8 informative families, the analysis revealed deletions occurred at the paternal allele.

Mutations in *SREBF1*, Encoding Sterol Regulatory Element Binding Transcription Factor 1, Cause Autosomal-Dominant IFAP Syndrome.
Wang H, Humbatova A, Liu Y, Qin W, Lee M, Cesarato N, Kortüm F, Kumar S, Romano MT, Dai S, Mo R, Sivalingam S, Motameny S, Wu Y, Wang X, Niu X, Geng S, Bornholdt D, Kroisel PM, Tadini G, Walter SD, Hauck F, Girisha KM, Calza AM, Bottani A, Altmüller J, Buness A, Yang S, Sun X, Ma L, Kutsche K, Grzeschik KH, Betz RC, Lin Z.
Am J Hum Genet. 2020 Jul 2;107(1):34-45.

IFAP syndrome is a rare genetic disorder characterized by ichthyosis follicularis, atrichia, and photophobia. Mutations in *MBTPS2*, encoding site-2-protease (S2P), underlie X-linked IFAP syndrome. The present report describes the identification via whole-exome sequencing of three heterozygous mutations in *SREBF1* in 11 unrelated, ethnically diverse individuals with autosomal-dominant IFAP syndrome. *SREBF1* encodes sterol regulatory element-binding protein 1 (SREBP1), which promotes the transcription of lipogenes involved in the biosynthesis of fatty acids and cholesterols. Study findings indicate that SREBP signaling plays an essential role in epidermal differentiation, skin barrier formation, hair growth, and eye function.

DYNC2H1 hypomorphic or retina-predominant variants cause nonsyndromic retinal degeneration.
Vig A, Poulter JA, Ottaviani D, Tavares E, Toropova K, Tracewska AM, Mollica A, Kang J, Kehelwathugoda O, Paton T, Maynes JT, Wheway G, Arno G; Genomics England Research Consortium, Khan KN, McKibbin M, Toomes C, Ali M, Di Scipio M, Li S, Ellingford J, Black G, Webster A, Rydzanicz M, Stawiński P, Płoski R, Vincent A, Cheetham ME, Inglehearn CF, Roberts A, Heon E.
Genet Med. 2020 Aug 5. Epub ahead of print.

Genome and exome sequencing were performed for five unrelated cases of IRD with no identified variant. In vitro assays were developed to validate the variants identified (fibroblast assay, induced pluripotent stem cell [iPSC] derived retinal organoids, and a dynein motility assay).
Four novel *DYNC2H1* variants and one previously reported variant were identified. The latter was previously associated with Jeune asphyxiating thoracic dystrophy (JATD).
This paper identifies *DYNC2H1* variants that are either hypomorphic or affecting a retina-predominant transcript and causing nonsyndromic IRD.

Human iPSC Modeling Reveals Mutation-Specific Responses to Gene Therapy in a Genotypically Diverse Dominant Maculopathy.
Sinha D, Steyer B, Shahi PK, Mueller KP, Valiauga R, Edwards KL, Bacig C, Steltzer SS, Srinivasan S, Abdeen A, Cory E, Periyasamy V, Siahpirani AF, Stone EM, Tucker BA, Roy S, Pattnaik BR, Saha K, Gamm DM.
Am J Hum Genet. 2020 Aug 6;107(2):278-292.

Dominantly inherited disorders are not typically considered to be therapeutic candidates for gene augmentation. In this report, induced pluripotent stem cell-derived retinal pigment epithelium (iPSC-RPE) allowed for testing the potential of gene augmentation to treat Best disease, a dominant macular dystrophy caused by over 200 missense mutations in *BEST1*. Gene augmentation in iPSC-RPE fully restored BEST1 calcium-activated chloride channel activity and improved rhodopsin degradation in an iPSC-RPE model of recessive bestrophinopathy as well as in two models of dominant Best disease caused by different mutations in regions encoding ion-binding domains. A third dominant Best disease iPSC-RPE model did not respond to gene augmentation, but showed normalization of BEST1 channel activity following CRISPR-Cas9 editing of the mutant allele. Additionally, all three dominant Best disease iPSC-RPE models were studied with gene editing, which produced premature stop codons specifically within the mutant BEST1 alleles. Single-cell profiling demonstrated no adverse perturbation of retinal pigment epithelium (RPE) transcriptional programs in any model, although off-target analysis detected a silent genomic alteration in one model. These results suggest that gene augmentation is a viable first-line approach for some individuals with dominant Best disease. Testing gene editing strategies for on-target efficiency and off-target events using personalized iPSC-RPE model systems is warranted. Personalized iPSC-RPE models can be used to select among a growing list of gene therapy options to maximize safety and efficacy while minimizing time and cost.

LONGITUDINAL STUDY OF RPE65-ASSOCIATED INHERITED RETINAL DEGENERATIONS
PIERRACHE M, GHAFARYASL G, KHAN M, YZER S, VAN GENDEREN M, SCHUIL J, BOONSTRA F, POTT J, DE FABER J, TJON-FO-SANG M, VERMEER K, CREMERS F, KLAVER C, VAN DEN BORN L,

RETINA 2020 Sep;40:1812–1828.

The study aimed to look at the disease course of RPE65-associated inherited retinal degenerations (IRDs) as a function of the genotype, define a critical age for blindness, and identify potential modifiers. Forty-five patients with IRD from 33 families with biallelic RPE65 mutations, 28 stemming from a genetic isolate. The authors collected retrospective data from medical charts. Coexisting variants in 108 IRD-associated genes were identified with Molecular Inversion Probe analysis. Most patients were diagnosed within the first years of life. Daytime visual function ranged from near-normal to blindness in the first four decades and met WHO criteria for blindness for visual acuity and visual field in the fifth decade. p.(Thr368His) was the most common variant (54%). Intrafamilial variability and interfamilial variability in disease severity and progression were observed. Molecular Inversion Probe analysis confirmed all RPE65 variants and identified one additional variant in LRAT and one in EYS in two separate patients. All patients with RPE65-associated IRDs developed symptoms within the first year of life. Visual function in childhood and adolescence varied but deteriorated inevitably toward blindness after age 40. In this study, genotype was not predictive of clinical course. The variance in severity of disease could not be explained by double hits in other IRD genes. This paper tried to provide a clinical approach to help prognosticate patient outcomes.

PHENOTYPE-GUIDED GENETIC TESTING OF PEDIATRIC INHERITED RETINAL DISEASE IN THE UNITED ARAB EMIRATES
ARIF O. KHAN
RETINA 2020 Sep;40:1829–1837.

Inherited retinal disease is relatively common in the Arabian Gulf, but details regarding pediatric inherited retinal disease in the region are lacking. The purpose of this study is to report the experience of a regional Ocular Genetics Service with childhood onset inherited retinal disease in the United Arab Emirates. This was a retrospective series of consecutive Emirati patients referred to the Ocular Genetics Service of Cleveland Clinic Abu Dhabi over a 3-year period (2016–2018) who were diagnosed with childhood-onset inherited retinal disease (onset before 16 years old) and underwent diagnostic genetic testing guided by clinical phenotype (single gene, nextgeneration panel, or exome sequencing). Seventy-one probands were identified (38 male and 33 females), the majority of whom were symptomatic with visual problems within the first 5 years of life. All patients had disease causing mutations in 1 of 26 retinal disease genes. Recessive disease was frequently due to homozygous mutations. The most frequently mutated genes (and number of probands) were ABCA4 (14), KCNV2 (8), CRB1 (6), and CNGA3 (5). Recurrent specific gene mutations included ABCA4 p.Gly1961Glu/p.Leu857Pro, KCNV2 p.Glu143*, MERTK p.Cys738Trpfs*32, and RS1 c.52+3A.G. Some probands had mutations in syndromic genes and were confirmed to have extraocular findings. Phenotype-guided genetic testing had a remarkable yield for this patient population. Recessive disease is often from homozygous mutations. Cone-dominated phenotypes are common. There are apparent founder mutations for several genes that could be used in a targeted genetic testing strategy. Molecular diagnosis is particularly important in affected children when inherited retinal dystrophy could be a sign of syndromic disease as proper earlier diagnosis minimizes potential extraocular morbidity.

PHENOTYPIC CHARACTERISTICS OF ROD–CONE DYSTROPHY ASSOCIATED WITH MYO7A MUTATIONS IN A LARGE FRENCH COHORT
KHATEB S, MOHAND-SAÏD S, NASSISI M, BONNET C, ROUX A, ANDRIEU C, ANTONIO A, CONDROYER C, ZEITZ C, DEVISME C, LOUNDON N, MARLIN S, PETIT C, BODAGHI B, SAHEL J, AUDO I.
RETINA 2020 Aug;40:1603–1615.

The study aimed to document the rod–cone dystrophy phenotype of patients with Usher syndrome type 1 (USH1) harboring MYO7A mutations. Methods: Retrospective cohort study of 53 patients (42 families) with biallelic MYO7A mutations who underwent comprehensive examination, including functional visual tests and multimodal retinal imaging. Genetic analysis was performed either using a multiplex amplicon

panel or through direct sequencing. Data were analyzed with IBM SPSS Statistics software v. 21.0. Fifty different genetic variations including 4 novel were identified. Most patients showed a typical rod–cone dystrophy phenotype, with best-corrected visual acuity and central visual field deteriorating linearly with age. At age 29, binocular visual field demonstrated an average preservation of 50 central degrees, constricting by 50% within 5 years. Structural changes based on spectral domain optical coherence tomography, short wavelength autofluorescence, and near-infrared autofluorescence measurements did not however correlate with age. Our study revealed a higher percentage of epiretinal membranes and cystoid macular edema in patients with MYO7A mutations compared with rod–cone dystrophy patients with other mutations. Subgroup analyses did not reveal substantial genotype–phenotype correlations. Conclusion: To the best of our knowledge, this is the largest French cohort of patients with MYO7A mutations reported to date. Functional visual characteristics of this subset of patients followed a linear decline as in other typical rod–cone dystrophy, but structural changes were variable indicating the need for a case-by-case evaluation for prognostic prediction and choice of potential therapies.

PAX6 Mutational Status Determines Aniridia-Associated Keratopathy Phenotype
Neil Lagali, Bogumil Wowra, Fabian Norbert Fries, Lorenz Latta, Kayed Moslemani, Tor Paaske Utheim, Edward Wylegala, Berthold Seitz, Barbara Käsmann-Kellner
Ophthalmology. 2020 Feb(2);127:273-5.

Congenital aniridia can result from more than 400 unique mutations in the PAX6 gene. This study attempted to quantify the genotype-phenotype correlation for aniridia-associated keratopathy. Multiple techniques were used to objectively quantify the keratopathy – corneal thickness, anterior segment OCT, Cochet-Bonnet Esthesiometry, and laser confocal microscopy. The severity of keratopathy was found to correlate with the severity of the PAX6 mutations, from single amino acid substitution to deletion of the entire PAX6 gene. Several subtypes also showed age dependence. The mildest genetic defect (no detectable PAX6 mutation), had preserved vision and modestly reduced corneal sensitivity. These results should allow clinicians to provide better prognostic guidance on the progression and severity of aniridia-associated keratopathy based on the genetic evaluation.

Association of Genetic Variation With Keratoconus.
McComish BJ, Sahebjada S, Bykhovskaya Y, Willoughby CE, Richardson AJ, Tenen A, Charlesworth JC, MacGregor S, Mitchell P, Lucas SEM, Mills RA, Mackey DA, Li X, Wang JJ, Jensen RA, Rotter JI, Taylor KD, Hewitt AW, Rabinowitz YS, Baird PN, Craig JE, Burdon KP.
JAMA Ophthalmol. 2020 Feb 1;138(2):174-181.

Keratoconus is a major indication for corneal transplant. This study attempts to identify genetic susceptibility regions for keratoconus in the human genome. It was conducted with data from eye clinics in Australia, the United States, and Northern Ireland. The discovery cohort of individuals with keratoconus and control participants from Australia was genotyped using the Illumina Human Core Exome single-nucleotide polymorphism array. After quality control and data cleaning, genotypes were imputed against the 1000 Genomes Project reference panel, and association analyses were completed using PLINK version 1.90. Single-nucleotide polymorphisms with $P < 1.00 \times 10\text{-}6$ were assessed for replication in 3 additional cohorts. Control participants were drawn from the cohorts of the Blue Mountains Eye Study and a previous study of glaucoma. Replication cohorts were from a previous keratoconus genome-wide association study data set from the United States, a cohort of affected and control participants from Australia and Northern Ireland, and a case-control cohort from Victoria, Australia. Data were collected from January 2006 to March 2019. Associations between keratoconus and 6 252 612 genetic variants were estimated using logistic regression after adjusting for ancestry using the first 3 principal components. The discovery cohort included 522 affected individuals and 655 control participants, while the replication cohorts included 818 affected individuals and 3858 control participants. Two novel loci reached genome-wide significance , with a P value of $7.46 \times 10\text{-}9$ at rs61876744 in patatin-like phospholipase domain-containing 2 gene (PNPLA2) on chromosome 11 and a P value of $6.35 \times 10\text{-}12$ at rs138380, 2.2 kb upstream of casein kinase I isoform epsilon gene on chromosome 22. One additional locus was identified with a P value less than $1.00 \times 10\text{-}6$ in mastermind-like transcriptional coactivator 2

on chromosome 11. The novel locus in PNPLA2 reached genome-wide significance in an analysis of all 4 cohorts.

Clinical utility of genetic testing in 201 preschool children with inherited eye disorders.
Lenassi E, Clayton-Smith J, Douzgou S, Ramsden SC, Ingram S, Hall G, Hardcastle CL, Fletcher TA, Taylor RL, Ellingford JM, Newman WD, Fenerty C, Sharma V, Lloyd IC, Biswas S, Ashworth JL, Black GC, Sergouniotis PI.
Genet Med. 2020 Apr;22(4):745-751.

A key property to consider in all genetic tests is clinical utility, the ability of the test to influence patient management and health outcomes. This study assesses the current clinical utility of genetic testing in diverse pediatric inherited eye disorders (IEDs). Two hundred one unrelated children (0-5 years old) with IEDs were ascertained through the database of the North West Genomic Laboratory Hub, Manchester, UK. The cohort was collected over a 7-year period (2011-2018) and included 74 children with bilateral cataracts, 8 with bilateral ectopia lentis,28 with bilateral anterior segment dysgenesis, 32 with albinism, and 59 with inherited retinal disorders. All participants underwent panel-based genetic testing. The diagnostic yield of genetic testing for the cohort was 64% (ranging from 39% to 91% depending on the condition). The test result led to altered management (including preventing additional investigations or resulting in the introduction of personalized surveillance measures) in 33% of probands (75% for ectopia lentis, 50% for cataracts, 33% for inherited retinal disorders, 7% for anterior segment dysgenesis, 3% for albinism). Thus, genetic testing helped identify an etiological diagnosis in the majority of preschool children with IEDs. This prevented additional unnecessary testing and provided the opportunity for anticipatory guidance in significant subsets of patients.

Copy-number variation contributes 9% of pathogenicity in the inherited retinal degenerations.
Zampaglione E, Kinde B, Place EM, Navarro-Gomez D, Maher M, Jamshidi F, Nassiri S, Mazzone JA, Finn C, Schlegel D, Comander J, Pierce EA, Bujakowska KM.
Genet Med. 2020 Jun;22(6):1079-1087.

Current sequencing strategies can genetically solve 55-60% of inherited retinal degeneration (IRD) cases, despite recent progress in sequencing. This can partially be attributed to elusive pathogenic variants (PVs) in known IRD genes, including copy-number variations (CNVs), which have been shown as major contributors to unsolved IRD cases.
Five hundred IRD patients were analyzed with targeted next-generation sequencing (NGS). The NGS data were used to detect CNVs with ExomeDepth and gCNV and the results were compared with CNV detection with a single-nucleotide polymorphism (SNP) array. Likely causal CNV predictions were validated by quantitative polymerase chain reaction (qPCR). Likely disease-causing single-nucleotide variants (SNVs) and small indels were found in 55.6% of subjects. PVs in USH2A (11.6%), RPGR (4%), and EYS (4%) were the most common. Likely causal CNVs were found in an additional 8.8% of patients. Of the three CNV detection methods, gCNV showed the highest accuracy. Approximately 30% of unsolved subjects had a single likely PV in a recessive IRD gene.
This study shows that CNV detection using NGS-based algorithms is a reliable method that greatly increases the genetic diagnostic rate of IRDs. Experimentally validating CNVs helps estimate the rate at which IRDs might be solved by a CNV plus a more elusive variant.

Phenotype-guided Genetic Testing of Pediatric Inherited Retinal Disease in the United Arab Emirates.
Khan AO.
Retina. 2020 Sep;40(9):1829-1837.

The purpose of this study was to report the experience of the Ocular Genetics Service at Cleveland Clinic Abu Dhabi with phenotypes and genotypes of childhood onset inherited retinal disease in Emirati patients. This is a retrospective chart review performed from 2016-2018. Patients underwent genetic tested guided by the phenotype. 71 probands were identified who presented within the first 5 years of life with

nystagmus and decreased vision. All families were consanguineous or endogamous. This paper had a high yield for this population. This was likely due to the recessive nature of childhood onset diseases and history of consanguinity. This method can be useful in certain situations.

GUCY2D-associated Leber congenital amaurosis: a retrospective natural history study in preparation for trials of novel therapies.
Bouzia Z, Georgiou M, Hull S, Robson AG, Fujinami K, Rotsos T, Pontikos N, Arno G, Webster AR, Hardcastle AJ, Fiorentino A.
American Journal of Ophthalmology. 2020 Feb 1;210:59-70.

GUCY2D-associated Leber congenital amaurosis is a severe early-onset retinal dystrophy. Twenty-one subjects with GUCY2D-LCA were included, with a mean follow-up ± standard deviation (SD) of 10 ± 11.85 years. Marked reduction in visual acuity (VA) and nystagmus was documented in all patients within the first 3 years of life. 57% had photophobia and 38% had nyctalopia. Longitudinal assessment of VA showed stability in all patients, except 1 patient who experienced deterioration over a follow-up of 44 years. Eighteen subjects had either normal fundus appearance (n = 14) or a blond fundus (n = 3), while only 4 of the eldest subjects had mild retinal pigment epithelium (RPE) atrophy (mean, 49 years; range 40-54 years). OCT data were available for 11 subjects and 4 different grades of ellipsoid zone (EZ) integrity were identified: (1) continuous/intact EZ (n = 6), (2) focally disrupted EZ (n = 2), (3) focally disrupted with RPE changes (n = 2), and (4) diffuse EZ disruption with RPE changes (n = 1). All examined subjects had stable OCT findings over the long follow-up period. Full-field ERGs showed evidence of a severe cone-rod dystrophy in 5 of 6 patients and undetectable ERGs in 1 subject. Novel genotype-phenotype correlations are also reported. There is severe cone and rod dysfunction but with preserved photoreceptor structure evident on optical coherence tomography. Stable natural history suggests a wide therapeutic window for intervention.

Expanding the retinal phenotype of RP1: from retinitis pigmentosa to a novel and singular macular dystrophy.
Riera M, Abad-Morales V, Navarro R, Ruiz-Nogales S, Méndez-Vendrell P, Corcostegui B, Pomares E.
British Journal of Ophthalmology. 2020 Feb 1;104(2):173-81.

This study aimed to identify the underlying genetic cause(s) of inherited retinal dystrophy (IRD) in 12 families of Kuwaiti origin affected by macular dystrophy and four Spanish patients affected by retinitis pigmentosa (RP). Panel-based whole exome sequencing was used to simultaneously analyse 224 IRD genes in one affected member of each family. The putative causative variants were confirmed by Sanger sequencing and cosegregation analyses. Haplotype analysis was performed using single nucleotide polymorphisms. A homozygous missense mutation c.606C>A (p.Asp202Glu) in RP1 was found to be the molecular cause of IRD in all 12 families from Kuwait. These patients exhibited comparable symptoms, including progressive decline in visual acuity since adolescence. Fundus autofluorescence images revealed bilateral macular retinal pigment epithelium disturbances, with neither perimacular flecks nor peripheral alterations. A shared haplotype spanning at least 1.1 Mb was identified in all families, suggesting a founder effect. Furthermore, RP1 variants involving nonsense and/or frameshifting mutations (three of them novel) were identified in three Spanish autosomal-recessive RP families and one dominant RP pedigree. This study describes, for the first time, a macular dystrophy phenotype caused by an RP1 mutation; establishing a new genotype-phenotype correlation in this gene, expanding its mutation spectrum and further highlighting the clinical heterogeneity associated with IRD.

Bi-allelic Variants in TKFC Encoding Triokinase/FMN Cyclase Are Associated with Cataracts and Multisystem Disease.
Wortmann SB, Meunier B, Mestek-Boukhibar L, van den Broek F, Maldonado EM, Clement E, Weghuber D, Spenger J, Jaros Z, Taha F, Yue WW.
The American Journal of Human Genetics. 2020 Feb 6;106(2):256-263.

An inborn error of metabolism caused by TKFC deficiency in two unrelated families is reported. Rapid trio genome sequencing in family 1 and exome sequencing in family 2 excluded known genetic etiologies, and further variant analysis identified rare homozygous variants in TKFC. TKFC encodes a bifunctional enzyme involved in fructose metabolism through its glyceraldehyde kinase activity and in the generation of riboflavin cyclic 4′,5′-phosphate (cyclic FMN) through an FMN lyase domain. The TKFC homozygous variants reported here are located within the FMN lyase domain. Functional assays in yeast support the deleterious effect of these variants on protein function. Shared phenotypes between affected individuals with TKFC deficiency include cataracts and developmental delay, associated with cerebellar hypoplasia in one case. Further complications observed in two affected individuals included liver dysfunction and microcytic anemia, while one had fatal cardiomyopathy with lactic acidosis following a febrile illness. We postulate that deficiency of TKFC causes disruption of endogenous fructose metabolism leading to generation of by-products that can cause cataract. In line with this, an affected individual had mildly elevated urinary galactitol, which has been linked to cataract development in the galactosemias. Further, in light of a previously reported role of TKFC in regulating innate antiviral immunity through suppression of MDA5, we speculate that deficiency of TKFC leads to impaired innate immunity in response to viral illness, which may explain the fatal illness observed in the most severely affected individual.

PAX6 Mutational Status Determines Aniridia-Associated Keratopathy Phenotype
Neil Lagali, Bogumil Wowra, Fabian Norbert Fries, Lorenz Latta, Kayed Moslemani, Tor Paaske Utheim, Edward Wylegala, Berthold Seitz, Barbara Käsmann-Kellner
Ophthalmology. 2020 Feb;127:27-5.

Congenital aniridia can result from more than 400 unique mutations in the PAX6 gene. This study attempted to quantify the genotype-phenotype correlation for aniridia-associated keratopathy. Multiple techniques were used to objectively quantify the keratopathy – corneal thickness, anterior segment OCT, Cochet-Bonnet Esthesiometry, and laser confocal microscopy. The severity of keratopathy was found to correlate with the severity of the PAX6 mutations, from single amino acid substitution to deletion of the entire PAX6 gene. Several subtypes also showed age dependence. The mildest genetic defect (no detectable PAX6 mutation), had preserved vision and modestly reduced corneal sensitivity. These results should allow clinicians to provide better prognostic guidance on the progression and severity of aniridia-associated keratopathy based on the genetic evaluation.

17. TRAUMA

Pediatric Eye Injuries by Hydroalcoholic Gel in the Context of the Coronavirus Disease 2019 Pandemic.
Martin GC, LeRoux G, Guindolet D, Boulanger E, Hasle D, Morin E, Vodovar D, Vignal C, Gabison E, Descatha A for the French PCC Research Group.
JAMA Ophthalmol. Published online January 21, 2021.

This is a retrospective case series from April 2020 to August 2020 to evaluate the epidemiologic trend of pediatric eye exposures to alcohol-based hand sanitizers (ABHS). The data was collected from the national database of the French Poison Control Centers (PCC) and from a pediatric ophthalmology referral hospital in Paris, France and a comparison was made between April to August 2020 and April to August 2019. Results indicate, not surprisingly, there were 7 times more pediatric cases of ABHS eye exposures during the 2020 months (9.9%) versus during the 2019 months (1.3%) with $P < 0.001$. Similarly, admissions to the eye hospital for ABHS exposure increased during the 2020 months (16 children with mean age of 3 years old) versus during the 2019 months (1 child age at 16 months old). From the children presenting with eye injuries from ABHS, eight children had corneal and/or conjunctival ulcer involving > 50% corneal surface and two children required an amniotic membrane transplant with surgical intervention. Limitations of this case series is the small sample size and the data collection from France and one pediatric ophthalmology hospital in Paris. However, the case series have an important international message, as each country confronts the widespread use of ABHS and public safety for children during the COVID-19 pandemic. In summary, this article provides a cautionary tale for adults to keep ABHS away from young children's view and away from the proximity of young children's faces/eyes. Future studies will address how the international community of pediatric eye doctors treated pediatric eye exposures from ABHS in 2020 and 2021.

Utility of Pupillary Light Reflex Metrics as a Physiologic Biomarker for Adolescent Sport-Related Concussion.
Master CL, Podolak OE, Ciuffreda KJ, Metzger KB, Joshi NR, McDonald CC, Margulies SS.
JAMA Ophthalmol. 2020 Sep 24;138(11):1135–41.

This is a prospective cohort study of adolescent athletes between ages 12 and 18 years at a specialty concussion program and private suburban high school recruited between August 2017 to December 2018. The study included healthy control individuals (N=134) and athletes with a diagnosis of sport-related concussion (SRC) (N=98). Results of the pupillary light reflex (PLR) metrics of 134 healthy control individuals and 98 athletes with concussion were recorded a median of 12 days following injury (range of 5 to 18 days). Eight of the 9 PLR metrics were significantly greater among athletes with concussion (maximum and minimum pupillary diameter, peak and average constriction/dilation velocity, percentage constriction, and time to 75% pupillary re-dilation [T75]). The authors noted that teenage girls with concussion exhibiting a longer T75 and this is supported in previous research about the sex-based differences following concussion. This study also found no sex differences in T75 in the control group, similar to previous research. The authors sought to distinguish adolescent SRC from healthy controls using the PLR metrics and advance the utility and importance of an objective physiologic biomarker for concussion. Limitations of the study is that the PLR metrics were measured throughout the day and in turn, the authors were not able to control for diurnal variation. Also, limitations include the setting of private suburban high school and homogenous racial background with 81% control group and 85% athletes with SRC identified as White. In summary, evaluating the PLR metrics in athletes with SRC as compared to healthy teenagers is reminder that objective measurements, such as pupillary light reflex measurements, are an important part of the eye exam. Of note, at this time, the utility of abnormal PLR metrics found in athletes with SRC is not known.

Predictors of visual outcomes in pediatric open globe injuries.

Jacobson A, Liles N, Besirli CG, Bohnsack BL.
J AAPOS. 2020 Dec 1:S1091-8531(20)30298-6. Epub ahead of print.

Ocular trauma continues as a significant cause of morbidity in children. Specific challenges include poor or inaccurate history and poor cooperation for preoperative evaluation. There continues to be study attempting to provide information that can be used to predict final visual outcome. The ocular trauma score (OTS), pediatric ocular trauma score (POTS) and toddler/infant ocular trauma score (TOTS) all try to predict visual prognosis and have demonstrated presenting visual acuity is significantly associated with final visual outcome. Challenges encountered were the difficulty in obtaining acuity in young patients as well as creation of these tools using small studies. The authors sought to identify predictors of visual outcomes using a large cohort in the United States .Authors found that POT and TOTS predict visual outcome moderately well. Amblyopia in younger children remains a challenge especially when the injury results in unilateral aphakia or pseudophakia with subsequent amblyopia. It follow that when presenting visual acuity could not be obtained, age and lens damage were significant predictors for final visual acuity. The authors found that retinal detachment and presenting visual acuity were independently significant predictors of final visual outcome. Authors find that current models have limited predictive value and a large multicenter study population would be useful to create an accurate pediatric ocular trauma predictive model.

Pediatric retinal damage due to soccer-ball-related injury: Results from the last decade.
Leshno A, Alhalel A, Fogel-Levin M, Zloto O, Moisseiev J, Vidne-Hay O.
Eur J Ophthalmol. 2021 Jan;31(1):240-244.

Soccer ball injuries to the eye were previously assumed to be less harmful; however, this study is to report ocular injuries in the last decade. This is a study at a single center examining the incidence of soccer ball related retinal trauma in children. Subjects were divided in 2 groups based on severity: Group 1 (non severe-mild signs of retinal trauma and edema involving up to 1 quadrant) and Group 2 (severe-VH, retina tear or detachment, macular hole, retina edema in more than 1 quadrant). 14 patients were treated with injuries related to a soccer ball. All patients were early to mid teens. Group 1-7 eyes. All patients recovered vision. Group 2-7 eyes. 2 patients had decreased vision. 4 had retinal tears. One required surgical repair for a detachment. Ocular injuries in soccer are uncommon. The authors concluded recommending ocular protection.

Long-term outcomes of pediatric traumatic cataracts and retinal detachments due to self-inflicted injuries.
Felfeli T, Mireskandari K, Ali A.
Eur J Ophthalmol. 2021 Jan;31(1):271-276

Vision threatening complications following trauma can result in cataract, retina breaks, and detachments. The purpose of this study was to review the characteristics and outcomes of traumatic cataracts and retina detachments due to self-inflicted injuries (SII). This was a retrospective chart review of 11 patients with traumatic cataracts following SII. All patients had intellectual disability. 5 patients had unilateral cataracts, 6 bilateral cataracts, and 5 had concurrent unilateral retinal detachments. Following cataract surgery, post-operative complications included uveitis (3/13) and retinal detachment (10/13). An overall primary or secondary anatomical success rate was achieved in 71 % of retinal detachment cases. Development of a retinal detachment was one of the major contributors to poor vision in this patient population. Vision declined in 23% of the patients in this study at last follow up from initial presentation. The authors concluded that repeated attempts at surgical repair of recurrent RD may not be justified given poor visual outcomes. This needs to be considered if there is functional vision in the contralateral eye versus the possibility of the same outcome occurring with SII behavior of the better eye.

Long-term evaluation of pars plana vitrectomy in children with abusive head trauma.
Kozner P, Stepankova J, Dotrelova D.

Eur J Ophthalmol. 2020 Oct 29: Epub ahead of print.

Abusive head trauma (AHT) is defined as injury to the skull or intracranial content in children younger than 5 years of age due to abrupt impact and can be associated with intraocular hemorrhages (IOH). These IOH can be found in up to 80% of children with AHT. Pars plana vitrectomy (PPV) is a routine procedure to eliminate persistent pre-retinal hemorrhages in patients of any age. The authors of this paper present their long-term retrospective analysis of children requiring PPV for IOH due to AHT. At their institution, the incidence of IOH with AHT was 29.6/100,000. In total, 18 children were identified with AHT and IOH. 44% of children (36% of eyes) underwent PPV. Indication for surgery was non absorbing axial vitreous hemorrhage and extensive macular pre-retinal hemorrhage. Vision in 50% of eyes improved after surgery. 20% remained poor due to optic disc atrophy and choroidal rupture. Vision in 30% of eyes was not possible to test due to serious brain damage and disability. 16.7% of children in this cohort did not survive. The authors recommend to wait and observe IOH in children with AHT for.2 weeks for spontaneous resporption and then to consider PPV between 2-5 weeks. Overall, this is a smaller cohort and provides some guideline to when to perform a PPV and potential results. A larger cohort and risk of amblyopia by age of onset of hemorrhages would help provide stronger guidelines.

Rate of ocular trauma in children operated on for unilateral cataract in infancy-data from the Infant Aphakia Treatment Study.
Traboulsi EI, Drews-Botsch CD, Christiansen SP, Stout AU, Hartmann EE, Lambert SR; IATS Investigator Group.
J AAPOS. 2020 Oct;24(5):301-303.

This is a retrospective review of medical records of 109 of 114 children enrolled in the Infant Aphakia Treatment Study (IATS) prospective followed to age 10.5 to determine whether the fellow eye of children who have undergone unilateral cataract extraction in the first year of life are at increased risk of injury and vision loss. Based on this limited data, it was estimated that the fellow eye is at greater risk of injury than the operated eye. The data did not support the risk being higher in children with the worst vision in the treated eye.

Pediatric Ocular Injuries: A 3-Year Follow-up Study of Patients Presenting to a Tertiary Care Clinic in Canada
Archambault, Cyril; Mekliche, Assia; Isenberg, Jordan; Fallaha, Nicole; Hamel, Patrick; et al.
J Pediatr Ophthalmol Strabismus 2020 May 1;57(3):185-189.

A retrospective chart review from a tertiary eye care center in Canada over a three year period identified 409 cases of pediatric ocular trauma. The average age was 7.7 years and boys were more commonly injured than girls. Most young children (<10 years old) were injured during free play while older children were most frequently injured playing sports. Soccer was the most common sport, followed by hockey and ball sports. Most injuries were caused by blunt objects. Final visual acuity was 20/40 or better in 77% of patients and 9% percent of patients required surgery. The authors' results were similar to a prior Canadian study. Additionally, as in a study from the United Kingdom, soccer was the most common sports related cause of ocular trauma. Soccer is a very popular sport and might not seem an obvious cause of eye injury, therefore emphasizing this to patients, especially those with monocular vision loss is advisable.

Rate of ocular trauma in children operated on for unilateral cataract in infancy—data from the Infant Aphakia Treatment Study.
Traboulsi EI, Drews-Botsch CD, Christiansen SP, Stout AU, Hartmann EE, Lambert SR, Group II.
J AAPOS. 2020 Oct;24(5):301-303.

There is some body of evidence in the adult literature that those with low vision in one eye are more likely to experience injury to their better seeing eye. In that vein, this is a study assessing prospectively collected data as a part of the 10 year data from the Infant Aphakia Treatment Study evaluating children who underwent unilateral cataract extraction in the first year of life with the goal of determining the incidence of injury to the non-operative eye. In the 109 children included in this study, 4 (3.7%) sustained injury to the non-operative eye and 2 (1.8%) to the operative eye during the study period. These injuries ranged from corneal abrasion, traumatic subconjunctival hemorrhage to subluxed intraocular lens. The risk of injury was higher in boys than girls and there was no clear correlation with injury and best corrected visual acuity in the operative eye. This paper is limited by the small number of cases, but the authors conclude that non-operative eyes of children with unilateral cataracts may be more injury prone than the operative eyes.

Nonaccidental trauma in pediatric patients: evidence-based screening criteria for ophthalmologic examination.
Ip SS, Zafar S, Liu TA, Srikumaran D, Repka MX, Goldstein MA, Woreta FA.
J AAPOS. 2020 Aug;24(4):226.e1-226.e5.

Ophthalmic examinations are routinely performed as part of the workup for suspected non-accidental injury, though prior studies have suggested that normal neuroimaging is typically associated with a normal dilated examination. This retrospective chart review of 192 patients who underwent eye examinations in the setting of non-accidental injury workup found that 8% of patients had retinal hemorrhages. Every single one of those children also had abnormal neuroimaging (the majority being subdural hemorrhage). The authors discuss the downsides associated with ophthalmic evaluation including inability to monitor pupillary examination and increased healthcare cost and patient stress. The authors suggest that eye examinations should be performed in children with abnormal neuroimaging but that an ophthalmologic consultation should not be routine in children with normal neuroimaging.

Ocular injury via epinephrine auto-injector.
Collett G, Elhusseiny AM, Scelfo C, Whitman MC, VanderVeen DK.
J AAPOS. 2020 Jun;24(3):179-181.

Intraocular injury secondary to an EpiPen is exceedingly rare and has only been reported twice (once previously, and the second time with this report). This is a case report of a 2 year old girl who accidentally hit her eye with an EpiPen Jr autoinjector. She presented with a dilated, non-reactive pupil, a Seidel-negative linear corneal wound, anterior capsular tear, and associated lens opacification. Cataract extraction with intraocular lens implantation was performed 1 week after the injury during which a pre-existing posterior capsule rupture was identified. The patient had a normal retinal examination and was 20/30 in that eye 3 months following surgery. The authors discuss the implications of intraocular epinephrine and preservative, confirming that this patient did not experience any untoward events. They suggest that further work is needed to understand the implications of high dose intraocular epinephrine.

Pediatric ocular surface disease associated with suspected abuse.
Aziz M, Mawn L, Zaidman GW, Coroneo MT, Donahue SP, Lenhart P, Shieh C.
J AAPOS. 2020 Jun;24(3):141.e1-141.e6.

The most common ocular manifestation of non-accidental injury is retinal hemorrhage, though this type of injury can also lead to anterior segment and ocular surface conditions as well. The goal of this multi-center, retrospective case series of 4 patients is to evaluate the ocular surface manifestations of non-accidental injury. The four cases presented contain a broad range of manifestations including preseptal cellulitis, corneal ulcer, symblepharon, limbal stem cell deficiency, recurrent erosions, keratitis, corneal neovascularization and scarring. They also include a literature review which includes 9 other case reports of anterior segment manifestations of non-accidental injury. The authors conclude that non-accidental

injury can present in myriad ways and that a hallmark of this condition is sudden improvement in the clinical condition with minimal change in management when the child is admitted and under close supervision.

Long-term outcomes of pediatric traumatic cataracts and retinal detachments due to self-inflicted injuries.
Felfeli T, Mireskandari K, Ali A.
Eur J Ophthalmol. 2021 Jan;31(1):271-276.

Self-inflicted injuries (SIIs) involving repetitive head banging or striking of the face and eyes have a prevalence of up to 50% in children with intellectual disabilities. This can lead to vision threatening complications following trauma such as cataracts and retina detachments. The authors review the characteristics and outcomes of traumatic cataracts and RD in patients with SII in this retrospective chart review over a 14 year period at the Hospital for Sick Children. The authors identified 11 patients to fit their criteria. All patients had intellectual disability include autism spectrum disorder. All patients presented with a traumatic cataract secondary to SII. 9 patients were deemed appropriate for surgical intervention. Vision was improved or preserved in 77% of eyes but worse in the remaining cases due to a traumatic RD. The prognosis for vision is poor and can be attributed to the underlying etiology, continued SII, and burden of surgical interventions. The authors conclude that a high index of suspicion, preventive measures, and regular surveillance are critical for early detection and improving prognosis.

Intraocular foreign body injury in children: clinical characteristics and factors associated with endophthalmitis
Yang Y, Yang C, Zhao R, Lin L, Duan F, et al
Br J Ophthalmol 2020 Jun;104:780-784.

This was a retrospective analysis of patients <18 years old presenting with an intraocular foreign body (IOFB) between 2003 and 2016. 484 children (484 eyes) were included with mean age of 10.12 years. 84.% were male. Fireworks (28.5%) were the most common cause of injury. Endophthalmitis occurred in 116 patients (24.0%). Lower risk of endophthalmitis was associated with metallic IOFB, intraocular hemorrhage and uveal tissue prolapse. Higher risk was associated with zone II wounds and traumatic lens rupture. Culture was performed in 93 patients of which 26 specimens produced a positive culture. 63.0% were gram-positive bacteria, 29.6 % gram-negative and 7.4% fungal. A correlation between intravitreal antibiotic injection during repair and endophthalmitis could not be analyzed in this study, and visual prognosis was also not analyzed.

18. RETINA

Data Assessment of Peripapillary and Macular Vessel Density and Foveal Avascular Zone Metrics Using Optical Coherence Tomography Angiography in Children.
Kiziltoprak H, Tekin K, Cevik S, Kocer AM, Goker YS. Normative
J Pediatr Ophthalmol Strabismus. 2020 Nov 1;57(6):388-398.

OCTA can quantify retinal vessel perfusion density. Therefore, understanding the difference between normal and pathologic retinal vessel density is needed to identify vascular pathology such as ischemia and neovascularization. The study prospectively enrolled 92 eyes of 92 participants; the mean age was 13.4 years (range 7-18), with 42 boys and 50 girls enrolled. Only normal healthy eyes were included, and the study was done in Turkey. OCTA images were acquired and the authors studied the relationship between retinal vasculature and age, sex, BMI, and refractive status. The normative values of the FAZ area, the vessel density of the optic nerve and the macula in children can be incorporated into OCTA reports allowing for clinically useful interpretation. The study used AngioVue software and the RTVue XR Avanti device (Optovue, Inc). Further study in different regions of the world including various ethnicities, could produce a robust normative data set for pediatric patients. If this were included in the imaging system software it would be more useful.

Using the RETeval Device in Healthy Children to Establish Normative Electroretinogram Values.
Soekamto CD, Gupta R, Keck KM.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):17-22.

This prospective study provides a range of normative full-field ERG values in the pediatric population using the RETeval system. The RETeval handheld ERG device (LKC Technologies, Inc) can record full-field ERG responses compliant with ISCEV 5- and 6-step protocols. The test is simple to operate, and can be done without anesthesia. It uses skin electrodes that are similar to adhesive pads used in electrocardiogram recordings. In this study, thirty-eight eyes of 20 patients were included. This handheld system was tolerated in all patients (aged 4-17). The study is limited by its sample size, the lower limits of normal (5th percentile) may not be relevant for clinical use. Additionally, patients younger than 4 years old were not included. This system could be most useful for these young patients who often need general anesthesia for traditional full field ERG.

Developmental Changes in Retinal Microvasculature in Children: A Quantitative Analysis Using Optical Coherence Tomography Angiography.
Songshan Li, Xiao Yang, Mengke Li, Limei Sun, Xiujuan Zhao, Qiong Wang, Sijian Huang, Chonglin Chen, Zhirong Wang, Xiaoling Luo, Bilin Yu and Xiaoyan Ding.
American Journal of Ophthalmology, 2020 Nov; 219: 231-239.

The purpose of this prospective cross-sectional study was to quantify the macular microvascular structure in healthy children of various ages using optical coherence tomography angiography (OCTA). The authors imaged 333 normal children aged 4 to 16 years. The macular vascular density and perfusion density increased with age. However, once these values were adjusted for spherical equivalence and axial length, only the macular vascular density was associated with age. The FAZ area and perimeter did not change over age which is interesting because in healthy adults generally we do see an increase in the FAZ with age. The authors also noted that the younger children had more nonconsecutive vessel branching and vascular loops with irregular shapes in the FAZ. The conclusion of the authors was that macular vascular density and perfusion density continue to increase with age in children. And that even though the FAZ area and perimeter did not change with age, the structure of the FAZ became more smooth over time. The biggest weakness of the study is the homogeneous patient population as this was a study of only Chinese children and the results could differ by race and ethnicity. In sum, this study

establishes normal values in the general pediatric population with the goal of better defining pathology from normal growth when performing OCTA in a child, which is important as this becomes a more common imaging modality for ophthalmologists.

IMPAIRED DARK ADAPTATION ASSOCIATED WITH A DISEASED BRUCH MEMBRANE IN PSEUDOXANTHOMA ELASTICUM
Hess K, Gliem M, Birtel J, Müller P, Hendig D, Andrews C, Murray IJ, Holz FG, Charbel Issa P.Retina. 2020 Oct;40(10):1988-1995.

The prospective case–control study aimed to characterize dark adaptation in patients with pseudoxanthoma elasticum, a systemic disease leading to calcification of elastic tissue including the Bruch membrane. Dark adaptation thresholds were measured using a Goldmann-Weekers dark adaptometer. Additional assessments included best-corrected visual acuity testing, contrast sensitivity, low luminance deficit, and visionrelated quality of life. Dark adaptation thresholds were significantly higher, and adaptation periods were prolonged in patients with pseudoxanthoma elasticum (n = 35; 33 with 2 ABCC6 mutations) compared with controls (n = 35). The time to adapt 4 log units (20.6 ± 8.6 vs. 8.0 ± 1.3 minutes) and the mean dark adaptation threshold after 15 minutes (3.5 ± 1.1 vs. 1.8 ± 0.2 log units) were significantly different between patients and controls (both P , 0.001). Low luminance deficits (12.3 ± 6.4 vs. 6.1 ± 4.3 ETDRS letters), contrast sensitivity (1.4 ± 0.3 vs. 1.9 ± 0.1), and low luminance-related quality of life (LLQ score: 1,286 ± 355 vs. 2,167 ± 68) were also significantly worse in patients with pseudoxanthoma elasticum (all, P , 0.001). Two patients were treated with high-dose vitamin A which partially reversed impaired dark adaptation. Patients with pseudoxanthoma elasticum often have impaired dark adaptation. Positive effects of vitamin A supplementation may indicate restricted retinal access of vitamin A through the Bruch membrane as one possible underlying pathogenic factor.

HANDHELD SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY FINDINGS OF X-LINKED RETINOSCHISIS IN EARLY CHILDHOOD
Ling KP, Mangalesh S, Tran-Viet D, Gunther R, Toth CA, Vajzovic L.
Retina. 2020 Oct;40(10):1996-2003.

This retrospective analysis looked at using handheld spectral domain optical coherence tomography (SDOCT) imaging to investigate in vivo microanatomic retinal changes and their progression over time in young children with juvenile X-linked retinoschisis (XLRS). The handheld SD OCT images obtained under a prospective research protocol in children who had established XLRS diagnosis based on genetic testing or clinical history. Three OCT graders performed standardized qualitative and quantitative assessment of retinal volume scans, which were divided into foveal, parafoveal, and extrafoveal regions. Visual acuity data were obtained when possible. Spectral domain OCT images were available of both eyes in 8 pediatric patients with ages 7 months to 10 years. The schisis cavities involved inner nuclear layer in over 90% (15/16) of eyes in all 3 regions. Retinal nerve fiber and ganglion cell layer involvement was present only in the extrafoveal region in 63% (10/16) eyes and outer nuclear and plexiform layer in few others. In 7 children followed over 2 months to 15 months, the location of schisis remained consistent. Central foveal thickness decreased from the baseline to final available visit in 4/6 eyes. Ellipsoid zone disruption seemed to accompany lower visual acuity in 1/4 eyes. Early in life, the SD OCT findings in XLRS demonstrate differences in schisis location in fovea–parafoveal versus extrafoveal region, possible association between poor visual acuity and degree of ellipsoid zone disruption and decrease in central foveal thickness over time in this group. Furthermore, they illustrates that the pattern of XLRS in adults is already present in very young children, and unlike in older children and adults, those presenting with earlier disease may have a more aggressive course. Further studies in this early age group may provide more insights into treatment and prevention of progressive visual impairment in children with XLRS. This study helps with diagnosis and prognosis of XLRS in younger children.

VISUAL AND ANATOMIC OUTCOMES OF PEDIATRIC ENDOSCOPIC VITRECTOMY IN 326 CASES
Nagiel A, Yang U, Reid MW, Anulao KJ, Say EAT, Wong SC, Lee TC.

Retina. 2020 Nov;40(11):2083-2090.

This retrospective interventional case series aimed to report on the indications, outcomes, and complications of endoscopic vitrectomy in a large cohort of pediatric vitreoretinal patients.
The study consisted of 244 eyes of 211 patients aged 18 years or younger undergoing a total of 326 endoscopic vitrectomies from 2008 to 2017. A 23-gauge vitrectomy was performed with use of a 19-gauge endoscope. Two hundred and eleven patients with a mean age of 7.5 years (range: 0–18 years) and median follow-up since last surgery of 28 months (range: 3 months–8.7 years) were included. The most common indication for endoscopic vitrectomy was retinal detachment (234/326; 72%) with proliferative vitreoretinopathy (162/234; 69%). Other diagnoses included trauma (25%), retinopathy of prematurity (15%), and glaucoma (9%). Twenty-five percent of surgeries (80/326) were performed on eyes with significant corneal opacities. Retinal reattachment was achieved in 67% of eyes with retinal detachment (119/ 178). Visual acuity improved in 26% of retinal detachment eyes versus 53% of nonretinal detachment eyes (P = 0.005). Surgical complications included band keratopathy (15%), hypotony (8%), cataract (7%), and elevated intraocular pressure (3%). In this large series of pediatric endoscopic vitreoretinal surgeries, anatomic outcomes and complication rates were comparable with previous studies. The study provides data to help guide risk/benefit analysis for children requiring endoscopic surgery.

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY IN PATIENTS WITH RETINITIS PIGMENTOSA–ASSOCIATED CYSTOID MACULAR EDEMA
Yeo JH, Kim YJ, Yoon YH.
Retina. 2020 Dec;40(12):2385-2395.

The study aimed to investigate the microstructure of cystoid macular edema (CME) in retinitis pigmentosa (RP) and the associated vascular changes using optical coherence tomography (OCT) angiography. In this retrospective study, we included 42 eyes of 21 patients with RP and age-similar normally sighted controls who underwent both OCT and optical coherence tomography angiography. Using OCT, spatial distribution of CME and the retinal layer, which CME located, was examined. Optical coherence tomography angiography images of the superficial capillary plexus and deep capillary plexus were obtained. Foveal and parafoveal flow densities in each layer and foveal avascular zone area were measured. Of the 42 eyes with RP, 32 had CME. All CMEs were located in the inner nuclear layer and limited to the parafovea. The outer nuclear layer/ganglion cell layer was involved in 12 eyes (37.5%). Compared with RP without CME, RP with CME (RP-CME) did not show significant differences in flow density or extent of vascular disruption within the superficial capillary plexus, deep capillary plexus, or foveal avascular zone areas. RP-CME was mostly located in the inner nuclear layer of the parafoveal macula, without vascular disruption in optical coherence tomography angiography. Our findings may support the hypothesis that the pathogenesis of RP with CME differs from retinal vascular CME triggered by compromised deep capillary plexus. The study sheds light on variations in pathology associated with RP.

OPTICAL COHERENCE TOMOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY PARAMETERS IN PATIENTS WITH PHACOMATOSIS
Marta A, Malheiro L, Coelho J, Poças J, Gonçalves N, Sousa P, Figueiredo A, Araújo M, Maia S, Miranda V, Parreira R, Menéres P.
Retina. 2021 Feb 1;41(2):366-372.

The case- control observational study aimed to compare the retinal vasculature characteristics between eyes of patients with and without phacomatosis.
The retinal vasculature was evaluated by optical coherence tomography and optical coherence tomography angiography of the macula and disk. The study included 80 eyes. Neurofibromatosis Type 1 patients presented with a higher central macular thickness (P = 0.007), a lower optical disk nervous fiber layer (P = 0.006), a lower perimeter, area, and circularity of the foveal avascular zone (P , 0.05), a higher vascular density of macular avascular layer (AMVD) (P = 0.004), and a lower papillary vascular density of

superficial capillary plexus (SPVD) (P = 0.048). Patients with tuberous sclerosis presented with an increase in central macular thickness (P = 0.024) and in vascular densities (P , 0.05) [except for macular vascular density of deep capillary plexus (PMVD), AMVD, and SPVD]. Patients with Sturge–Weber syndrome showed a decrease in optical disk nervous fiber layer (P , 0.001), subfoveal choroid thickness (P = 0.011), macular vascular density of superficial capillary plexus (SMVD) (P = 0.036), and SPVD (P , 0.001). Phacomatosis patients showed statistically significant differences of retinal vasculature characteristics, compared to eyes without pathology. Further studies are needed to determine when and if these parameters change with the course of the disease and if they can be used as biomarkers for disease severity or progression. This is an interesting study looking to further our knowledge of phacomatoses characteristics.

Intravitreal ranibizumab treatment for advanced familial exudative vitreoretinopathy with high vascular activity
Lyu, Jiao MD; PhD; Zhang, Qi MD; Xu, Yu MD; PhD; Zhang, Xiang MD; Fei, Ping MD; PhD; Zhao, Peiquan MD; PhD
Retina. 2021 Jan 20. Volume Publish Ahead of Print

The retrospective interventional case study demonstrated the efficacy of intravitreal injection of ranibizumab for advanced familial exudative vitreoretinopathy with high vascular activity, in patients with varying clinical and genetic backgrounds. The study included 28 eyes (20 patients) that had IVR in combination or not with other treatment, for stage 3 to 5 FEVR with active fibrovascular proliferation (FP) and prominent subretinal exudation. Outcome measures were fundus featuresafter treatment, associated clinical variables and genetic mutations. The age of patients at the first IVR ranged from 0.2-36 months. An average of 1.3 IVR injections per eye were given. FEVR regressed in 16 (57%) eyes and progressed in 12 eyes (43%) after IVR. Laser and/or vitrectomy was performed on 13 eyes. The retina was reattached in 22 eyes (78%) after a 24 to 58 months follow-up. Clinical variables associated with progression after IVR were preexisting FP over one quadrant, and persistent vascular activity after the initial injection ($P < 0.05$). FEVR-causative genetic mutations in 11 patients were related to variable response to IVR treatment. IVR treatment may effectively regress advanced FEVR with high vascular activity in selected cases. Different treatment outcomes may be relevant to variable presentation and genetic heterogeneity of FEVR.

Unilateral ischemic retinopathy following traumatic intubation mimicking retinopathy of prematurity in a preterm newborn.
Theuriau A, Bremond-Gignac D, Daruich A.
J AAPOS. 2020 Oct;24(5):321-323.

A case report: A preterm child, born at 24 weeks' postmenstrual age (PMA), suffered a traumatic nasotracheal intubation at birth, with exteriorization of the tube through the right orbit. Delayed routine screening for retinopathy of prematurity (ROP) at 34 weeks' PMA revealed a right ischemic retinopathy. Right eye fundus examination at 39 weeks' PMA showed a neovascularized ridge delimiting the vascular retina from an avascular zone over 360°, with localized fibrosis and traction in the right eye, mimicking a zone II stage 3-4 ROP. The left fundus was normal. We suggest that the traumatic ocular contusion stunned the physiological vascularization process of the premature eye leading to permanent retinal sequalae.

Pediatric diabetic retinopathy telescreening
Strul S, Zheng Y, Gangaputra S, Datye K, Chen Q, Maynard L, Pittel E, Russell W, and Donahue S.
J AAPOS. 2020 Feb; 24:10.e1-5.

This is a retrospective study reviewing medical records of a telemedicine program at tertiary, academic medical center over 17 months. Patients visiting a pediatric endocrinology clinic who met guidelines underwent telescreening for pediatric pediatric diabetic retinopathy (DR) and risk factors for DR were

evaluated. Fundus photos of 852 patients age 10-23 were reviewed. 51 (6%) had DR. Older age, longer diabetes duration (*P*=0.003), type 1 diabetes, and higher average glycated hemoglobin (HbA1c) from the year prior to the photography (P=0.02) was associated with increased risk for DR. The duration and higher HbA1C were significant after adjusting for sex, race and age. Limitations of the study are the small sample size and lack of follow-up eye examinations. This study may encourage telescreening for DR in those with risk factors of type 1 diabetes of long duration or high HbA1c.

Effect of EnChroma glasses on color vision screening using Ishihara and Farnsworth D-15 color vision tests.
Varikuti VNV, Zhang C, Clair B, Reynolds AL.
J AAPOS. 2020 Jun;24(3):157.e1-157.e5.

There is no cure for color vision deficiency, but recently, the EnChroma filter and other iron-based filters have been designed to enhance color discrimination. This was a retrospective review of 19 patients with color vision deficiency who underwent color vision testing with Ishihara and Farnsworth D-15 tests with and without the EnChroma glasses. The authors found that the number of errors decreased significantly with the use of EnChroma glasses, though only for deutans on Ishihara testing. Number of correct Ishihara responses increased from 3.05 to 3.79 without and with the EnChroma glasses. The authors conclude that in this small group of patients with color vision deficiency, EnChroma glasses decreased errors and increased number of correct answers on formal color vision testing. While this was statistically significant, the small differences may not be clinically significant. Additionally, neither testers nor participants were masked to filter use, which could confound results.

Subclinical retinal microvascular alterations assessed by optical coherence tomography angiography in children with systemic hypertension.
Dereli Can G, Korkmaz MF, Can ME.
J AAPOS. 2020 Jun;24(3):147.e1-147.e6.

This is a prospective, cross-sectional, case-control comparative study from January to June 2019 at one institution in 40 eyes of 20 children from 10-18 years old with a diagnosis of primary hypertension (PH). The referral to the ophthalmology clinic was from the pediatric clinic of the same institution. Of note, the participants with PH met the criteria of the NHBPEP Working Group Report. Hypertension was defined as systolic and/or diastolic BP above the 95% for age, sex, height as measured on three separate occasions. None of the children were receiving treatment at the time of this study. 40 eyes of 20 age and sex-matched healthy pediatric patients who presented to the ophthalmology clinic for routine eye exams were assigned to the control group. In addtion to a full ophthalmic exam, all participants had OCT-A imaging with SS-ADA technology. Participants with PH had mean age of 15.2 years, SD 1.5 years and healthy control had mean age of 14.4 years, SD 2.8 years. The anterior segment exam was similar in both groups as was the mean refractive error, IOP, and BCVA. Results of the OCT-A showed a mean FAZ are 0.25mm2 in the PH patients and 0.25mm2 in control group (P=0.752). There was no statistical signficance in the superficial retinal capillary plexus (SCP) measurements for the OCT-A between the 2 groups. However, the deep retinal capillary plexus (DCP) measurements in the para- and perifoveal measurements were lower in PH participants compared to control group. Limitations include that it is a small study at one institution. Another limitation the authors address is that artifact on DCP and the authors used the 3D artifact removal algorithm in the OCT-A software. In summary, the authors note that although there is no clinical retinopathy in children with PH, use of the OCT-A reveals sub-threshold deep microvascular changes in the DCP in children with PH as compared to controls.

Clinical characteristics and surgical outcome of pediatric and early adulthood retinal detachment.
Eibenberger K, Sacu S, Rezar-Dreindl S, Schmidt-Erfurth U, Stifter E, Georgopoulos M.
Eur J Ophthalmol. 2020, E publication ahead of print. March 19.

The causes of retinal detachments (RD) in children include rhegmatogenous, tractive and exudative, whereas in adult it is primarily rhegmatogenous. The authors investigated and copared the various causes, clinical and anatomic characteristics, surgical approaches, and outcomes of RD in childhood and in early adulthood in this retrospective clinical analysis. The reviewed patients with RD in a preschool group (n=4, ages 0-6 years), the pediatric group (n=19, 7-16 years), and early adulthood group (n=13, 17-26 years). As expected, all causes of RD existed in the pediatric group, but only RRD in the early adult group. In both groups, the main intervention was PPV. The type of intraocular tamponade did vary between groups with silicone oil used mainly in the pediatric group, whereas the early adult group either had no tamponade or gas tamponade. This likely due to the head positioning and cooperation of a young adult group. Final attachment rate was similar between both groups. Better functional outcomes were observed in cases in the early adulthood group compared to the younger children group, however they did not compare this since formal vision is difficult to obtain in younger children. In conclusion, this studies showed similar results between the two groups. Larger sample size would make this a stronger study.

Multimodal evaluation of central and peripheral alterations in Stargardt disease: a pilot study.
Arrigo A, Grazioli A, Romano F, Aragona E, Marchese A, Bordato A, Di Nunzio C, Sperti A, Bandello F, Parodi MB.
British Journal of Ophthalmology. 2020 Sep 1;104(9):1234-8.

This study aims was to correlate peripheral ultrawide field (UWF) involvement with macular alterations, as assessed by structural optical coherence tomography (OCT) and OCT angiography (OCTA), in order to identify potentially different phenotypes in pts with STGD. Seventy STGD eyes (19 male; mean age 41.3±13.2 years) and 70 healthy eyes (35 male; 50%; mean age 41.2±9.8 years) were included in the analyses. Mean best-corrected visual acuity was 0.60±0.45 LogMAR for the STGD group and 0.0±0.0 LogMAR for controls ($p<0.01$). All clinical and imaging findings proved to be statistically worse in patients with STGD than in the control subjects ($p<0.01$). UWF types were distributed as follows: type I (49%), type II (34%), type III (17%). Type III patients proved to be significantly worse in terms of visual function and OCT and OCTA imaging parameters. The UWF autofluorescence performed in the present study suggests that there exist three different STGD phenotypes.

Longitudinal study of RPE65-associated inherited retinal degenerations.
Pierrache LH, Ghafaryasl B, Khan MI, Yzer S, van Genderen MM, Schuil J, Boonstra FN, Pott JW, de Faber JT, Tjon-Fo-Sang MJ, Vermeer KA.
Retina. 2020 Sep 1;40(9):1812-28.

Forty-five patients with IRD from 33 families with biallelic RPE65 mutations, 28 stemming from a genetic isolate. We collected retrospective data from medical charts. Coexisting variants in 108 IRD-associated genes were identified with Molecular Inversion Probe analysis. Most patients were diagnosed within the first years of life. Daytime visual function ranged from near-normal to blindness in the first four decades and met WHO criteria for blindness for visual acuity and visual field in the fifth decade. p.(Thr368His) was the most common variant (54%). Intrafamilial variability and interfamilial variability in disease severity and progression were observed. Molecular Inversion Probe analysis confirmed all RPE65 variants and identified one additional variant in LRAT and one in EYS in two separate patients. All patients with RPE65-associated IRDs developed symptoms within the first year of life. Visual function in childhood and adolescence varied but deteriorated inevitably toward blindness after age 40. In this study, genotype was not predictive of clinical course. The variance in severity of disease could not be explained by double hits in other IRD genes.

Recent developments in pediatric retina.
Cai S, Therattil A, Vajzovic L.
Curr Opin Ophthalmol. 2020 May;31(3):155-160.

The authors review current updates in the management of pediatric retinal disease which focuses mostly on advances in imaging and gene therapy. The paper discusses the use of OCT both of the macula and periphery in the diagnosis and management of ROP. The use of OCT imaging in patients with Coats' disease may prove useful in detecting features difficult to detect by fundus examination and help provide more objective and quantitative tracking of disease progression. The success of RPE65 associated LCA gene therapy and advances in subretinal injection techniques, as well as the increased research and development of gene therapy for other inherited retinal diseases will lead to further advancement for children with previously untreatable diseases. In the realm of ROP there have been advances in the use of machine learning and the ability to develop severity scores from fundus photographs that will provide further help in the screening and monitoring of ROP. The use of anti-VEGF agents may be superior to outcomes for laser therapy but dosing and monitoring studies are still ongoing to optimize treatment for patients and to assess for late recurrence. Lastly, improving surgical technology, as well as the integration of handheld OCT and other imaging modalities in the OR may be helpful in pediatric retinal surgery becoming safer and more effective.

Gene therapy beyond luxturna: a new horizon of the treatment for inherited retinal disease.
Prado DA, Acosta-Acero M, Maldonado RS.
Curr Opin Ophthalmol. 2020 May;31(3):147-154

The goal of gene therapy is to treat genetic disease by introducing corrective, healthy, genetic material into cells to either produce a functional protein or compensate for a specific diseased gene. There are multiple vectors under investigation with most being adenovirus-based vectors. Adenovirus, are DNA vectors with very large transgene capacity but that cause strong immune responses, adeno-associated virus (AAV) which is the predominant vector due to its tolerability and gene expression longevity, and lentiviruses. AAvs are nonpathogenic and non integrating DNA vectors with high retinal affinity and low immunogenicity but are limited by small gene carrying capacity. Lentiviruses are RNA vectors that have high gene transport capacity but may theoretically increase the risk of cancer mutagenesis. Lastly, dual AAVs are another emerging alternative that can accommodate large transgenes by splitting the material into two components which later become reconstituted when they are delivered to the target cells. These vehicles can be delivered by intravitreal injection to target the inner retina, while subretinal injection is preferred for the outer retina and RPE. Intravitreal injection has the advantage of greater ease of administration but less success due to the barriers posed by the vitreous cavity and ILM. The subretinal injection requires a PPV and because it provides direct access to the RPE is the most popular gene delivery technique for inherited retinal dystrophies (IRDs). There are different applications and targets of gene therapy. One is gene replacement which targets biallelic loss-of-function recessive disease and is most advantageous in early disease. In diseases with gain-of-function mutations a combined approach is warranted utilizing gene suppression and replacement. Gene editing has recently become a focus, such as CRISPR technology which can cut and remove the target cell's genome and also add the desired functional gene. Lastly, optogenetics, which can be used in diseases with significant photoreceptor loss aims to convert remaining inner retinal cells into photosensitive cells to serve as artificial photoreceptors. This gene independent approach is not specific to a genetic mutation and may potentially be used for a wider variety of disease. The limitations of all of these therapies are the safety risks which are, the inability to halt treatment effects once the treatment is delivered, it requires a surgical procedure and relies on complex skills and special training which limits the number of providers who can administer these therapies. The authors provide a comprehensive review of the modalities, delivery techniques and possibilities and applications for novel approaches to the burgeoning field of gene therapy.

Macular dystrophies: clinical and imaging features, molecular genetics and therapeutic options.
Rahman N, Georgiou M, Khan KN, Michaelides M.
British Journal of Ophthalmology. 2020 Apr 1;104(4):451-60.

Macular dystrophies (MDs) consist of a heterogeneous group of disorders that are characterised by bilateral symmetrical central visual loss. Advances in genetic testing over the last decade have led to improved knowledge of the underlying molecular basis. The developments in high-resolution multimodal

retinal imaging have also transformed our ability to make accurate and more timely diagnoses and more sensitive quantitative assessment of disease progression and allowed the design of optimised clinical trial endpoints for novel therapeutic interventions. The aim of this review was to provide an update on MDs, including Stargardt disease, Best disease, X-linked retinoschisis, pattern dystrophy, Sorsby fundus dystrophy and autosomal dominant drusen. It highlights the range of innovations in retinal imaging, genotype–phenotype and structure–function associations, animal models of disease and the multiple treatment strategies that are currently in clinical trial or planned in the near future, which are anticipated to lead to significant changes in the management of patients with MDs.

Clinical implications and cost of electroretinography screening for vigabatrin toxicity
Jastrzembski B, Locke J, Wan M
Can J Ophthalmol. 2020 Jun;55:e98-e100

Although Vigabatrin has been reported to cause permanent peripheral visual field loss due to retinal toxicity, monitoring visual function of children on vigabatrin is challenging. Some centers use electroretinography (ERG) to monitor for toxicity, but this is not in widespread use and the utility of this method has not been well studied. The authors of this short report performed a retrospective case series of children with infantile spams screening with ERG. Baseline ERG was performed within a few weeks of starting vigabatrin and then every 4 months on treatment. Dilated exam was also performed. 67 patients were screened over 3 years for a total of 147 ERGS (media 2 per patient). 3 patients had concern for toxicity, 2 based on findings on ERG and 1 due to parental concern. In once case, the concern of decreased flicker response was non consistent on consecutive ERG's. In another the medication was already weaned off by the time of second ERG. The patient with clinical concern did not show abnormalities on ERG. Overall none of the 67 patients had definitive evidence of toxicity on testing, and for the 3 patients who had suspicions of toxicity, the screening did not change clinical management. Average cost for ERG was $599 in outpatient setting and $1466 for inpatient setting, with average of $1716 per patient. The authors conclude that routine ERG screening for vigabatrin toxicity may not be justified given lack of influence on clinical decision making, risks of sedation, and costs.

HYPERREFLECTIVE FOCI AS A PATHOGENETIC BIOMARKER IN CHOROIDEREMIA ROMANO F, ARRIGO A, MACLAREN R, ISSA P, BIRTEL J, BANDELLO F, PARODI M.
RETINA Aug 2020; 40:1634–1640.

The goal was to assess hyperreflective foci (HF) number and distribution in choroideremia (CHM) using spectral domain optical coherence tomography. This was an observational, cross-sectional case series. Consecutive patients and matched controls (20 eyes each) underwent best-corrected visual acuity measurement, fundoscopy, blue-light autofluorescence (BL-FAF) and spectral domain optical coherence tomography. Hyperreflective foci were assessed on a horizontal spectral domain optical coherence tomography scan, in the 500-mm area centered on the umbo, and in the 500- mm-wide areas internal (preserved border) and external (pathologic border) to the chorioretinal atrophy of CHM patients, and in the parafovea of controls. Hyperreflective foci were subclassified as retinal or choroidal. The spared central islet was measured on BL-FAF. Primary outcome was HF quantification in CHM. Secondary outcomes included their relationships with atrophy extent. Choroideremia eyes disclosed a significantly higher HF number across the pathologic border and in the fovea when compared with controls; in particular, these HF were primarily located in the choroid (59–87%). Moreover, choroidal HF in the pathologic border inversely correlated with the area of the preserved central islet. Hyperreflective foci might turn out to be a potential biomarker of CHM activity or severity. In this regard, we hypothesize that HF may be related to macrophages activation or progressive retinal pigment epithelium degeneration.

ETIOLOGY AND CLINICAL CHARACTERISTICS OF MACULAR EDEMA IN PATIENTS WITH FAMILIAL EXUDATIVE VITREORETINOPATHY
RAO P, LERTJIRACHAI I, YONEKAWA Y, HASBROOK M, THOMAS B, WOOD E, MEHTA N, MANE G, DRENSER K, TRESE M, CAPONE A.

RETINA Jul 2020; 40:1367–1373.

The goal of this paper was to describe the etiology and clinical characteristics of macular edema (ME) in patients with familial exudative vitreoretinopathy. This was an observational, retrospective case series of 30 patients (34 eyes) with ME and familial exudative vitreoretinopathy who underwent spectral-domain optical coherence tomography imaging between 2009 and 2016. Baseline and follow-up optical coherence tomographies were correlated with color fundus photography and fluorescein angiography. The average age was 20.6 years (6.6–68.7). Eighteen eyes exhibited cystoid ME (52.9%), 14 noncystoid ME (41.2%), and 2 eyes (5.9%) with both. Macular edema was foveal in 52.9% (n = 18). Eighteen of 24 eyes (64.3%) with an available fluorescein angiography showed leakage from ME. The most common structural feature was posterior hyaloidal organization/ contraction (n = 15). Sixteen eyes were treated with topical or intravitreal steroids (n = 6), intravitreal anti–vascular endothelial growth factor (n = 3), or pars plana vitrectomy with membrane stripping (n = 7). There was no difference between mean preoperative and postoperative LogMAR visual acuity (0.63 [20/85] vs. 0.87 [20/148], P = 0.35) after vitrectomy despite a statistical improvement in the mean central foveal thickness (596 mm3 vs. 303 mm3, P = 0.04). Macular edema in familial exudative vitreoretinopathy occurs most commonly because of traction. Vitrectomy is effective for relieving tractional forces with anatomical improvement.

MACULAR CAPILLARY DROPOUT IN FAMILIAL EXUDATIVE VITREORETINOPATHY AND ITS RELATIONSHIP WITH VISUAL ACUITY AND DISEASE PROGRESSION
ZHANG J, JIANG C, RUAN L, YANG Q, CHANG Q, HUANG X
RETINA Jun 2020; 40:1140–1147.

The paper aimed to quantitatively detect the macular microvascular alterations of eyes with familial exudative vitreoretinopathy (FEVR) and analyze their associations with the severity and visual acuity of FEVR. This was a case–control study comprising 62 patients (62 eyes) with FEVR and 21 agematched healthy individuals (21 eyes) with normal vision was conducted. Parafoveal vascular density (VD) was measured using optical coherence tomography angiography. Visual acuity, intraocular pressure, and axial length were recorded. Parafoveal VD of eyes with FEVR was lower than that of the controls (P , 0.05). Parafoveal VD decreased with increasing FEVR stages (P , 0.05), and decreased VD in superficial capillary plexus (SCP) was independently correlated with FEVR severity (odds ratio: 1.558, P , 0.001) after controlling for other confounding variables. Vascular density in eyes with FEVR and decreased visual acuity was lower than eyes with FEVR and normal visual acuity (SCP, P , 0.001; deep capillary plexus, P = 0.001). Moreover, VD loss had independent association with visual loss in FEVR (SCP: odds ratio: 0.817, P = 0.019; deep capillary plexus: odds ratio: 0.763, P = 0.016). There may be parafoveal microvascular defects in FEVR and that VD loss in SCP may be correlated with the severity of FEVR. In addition, VD loss in SCP and deep capillary plexus may be associated with the visual loss in FEVR.

“There are Hills And Valleys”: Experience of Parenting a Son With X-Linked Retinoschisis
Turriff A, Nolen R, D’Amanda C, et al.
Am J Ophthalmol. April 2020; 212:98-104.

The goal of this study of parents of 13 families with sons with X-Linked Retinoschisis (XLRS) was to better understand the experiences of these parents. Data was collected via qualitative interview and quantitative survey of 11 mothers and 8 fathers of 13 families who were seen at the National Eye Institute over a 2-year period. The authors found that optimism, anxiety and personality traits were in the normative ranges. The initial diagnosis involved shock, grief, and devastation. Maternal guilt was also described as was fear of retinal detachment. Continued stress for these parents was around participation in sports and driving. Most parents also had perceived benefits such as gratitude and family cohesion. The conclusion from the authors was that most parents found a child’s diagnosis of XLRS as a challenge, but one that could be overcome. The largest limitation of this study was that it was a small, all white non-Hispanic cohort of patients that traveled to the NIH to enroll in a study and is unlikely generalizable to the general population.

Prospective Cohort Study of Childhood-Onset Stargardt Disease: Fundus Autofluorescence Imaging, Progression, Comparison with Adult-Onset Disease, and Disease Symmetry.
Georgiu M, Kane T, Tanna P, et al
Am J Ophthalmol. 2020 Mar; 211:159-175.

The purpose of this prospective cohort study was to determine the reliability and repeatability of a quantitative analysis of areas of decreased autofluorescence (DAF) in children with Stargardt disease. Additionally, the authors aimed to understand the phenotypic and genotypic correlations, the symmetry between eyes and the variability between families. The study was performed at one institution and patients were considered if they had annual visits for over 6 years. The authors longitudinally analyzed the fundus autofluorescence imaging of genetically confirmed patients and used semiautomatic measurements of the area of DAF to calculate the rate of progression. They also looked at the ERG at baseline, age of onset, acuity and intrafamilial variability. They examined 90 patients and found that the DAF quantification was reliable and symmetric between eyes. They found the rate of progression fastest for those with childhood onset Stargardt's disease that presented in childhood, and slowest in adults who weren't diagnosed until adulthood. The intrafamilial variability was limited and the authors concluded that DAF may be a solid structural endpoint to be considered in future clinical trials. This paper is important because it suggests that DAF could serve as an objective endpoint for clinical studies since it is a reliable and repeatable test. Additionally, the symmetry between eyes makes this a good test to use to follow in any studies where one of the eyes might be treated.

FLUORESCEIN ANGIOGRAPHY FINDINGS IN UNILATERAL PERSISTENT FETAL VASCULATURE
SHEN J, LIU L, WANG N, HWANG Y, CHEN K, CHAO A, LAI C, CHEN T, WU W
RETINA Mar 2020; 40:572–580.

This study aims to examine retinal vascular findings for affected eyes and contralateral eyes as well in typical cases of unilateral persistent fetal vasculature. The authors retrospectively reviewed all patients evaluated at Chang Gung Memorial Hospital, Linkou, for unilateral persistent fetal vasculature between January 2008 and July 2017. All patients underwent fluorescein angiography (FA) examination under general anesthesia. FA was performed using RetCam 3 (Clarity Medical Systems, Inc, Pleasanton, CA). Ten patients (eight male and two female) were identified as having adequate clinical data for the final analysis. The mean age at diagnosis was 13.7 ± 17.2 months (range 1–58). The mean axial length was shorter in the affected eyes as compared to the fellow eyes (17.27 ± 2.8 vs. 20.2 ± 1.7 mm; P = 0.024). In the affected eyes, nine cases (90.0%) showed a concomitant retrolental stalk, avascular peripheral retina, regional capillary dropout, and absence of foveal avascular zone. Hyperfluorescent stalk was seen in seven cases (70.0%). Four eyes (40.0%) showed leaking vessels. Terminal supernumerary branching was seen in two cases (20.0%). Popcorn hyperfluorescence was noted in one case (10.0%). In the fellow eyes, peripheral avascular zone was noted in nine eyes (90.0%), of which six (60.0%) had peripheral zones greater than two-disk diameters. Seven eyes (70.0%) presented with regional capillary dropout and abnormal choroidal filling. Three eyes (30.0%) had abnormal vessel straightening. Aberrant circumferential vessels and leaking spots were seen in two eyes (20.0%). Regional dilation of disk vessels, peripheral vessel dilation, and terminal bulbing were noted in one eye (10.0%). The mean best-corrected visual acuity of the fellow eyes was 20/39 (0.29 in logarithm of the minimum angle of resolution). Retinal vascular abnormalities in the affected eyes and fundoscopically normal fellow eyes of unilateral persistent fetal vasculature patients were found in 100% and 90.0% of patients, respectively. Fellow eyes had some subtle abnormalities that were only revealed through FA. These unilateral persistent fetal vasculature cases were still bilaterally affected.

Phenotypic Spectrum of the Foveal Configuration and Foveal Avascular Zone in Patients With Alport Syndrome.
Hess K, Pfau M, Wintergerst MWM, Loeffler KU, Holz FG, Herrmann P.
Invest Ophthalmol Vis Sci. 2020 Feb 7;61(2):5.

This study investigates characteristics of the foveal pit and the foveal avascular zone (FAZ) in patients with Alport syndrome (AS), a rare monogenetic disease due to mutations in genes encoding for collagen type IV. Twenty-eight eyes of nine patients with AS, and five autosomal-recessive carriers and 15 eyes from 15 age-similar healthy control subjects were examined using optical coherence tomography (OCT) and OCT-angiography (OCT-A). Foveal configuration and FAZ measures including the FAZ area, circularity, and vessel density in the central 1° and 3° were correlated. Foveal hypoplasia was found in 10 eyes from seven patients with either genotype. In contrast, a staircase foveopathy was found in seven eyes of four X-linked AS patients. The average FAZ area did not differ significantly between AS patients and control subjects (mean ± SD 0.24 ± 0.24 mm2 vs. 0.21 ± 0.09 mm2; P = 0.64). Five eyes showed absence or severe anomalies of the FAZ with crossing macular capillaries that was linked to the degree of foveal hypoplasia on OCT images leading to a significant inverse correlation of FAZ area and foveal thickness (r = -0.88; P < 0.001). In contrary, female patients with X-linked mutations exhibited a significantly greater FAZ area (0.48 ± 0.30 mm2 vs. 0.21 ± 0.09 mm2; P = 0.007), in line with OCT findings of a staircase foveopathy.
The foveal phenotypic spectrum in AS ranges from foveal hypoplasia and absence of a FAZ to staircase foveopathy with an enlarged FAZ. Because the development of the FAZ and foveal pit are closely related, these findings suggest an important role for collagen type IV in foveal development and maturation.

Etiologies, Characteristics, and Management of Pediatric Macular Hole.
Liu J, Peng J, Zhang Q, Ma M, Zhang H, Zhao P.
Am J Ophthal. 2020 Feb; 210: 174-183.

The authors present a retrospective case series regarding the etiologies and prognosis of macular hole (MH) in children aged less than 16 years old. The data was collected from 2013 to 2019 in a tertiary care center in China. Forty eyes of 40 patients with a mean age of 8.3 years old with nearly all male patients. The major cause of MH in this case series was trauma (72.5%). All of the traumatic MH achieved hole closure. Spontaneous closure was noted in 10 eyes (25%) for an average of 2 months after the trauma. Regression analysis indicated that a smaller MH (P= 0.006) was more likely to spontaneously close. The most significant risk factor for poor visual outcome was the presence of macular lesions (P = 0.001). The authors report in this case series of 40 children the most common etiology as blunt trauma. The limitations of this study include the retrospective nature, unequal representation of male and female children, and evaluation of 40 eyes.

19. RETINOBLASTOMA / INTRAOCULAR TUMORS

TOXICITY AND EFFICACY OF INTRAVITREAL MELPHALAN FOR RETINOBLASTOMA: 25 µg Versus 30 µg.
Liao A, Hsieh T, Francis JH, Lavery JA, Mauguen A, Brodie SE, Abramson DH.
Retina. 2021 Jan 1;41(1):208-212.

The study aimed to compare retinal toxicity as measured by electroretinogram, ocular, and patient survival in retinoblastoma treated with intravitreal melphalan at two concentrations (25 vs. 30 mg). Single-center, retrospective analysis of retinoblastoma eyes receiving 25-mg or 30-mg intravitreal melphalan from September 2012 to January 2019. Ocular toxicity was measured by electroretinogram of evaluable injections in 449 injections in 136 eyes. A repeated-measures linear mixed model with a random intercept and slope was applied to account for repeated measures for each eye. Average decline in electroretinogram after each additional injection was 24.9 mV (95% confidence interval 26.3 to 23.4); electroretinogram declined by 24.6 mV (95% confidence interval 27.0 to 22.2) after 25-mg injections and 25.2 mV (95% confidence interval 26.6 to 23.8) after 30-mg injections (P = 0.66). Injection at a new clock site hour was associated with a 23.91-mV lower average (95% confidence interval 27.8 to 20.04). Electroretinogram-measured toxicity in retinoblastoma eyes treated with intravitreal injections was not found to be different across 25-mg and 30-mg injections. There were no cases of extraocular extension or metastatic deaths in our patient population. Study showed that a higher dose doesn't cause more retinal toxicity.

A Multicenter, International Collaborative Study for American Joint Committee on Cancer Staging of Retinoblastoma: Part I: Metastasis-Associated Mortality.
Tomar AS, Finger PT, Gallie B, Mallipatna A, Kivelä TT, Zhang C, Zhao J, Wilson MW, Kim J, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Yousef YA, Nummi K, Ushakova TL, Yugay OV, Polyakov VG, Ramirez-Ortiz MA, Esparza-Aguiar E, Chantada G, Schaiquevich P, Fandino A, Yam JC, Lau WW, Lam CP, Sharwood P, Moorthy S, Long QB, Essuman VA, Renner LA, Català J, Correa-Llano G; American Joint Committee on Cancer Ophthalmic Oncology Task Force.
Ophthalmology. 2020 Dec;127(12):1719-1732.

This study looked at the reliability of the latest edition of the American Joint Committee on Cancer Staging Manual in estimating metastatic and mortality rates in children with retinoblastoma. Retrospective data was accumulated in 2190 children from 18 oncology centers in 13 countries. Clinical and pathologic criteria were evaluated. The overall survival rate was high (>95%) until third level of clinical tumor category was reached, when the survival rate dropped to 89%, and further dropped to 45% with the fourth level of clinical tumor category. Likewise, the risk of metastasis increased with increasing clinical tumor categories. Although the methodology was confirmed to show a stepwise increase in metastasis and mortality with increasing clinical grading, significant compression of the mortality rates in the lower categories of clinical tumor categories limits the effectiveness of those categories in differentiating between survival rates. A simpler classification system might reliably identify good, intermediate, and worse prognoses without all of the various sub-classifications.

A Multicenter, International Collaborative Study for American Joint Committee on Cancer Staging of Retinoblastoma: Part II: Treatment Success and Globe Salvage.
Tomar AS, Finger PT, Gallie B, Mallipatna A, Kivelä TT, Zhang C, Zhao J, Wilson MW, Brenna RC, Burges M, Kim J, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Yousef YA, Nummi K, Ushakova TL, Yugay OV, Polyakov VG, Ramirez-Ortiz MA, Esparza-Aguiar E, Chantada G, Schaiquevich P, Fandino A, Yam JC, Lau WW, Lam CP, Sharwood P, Moorthy S, Long QB, Essuman VA, Renner LA,

Semenova E, Català J, Correa-Llano G, Carreras E; American Joint Committee on Cancer Ophthalmic Oncology Task Force.
Ophthalmology. 2020 Dec;127(12):1733-1746.

This study looked at the reliability of the latest edition of the American Joint Committee on Cancer Staging Manual in estimating treatment success and globe salvage in children with retinoblastoma. Retrospective data was accumulated in 2097 children from 18 oncology centers in 13 countries. Clinical and pathologic criteria were evaluated. As predicted, clinical tumor category level 1 had a high (>88%) rate of globe salvage, with progressively worse outcomes for clinical tumor category level 2 (>57%) and clinical tumor category level 3 (>25%). The risk of treatment, likewise, was significantly greater with increasing clinical tumor category level. Among the oncology centers, however, there was a wide variation in treatment modalities used – enucleation, systemic chemotherapy with focal consolidation, plaque brachytherapy, intra-arterial chemotherapy, and external beam radiation therapy. The existence of so many treatment modalities resulting in similar rates of success suggest that the tumor characteristics, not the treatment modality, might have the most influence on treatment success. Regardless, the data showed that the classification system accurately stratified tumor severity and thus was validated.

Inflamed nonlimbal scleral dermoid masquerading as nodular scleritis.
Hamid MS, Steen DW, Ormsby AH, Lin X, Le KH.
J AAPOS. 2020 Oct;24(5):319-321.

A 5-year-old boy presented with unilateral, focal superonasal conjunctival injection in the absence of vision changes or trauma. He was treated with a topical steroid for possible phlyctenule or episcleritis, but the lesion progressed to an elevated nodule, raising concern for nodular scleritis with no evidence of posterior involvement. Systemic work-up for underlying inflammatory conditions was unremarkable. There was some improvement in the level of injection with topical steroid, topical fluoroquinolone, and oral nonsteroidal anti-inflammatory drugs, but the nodular lesion persisted. Excisional biopsy revealed an inflamed dermoid cyst in the sub-Tenon's space.

How Telemedicine and Centralized Care Changed the Natural History of Retinoblastoma in a Developing Country: Analysis of 478 Patients
Yacoub A Yousef , Ibrahim Al-Nawaiseh Mustafa Mehyar , Iyad Sultan , Maysa Al-Hussaini , Imad Jaradat , Mona Mohammad, Reem AlJabari, Nakhleh Abu-Yaghi, Carlos Rodriguez-Galindo, Ibrahim Qaddoumi, Matthew Wilson
Ophthalmology. 2021 Jan;128(1):130-137.

This retrospective study conducted at the King Hussein Cancer Centre in Amman, Jordan evaluated 478 patients (813 eyes) managed between 2003 and 2019. The purpose of the study was to compare outcomes for retinoblastoma patients treated after their telemedicine-based salvage program was implemented (2003-2009) versus before (1992-2002). 70% had bilateral disease. Most notably, since the implementation of the telemedicine program which was a collaborative effort amongst pediatric oncologists, ophthalmologists, ocular oncologists, and radiation oncologists, mortality was significantly reduced (38% versus 5%, $P < 0.0001$) and eye salvage rate improved (4% versus 61%, $P < 0.0001$). This significant impact was attributed to the role of twinning which involved a mentor at St. Jude who reviewed all clinical data and proposed treatment plans. Initially, all consults were reviewed by the twinning program, but by 10 years later, only 3% of cases required discussion. Videoconferences and exchange visits were utilized in this program. Fundus drawings were replaced by RetCam II photos and more modalities of treatment became available over the years. This model of twinning via telemedicine may be useful in other diseases in which outcomes vary widely depending on location and access to resources. Impact is immediate instead of patient outcomes paralleling the skills and knowledge of a team who is continuing to learn.

Risk Factors for Tumor Recurrence Following Primary Intravenous Chemotherapy (Chemoreduction) for Retinoblastoma in 869 Eyes of 551 Patients
Lauren A. Dalvin, MD; Zeynep Bas, MD; Sameeksha Tadepalli, MD; Raksha Rao, MD; Sarangdev Vaidya, BA; Richard Pacheco, BA; Carol L. Shields, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):224-234.

The purpose of the retrospective study was to identify risk factors for retinoblastoma recurrence following chemoreduction (six cycle regimen of vincristine, etoposide and carboplatin). There were 869 eyes of 551 patients with retinoblastoma treated with chemoreduction. The minimum follow up for study inclusion was 3 months and 556 eyes met that minimum follow up. Recurrence was defined as recurrent tumor 3 months or more after initial tumor regression from chemoreduction. Among the 556 eyes, there was main solid tumor recurrence (n = 355, 64%), subretinal seed recurrence (n = 244, 44%), vitreous seed recurrence (n = 162, 29%), and/or new tumor (n = 118, 21%) requiring management with focal therapy (transpupillary thermotherapy, cryotherapy) (n = 294, 53%), intra-arterial chemotherapy (n = 125, 22%), intravitreal chemotherapy (n = 36, 6%), plaque radiotherapy (n = 120, 22%), external beam radiotherapy (n = 57, 10%), and/or enucleation (n = 49, 9%). Of all recurrences, 62% were detected by 1 year, 86% by 2 years, 94% by 3 years, 98% by 5 years, 99% by 10 years, and 100% by 15 years. Risk factors for recurrence on multivariate analysis included younger patient age at presentation (odds ratio [OR] = 1.02 [1.00 to 1.04] per 1 month decrease, P = .02), greater International Classification of Retinoblastoma group (OR = 1.24 [1.05 to 1.47] per 1 more advanced group, P = .01), shorter tumor distance to optic disc (OR = 1.11 [1.01 to 1.21] per 1 mm decrease, P = .03), and presence of subretinal seeds (OR = 1.66 [1.09 to 2.53], P = .02). Retinoblastoma recurrence after chemoreduction is usually detected within the first 3 years following treatment, but there are outliers of recurrence as late as 15 years after diagnosis. Younger patients with more advanced, posteriorly located tumors and subretinal seeds at presentation are at increased recurrence risk.

Screening for Pineal Trilateral Retinoblastoma Revisited: A Meta-analysis
Marcus C de Jong PhD, Wijnanda A Kors MD, Annette C Moll MD PhD, Pim de Graaf MD PhD, Jonas A. Castelijns MD PhD, Robin W. Jansen MD, Brenda Gallie MD, Sameh E. Soliman MD, Furqan Shaikh MD, Helen Dimaras PhD, Tero T. Kivela MD.
Ophthalmology. 2020 May; 127(5):601-607.

This meta-analysis aimed to answer two questions including (1) which age are patients with heritable retinoblastoma at risk of pineal trilateral retinoblastoma (TRb) and (2) does pineal TRb develop earlier if diagnosis of retinoblastoma is made at less than or equal to 6 months of age. PubMed and Embase were used to systematically review the literature. Main analyses of the data only included the studies published in 1995 or later when chemotherapy was introduced as part of the routine management for retinoblastoma. After 185 PubMed search results were reviewed, eighteen articles were deemed to meet inclusion criteria. Review of these manuscripts yielded 15 unique patients with TRb which were then added to the 174 patients that were published in an earlier systematic review. Of these patients, 73% had pineal TRb, 22% had suprasellar, paraseallar or ventricular TRb, 2% had both pineal and nonpineal TRb. 3% of the patients had TRb without specified location. 95% (21/22) of asymptomatic patients were diagnosed before 40 months of age. Whether intraocular retinoblastoma was diagnosed at the age of or less than 6 months versus later did not affect the age at which a pineal TRb was diagnosed. One year was the lead time from asymptomatic to symptomatic pineal TRb. Hence, based on these results, neuroimaging every 6 months was recommended by the authors. Limitations of this study include the heterogeneity of the patients in each separate publication and any case not reported in the literature would not be accounted for by this meta-analysis. The authors also mention that false positive diagnoses of pineal TRb cannot be ruled out based on their review of the published cases.

Association Between Genotype and Phenotype in Consecutive Unrelated Individuals With Retinoblastoma.
Salviat F, Gauthier-Villars M, Carton M, Cassoux N, Lumbroso-Le Rouic L, Dehainault C, Levy C, Golmard L, Aerts I, Doz F, Bonnet-Serrano F, Hayek S, Savignoni A, Stoppa-Lyonnet D, Houdayer C.

JAMA Ophthalmol. 2020 Aug 1;138(8):843-850.

This was a single-center retrospective cohort study at Institut Curie of 1404 consecutive unrelated pediatric patients with retinoblastoma (RB) from January 1, 2000 to September 30, 2017. All patients had genotypic analysis of the whole spectrum of *RB1* pathogenic variations and phenotypic description of demographics (age at diagnosis, sex, laterality, and the International Intraocular Retinoblastoma Classification (IIRC) group at diagnosis. The authors sought to further understand genotype-phenotype relationships in patients with RB, since RB is a complex disease and is the most common pediatric intraocular neoplasm. Among the 1404 study patients with RB, 734 (52.3%) were female with a mean age of 20.2 months with SD of 21.2 months. 866 patients (61.7%) were unilateral and 538 patients (38.3%) were bilateral. For this study, the IIRC group were pooled into categories based upon the rate risk of loss of the eye: A, B, C (very low, low, moderate) and D and E (high and very high, respectively). Results indicated that loss of function variants throughout the coding sequence for *RB1* with 259 of 272 (95.2%) somatic pathogenic variants and 537 of 606 (88.6%) germline pathogenic variants (P<0.001) after the exclusion of tumor-specific pathogenic variants. Furthermore, the authors report that germline pathogenic variants which abrogate RB protein expression rather than retain RB protein expression were associated with earlier mean age of diagnosis (12.3 months, SD 11.3 months) among 457 patients versus 16.3 months, SD 13.2 months) among 55 patients with difference of 4 months (P=0.01). This genotypic pathogenic variant finding was also more prevalent with bilateral involvement (84.2% of 452 patients versus 65.2% of 45 patients) and more advanced IIRC grouping (85.3% among 339 patients versus 73.9% among 34 patients). In addition, the authors reported a sex-linked mechanism for nongermline carriers; among the 765 nongermline carriers of an *RB1* pathogenic variant, most were female (419 females [54.8%] versus 346 males [45.2%] P=0.008) and more males had bilateral involvement (23 males [71.4%] versus 12 females [34.3%] P=0.01). In summary, this RB genotype-phenotype study furthers our understanding about RB risk and its relationship with severity of disease and germline pathogenic variant, sex-linked mechanism and nongermline carriers, and RB laterality in males versus females.

20. ORBIT

Reconstruction of the Orbit and Anophthalmic Socket. Using the Dermis Fat Graft: A Major Review
Jovanovic N, Carniciu AL, Russell WW, Jarocki A, Kahana A.
Ophthalmic Plast Reconstr Surg. 2020 Nov/Dec;36(6):529-539.

This was a retrospective review of use of dermis fat graft (DFG) in socket reconstruction and illustrate the technical nuances and outcomes. A literature search of 143 texts was reviewed. A retrospective case series of 34 patients following primary or secondary DFG after enucleation at a single institution (2009–2019) was performed. Variables investigated included age, sex, race, surgical indication, muscle reattachment, complications, motility, eyelid position, prosthesis fit, and need for additional surgery. The history of DFG, use in socket reconstruction, primary and secondary indications, and surgical techniques are described. Thirty-two adults and 2 pediatric cases of DFG were reviewed; 18.75% indications were primary and 81.25% were secondary. Good eyelid position was observed in 83.3% of patients with primary DFG versus 37.5% with secondary DFG ($p = 0.07$). Postoperative complications occurred in 58.8% of patients, were typically mild, and resolved with minimal or no intervention. No statistically significant differences were found between occurrence of any particular complication in primary versus secondary DFG placement ($p = 0.36$) or between primary and secondary DFG placement and the need for additional surgery ($p = 1.0$). Among the 67.7% patients who had implant exposure or extrusion as an indication for DFG, 39.1% required additional surgery within 2 years. Advanced age was not associated with higher complication rates ($p = 0.12$). The study showed that DFG is an excellent option for socket reconstruction, particularly in cases involving pediatric patients, complicated orbits, history of multiple previous surgeries, and inflamed, contracted, or scarred sockets.
The paper had a small number of pediatric cases included.

Adult Versus Pediatric Relapse and Recurrence in Orbital Inflammatory Syndrome
Keen JA, Kennedy BJ, Mishulin A, Winkler K, Fernandez-Ruiz M, Black EH, Roarty J. Adult Versus Pediatric Relapse and Recurrence in Orbital Inflammatory Syndrome.
Ophthalmic Plast Reconstr Surg. 2021 Jan-Feb 01;37(1):77-80.

Orbital inflammatory syndrome (OIS) is a diagnosis of exclusion that has a variable presentation and unpredictable course. Many studies report incomplete or lack of OIS resolution with high recurrence and relapse rates. No studies to date have investigated the characteristics of both recurrence and relapse in OIS. We sought to determine this in both pediatric and adult patients. A retrospective chart review of 56 patients with OIS was performed between 2004 and 2018. Forty-one patients were identified as adults greater than 18 years of age and 15 were identified as pediatric patients less than 18 years of age. Among 56 (41 adult and 15 pediatric) cases of OIS, 18 cases of recurrent disease (32.1%) were identified and 15 (26.8%) patients experienced relapses. All 6 (100%) pediatric patients that had recurrent disease initially suffered from relapses. In contrast, only 1 of the 12 (8.3%) recurrent adult cases initially experienced relapse. Of the 18 patients with recurrent disease, 9 (50%) had multiple recurrences. Underlying etiologies were confirmed in 5 of 18 recurrent cases (27.8%) and 5 of 38 (13.2%) non-recurrent cases. Of the 5 patients with recurrent OIS and an identified etiology, all 5 (100%) demonstrated multiple recurrences. In pediatric cases, relapse was more common and prior episodes of relapse were predictive of later recurrence. Recurrence was relatively common in both groups with half of the patients having multiple recurrences. Identifiable underlying etiologies were more common in patients with recurrent OIS and those cases all demonstrated multiple recurrences.

Feasibility of rapid magnetic resonance imaging (rMRI) for the emergency evaluation of suspected pediatric orbital cellulitis.
Jain SF, Ishihara R, Wheelock L, Love T, Wang J, Deegan T, Majerus CR, Oarhe C, Allbery S.
J AAPOS. 2020 Oct;24(5):289.e1-289.e4.

This is a prospective study of 14 patients enrolled over a 22 month period (July1, 2017 to April 30,2019) to evaluate the feasibility of noncontrast rapid magnetic resonance imaging (rMRI), compared with traditional contrast-enhanced computed tomography (CT) in assessing pediatric emergency department patients with suspected orbital cellulitis or orbital abscess. Participants received both contrast orbital CT, with the addition of the noncontrast rMRI. No sedation was used for either examination. All clinical decisions were based on CT findings; rMRI was interpreted within 24 hours of the visit. Three pediatric radiologists, with 8-21 years' experience of pediatric neuroradiology, interpreted the rMRI, masked to the CT and clinical results. Results were analyzed for interobserver bias. Mean age was 5.9 years (range, 0.33-13). Of the 14 patients, 13 (93%) were able to complete the rMRI at 1.5 and 3T; 1 patient (1.67 years of age) was unable to complete the rMRI (no images obtained). Of the 26 unilateral orbital units assessed, 3 were positive for retro septal orbital cellulitis by CT and were diagnosed correctly by rMRI. CT and rMRI findings were concordant in 100% of cases in differentiating preseptal vs orbital cellulitis. The study is limited by the small sample size. This study suggests that an accurate diagnosis of orbital cellulitis can be obtained with an rMRI concordant with contrast-enhanced CT, while sparing the need for intravenous access, no significant difference in time of completion and sparing the child from potential detrimental effects of ionizing radiation.

A rare case of pediatric Tolosa-Hunt syndrome.
Sohal P, Bregman J, Stokes S, Whitehead MT, Karwoski B.
J AAPOS. 2020 Oct;24(5):316-319.

A case report of an 8-year-old girl with Tolosa-Hunt syndrome who presented, atypically, without the hallmark finding of pain. This case of pediatric Tolosa-Hunt syndrome is the only reported example to date lacking what is considered its pathognomonic feature and thus brings to light the clinical variability of this already inconspicuous disorder.

Simultaneous Bilateral Orbital Cellulitis With Meningitis Caused by Methicillin-Resistant Staphylococcus aureus in an Immunocompetent Infant.
Nair AG, Rathi N, Apte MK, Marathe TR, Potdar NA, Shinde CA.
J Pediatr Ophthalmol Strabismus. 2020 Jun 23;57:e34-e37

In this case report, the authors describe a 17 day old immunocompetent infant who presented with bilateral methicillin-resistant Staphylococcus aureus (MRSA) orbital cellulitis. There were no other systemic issues and the child was feeding well. Work up included CT of the brain and orbits, blood and CSF analysis, and an evaluation for immunodeficiency. The patient was treated with transcutaneous ultrasound guided aspiration of the loculated abscesses, intravenous and oral antibiotics, and steroids. Both the CSF fluid and contents of the orbital abscesses grew MRSA. The patient did well with no signs of visual, orbital or systemic sequela at one year follow up. The authors emphasize the poor prognosis of orbital cellulitis in the pre-antibiotic era (17% mortality and 20% blindness) and the importance of CSF evaluation when bilateral presentation occurs during infancy, as not all patients with meningitis secondary to orbital cellulitis exhibit clinical signs of CNS involvement.

Hemicentral Retinal Artery Occlusion: A Rare Complication of Orbital Cellulitis
Erbil Seven, Tuncay Artuç, Serek Tekin, Muhammed Batur, Muhammet Derda Özer
J Pediatr Ophthalmol Strabismus. 2020 Aug 19;57:

A 14 year old boy with right sided orbital cellulitis and pansinusitis presented with hand motion vision, an APD, and hemiretinal artery occlusion. He was admitted to the hospital and treated with intravenous antibiotics, glaucoma eye drops, intravenous acetazolamide a mannitol infusion and hyperbaric oxygen. His intraocular pressure at presentation was 17 mm Hg in the affected eye. On his second day of admission his clinical situation deteriorated and functional endoscopic sinus surgery was performed. Ethmoid sinus culture grew Streptococcus viridans. After thirteen days the patient was discharged, during his hospitalization he continued to receive hyperbaric oxygen along with antibiotics. His vision slowly

improved and after four months of follow up returned to 20/20. He had a persistent APD and exotropia. Several cases of central retinal artery occlusion with orbital cellulitis have been reported, this case is the first report of a hemiretinal artery occlusion in this condition. The authors emphasize the use of oxygen (inspired and hyperbaric) in the treatment of retinal artery occlusion. Indications for surgical treatment of orbital cellulitis such as the Harris Garcia criteria, the use of steroids, and evidence for IOP lowering medications were not discussed.

Painful Proptosis in a 12-Year-Old Boy
Jamie H Choi, Wasim A Samara, Adam E Pflugrath, William H Benson
J Pediatr Ophthalmol Strabismus. 2020 May 1;57(3):204

A 12 year old boy presented with eyelid swelling, proptosis, and limited extraocular motility days after minor orbital trauma. He was found to have ethmoid sinusitis on CT scan and a dilated superior ophthalmic vein (SOV). No subperiosteal abscess was found. Given the orbital signs, dilated SOV and lack of a subperiosteal abscess, the diagnosis of SOV thrombosis (SOVT) was made. The most common cause of SOVT is paranasal sinusitis, other causes include hematologic abnormalities, trauma, and inflammation not associated with infection. In this case the trauma was felt to likely be incidental. An important goal of treatment is to prevent cavernous sinus thrombosis which can lead to permanent blindness or death. Treatment with systemic antibiotics guided by culture and anticoagulation therapy is recommended. This case highlights the importance of looking for alternative causes of orbital signs when a patient presents with sinusitis, despite subperiosteal abscess being very frequently encountered clinically.

Quality of Life in Thyroid Eye Disease: A Systematic Review
Howe T, Lee B, Sundar G
Ophthalmic Plast Reconstr Surg. March/April 2020;36:118–126

The aim of this systematic review is to provide 1) an understanding of the components of quality of life (QOL) questionnaires and 2) an up-to-date insight of the types of QOL questionnaires available, strengths and limitations based on current literature. A literature search was conducted from 18 to 21 of February 2019 using 6 major databases: Cochrane Library, Ovid Medline, PubMed, Scopus, Taylor and Francis, and Web of Science. All papers were skimmed by title and abstract to determine whether the paper fulfilled the screening criteria. In cases of uncertainty, the paper was read in totality to justify its inclusion. After that, duplicates were eliminated and the remainder was subjected to a second set of inclusion and exclusion criteria before finalizing the list of included studies. An initial search returned with 402 studies, which were subsequently filtered using prespecified criteria to 27 studies to collate information regarding questionnaires assessing QOL of thyroid eye disease patients. Conclusions: The QOL of thyroid eye disease patients is best assessed using disease-specific questionnaires. Among the different types of questionnaires, the Graves Ophthalmopathy Quality of Life (GO-QOL) questionnaire is preferred due to its' ability to explore QOL in-depth and proven efficacy in many countries after cultural adaptation at the expense of time. Single-item questionnaires like the Thyroid Eye Disease Quality of Life (TED-QOL) are more suitable as screening tools in busy metropolitan settings while semi-structured interviews are important in developing new ways of assessing the QOL of thyroid eye disease patients. As pediatric ophthalmologists, we are often dealing with TED and its repercussions and it's important for us to know about the thyroid related issues that are relevant to our patients.

En-Bloc Resection Versus Resection After Evacuation and Suction of the Content for Orbital Optic Nerve Glioma Causing Visual Loss and Disfiguring Proptosis

El-Nasser A, Mohammad A
Ophthalmic Plast Reconstr Surg July/Aug 2020;36:399–402

The study aimed to evaluate the surgical outcomes of two different techniques of resection for optic nerve gliomas confined to the intra-orbital segment. This was a prospective, comparable, clinical interventional case series that was conducted at the orbital clinic of Assiut University Hospital between 2006 and 2018. The study included 10 children with optic nerve gliomas confined to the intra-orbital part without intracanalicular or intracranial extension and causing severe visual loss and disfiguring proptosis. In all cases, lateral orbitotomy was performed to expose the mass. In 5 cases (group A), the glioma was resected en-bloc. In 5 cases (group B), a new technique of resection was introduced. The wall of the glioma was incised, the content was evacuated and suctioned and followed by resection under good visualization of the markedly reduced mass in size. In the 2 groups, no tumour regrowth was reported during the follow-up period of 3–12 years. In group A, the 5 cases developed postoperative third nerve damage with paralytic ptosis and one case had severe neurotrophic keratitis ended by dense corneal opacity. In group B, a healthy ipsilateral eye was preserved in all cases and no one case developed postoperative paralytic ptosis. Although the sample size was small, the authors felt that reduction of size of an intra-orbital optic nerve glioma by evacuation and suction of the content before resection is highly recommended. This makes the surgical field during resection more visible and minimizes the possibility of third or other nerves damage. A rare procedure but interesting to see how we can improve outcomes of this debilitating condition.

21. OCULOPLASTICS

Pattern of Presentation and Surgical Outcomes of Canalicular Laceration Repair in a Pediatric Population.
Agarwal R, Patidar N, Mohan A, Singh R, Sen P.
J Pediatr Ophthalmol Strabismus. 2021 Jan 1;58(1):42-47.

The retrospective cohort observational study characterized 18 canilicular lacerations in children under 10 years old. Twelve patients had lower, and six had upper canilicular lacerations. A blouse hook was the most common cause of injury. Anatomical and functional success was achieved in 88.9% and 94.4% of patients respectively. Repair was done with the Mini Monoka stent and no difference was found between early (<48 hours) and late repair.

Orbital and periorbital dermoid cysts: Comparison of clinical features and management outcomes in children and adults.
Dave TV, Gupta Rathi S, Kaliki S, Mishra D.
Eur J Ophthalmol. 2020 Nov 16. Epub ahead of print.

Orbital and periorbital dermoid cysts are benign cysts that are painless masses that occur at suture lines. Currently, there are no studies that define the exact timing of surgical intervention of these cysts. The authors aim was to describe a large series of proven dermoids and compare the difference to clinical presentation and management outcomes between pediatric and adult presentations. This was a retrospective single center interventional comparative consecutive case series. The study included 148 children and 55 adults with histopathologically proven dermoid cysts. The study showed that adults had more complicated presentations with a higher possibility of vision loss. Intraoperative rupture was more common in adults. The rate of recurrence was no different between the two groups. They found a higher incidence of inflammation in adults with dermoid cysts and hypothesize that this may be responsible for the higher incidence of rupture during surgery. The authors concluded that adults may require for excisional biopsy earlier. This is an important consideration when counselling patients on dermoid removal.

Is there an association between congenital nasolacrimal duct obstruction and cesarean delivery?
Alakus MF, Dag U, Balsak S, Erdem S, Oncul H, Akgol S, Diri H.
Eur J Ophthalmol. 2020 Nov;30(6):1228-1231

Congenital nasolacrimal duct obstruction (CNLDO) is a common cause of neonatal epiphora. 6-30% of full term infants can have CNLDO at birth, but 2-6% continues to be symptomatic later in life. This may require further treatment such as massage, or irrigation and probing of the nasolacrimal drainage system. The authors noted that the type of delivery (vaginal vs. cesarean) may be a risk factor for CNLDO and aimed to research this. 665 cases were included in this retrospective investigation. There was a significant positive family history of CNLDO in patients with CNLDO. When only first births were taken into consideration, comparisons of CNLDO vs non-CNLDO groups showed that the ratio of cesarean delivery was higher in the CNLDO group. They hypothesize that higher external pressure and collagenolytic activity during the first vaginal delivery decreases the risk of CNLDO. This study may show a potential risk factor for CNLDO, however the choice of delivery may not be chosen based on the potential to develop a CNLDO.

Marcus Gunn Jaw-Winking Synkinesis With Ipsilateral Eyelid Myokymia.
Althaqib RN, Khan AO, Alsuhaibani AH.
Ophthalmic Plast Reconstr Surg. 2020 Nov/Dec;36(6):566-568.

This was a retrospective case series that aimed to describe a novel observation of ipsilateral eyelid myokymia in the context of Marcus Gunn jaw-winking synkinesis (MGJWS). The series included 5 patients observed to have myokymia in the context of MGJWS in 2 tertiary hospitals in Riyadh, Saudi Arabia. Demographic profile including age and gender, and clinical features were analyzed. Five patients (3 males and 2 females) with MGJWS were noted to demonstrate the phenomenon of ipsilateral eyelid myokymia. All but 1 had right-sided MGJWS. The myokymia was seen as upper eyelid twitching in a vertical fashion along the levator palpebrae superioris muscle field of action. All subjects also had ipsilateral Monocular elevation deficiency. Ipsilateral upper eyelid myokymia is a potential feature of MGJWS. Monocular elevation seems to be a constant feature among MGJWS patients with levator muscle myokymia. The finding of myokymia has not been described previously in associated with MGJWS.

Day-Case Admission for External Dacryocystorhinostomy in Preschool Children
Juniat V, Rose GE, Timlin H, Wagh VJ, Abou-Rayyah Y, Uddin J, Verity DH.
Ophthalmic Plast Reconstr Surg. 2021 Jan-Feb 01;37(1):65-66.

This was a retrospective noncomparative series looking at epistaxis during or after dacryocystorhinostomy. The surgery may present a risk of circulatory compromise, particularly in young children. In view of this concern, we reviewed the outcome and complications of external dacryocystorhinostomy in preschool children, aged less than 4 years. A case-note review for a series of preschool children undergoing external dacryocystorhinostomy as a day-case admission at Moorfields Eye Hospital between 1992 and 2018; all surgery was consultant-led. Details were taken of the type of surgery, any intraoperative or postoperative complications (surgical or anesthetic), any unplanned admissions after surgery, and the functional outcome. To assess the veracity of the medical records, the parents for a sample of 67 children were contacted to check whether there had been any unrecorded events or concerns. The authors looked at anesthetic or surgical complications, unplanned admissions, and postoperative events. One-hundred and eighty-seven children (117 boys; 63%) underwent 228 external dacryocystorhinostomies during 201 admissions, the average admission age being 36.8 months (median, 37.5; range, 5.5–53.5 months). Forty-one children (20%) underwent bilateral dacryocystorhinostomy: the 27 having simultaneous bilateral surgery dacryocystorhinostomy were operated at a mean age of 38.2 months (median, 37.5; range, 15.5– 53.5 months), this being significantly different from the average age at first operation in 14 children undergoing sequential admission for bilateral dacryocystorhinostomy (mean, 24.9 months; median, 27.0; range, 5.5–42.5) ($p = 0.0023$). No adverse anesthetic events were recorded, 2 children (2 dacryocystorhinostomies) required temporary nasal packing at the end of surgery for epistaxis, and one further child was admitted for overnight observation because of persistent mild epistaxis after bilateral dacryocystorhinostomy. Three children (3 dacryocystorhinostomies) had a mild, selflimiting secondary epistaxis, and there were no unplanned emergency admissions. The telephone survey did not reveal any disparity in the medical records. With experienced surgeons and anesthetists in a suitable specialist hospital, external dacryocystorhinostomy in preschool children would appear to be a safe and effective procedure, with few and minor complications. Although facilities for overnight observation should be available, the surgery can typically be planned as a day-case admission, and simultaneous bilateral surgery is also possible in this age-group. The article shows that the procedure is safe in children even though they have higher risks of hemodynamic compromise due to lower blood volume than in adults.

Treatment of Congenital Ptosis in Infants With Associated Amblyopia Using a Frontalis Muscle Flap Eyelid Reanimation Technique
Eton EA, Carniciu AL, Prabhu SS, Wang GM, Kahana A.
Ophthalmic Plast Reconstr Surg. 2021 Jan-Feb 01;37(1):67-71.

The paper aimed to determine the efficacy of a frontalis muscle flap eyelid reanimation technique for correction of severe congenital ptosis and associated amblyopia in infants. The authors performed a retrospective chart review of patients 12 months of age or younger with unilateral or bilateral congenital

ptosis and associated amblyopia or deemed at high risk for amblyopia due to visual deprivation. Following ptosis repair via a frontalis muscle flap technique, primary outcomes of postoperative eyelid position and amblyopia reversal were assessed. Seventeen eyes of 12 participants were included for study. Seven of these patients had simple congenital ptosis, and the remainder had ptosis as part of a syndrome. Nine were diagnosed with amblyopia preoperatively, and the remaining 3 were too young for acuity testing but had occlusion of the visual axis by the ptotic eyelid in primary gaze. Postoperatively, the mean margin-to-reflex distance 1 was 2.4 mm (range: 0.0–4.0), and 9 patients (75%) demonstrated no evidence of amblyopia. Only 2 patients had eyelid asymmetry greater than 2 mm, which in both cases was due to lack of frontalis activation by the patient secondary to ongoing visual impairment. The most common complication was lagophthalmos in 6 eyes (35.3%), with no significant associated surface keratopathy. The frontalis muscle flap technique may offer a new and effective approach to treating infants with severe congenital ptosis causing poor eyelid excursion and associated amblyopia while avoiding use of an implant. This technique has not been described in infants in the past although has been used in kids and adults.

Single-triangle versus Fox pentagon frontalis suspension for unilateral severe congenital ptosis correction.
Mohammed NM, Kamal MA, Abdelhafez MA, Diab MM.
J AAPOS. 2020 Oct;24(5):295.e1-295.e6.

This is a randomized controlled trial of 60 eyes of 60 patients with severe unilateral simple congenital ptosis and poor levator function ($\leq$ 4mm) comparing the functional and cosmetic outcomes of two different frontalis sling techniques for correction of severe unilateral congenital ptosis: single triangle (ST) and Fox pentagon (FP) techniques using expanded polytetrafluoroethylene (ePTFE) suture. Participants were randomly assigned to either procedure. Functional outcome measures were margin reflex distance (MRD1), palpebral fissure height (VFH), and lagophthalmos. Cosmetic outcome parameters (lid contour, lid crease, and height symmetry) were graded as 3 (excellent), 2 (good), or 1 (poor), with a minimum of 18 months' follow-up. At final follow-up, there was a significant improvement in the MRD1 and VFH in both groups, with no statistical difference (P 5 0.9). Both groups showed comparative cosmetic results regarding lid height symmetry, crease, and contour. The patients in the singletriangle group showed more rapid recovery of postoperative edema and lagopthalmos with less visible forehead scarring. There were no serious ePTFE sling–related complications. The limitation of the study was that the grader was not masked to the technique performed. In this study cohort, the single-triangle and Fox pentagon frontalis suspension techniques had similar outcomes with respect to MRD1 and VFH and comparable cosmetic results. However, the single-triangle technique avoids two forehead incisions and was associated with less postoperative edema, lagophthalmos, and scarring.

Periocular infantile hemangioma masquerading as dacryocele.
Bonafede L, Go M, Cheng J, Belcastro AA, Bellet JS, Gabr H, Freedman SF, Velez FG.
J AAPOS. 2020 Oct;24(5):326-328.

A case report of a 2-month-old boy developed a protuberant, blue nodule inferomedial to the left medial canthus. It was unresponsive to oral and intramuscular antibiotics. After developing difficulty breathing, he was admitted, with the diagnosis of a dacryocele, and, after an inconclusive ultrasound, underwent probing and irrigation with nasal endoscopy. Intraoperatively, the lesion appeared discontinuous with the nasolacrimal system and could not be decompressed. Postoperative magnetic resonance imaging suggested a hemangioma or possible collapsed dacryocele. Doppler ultrasound confirmed a perinasolacrimal duct hemangioma. Systemic propranolol treatment was initiated.

Evaluation of All Causes of Visual Function Loss in Children With Congenital Blepharoptosis
Ozlem Ural, Mehmet C Mocan, Ugur Erdener
J Pediatr Ophthalmol Strabismus. 2020 Mar 1;57(2):97-102.

In this descriptive retrospective study, 134 consecutively operated on pediatric patients with congenital blepharoptosis with at least one year of postoperative follow up underwent chart review. All causes of congenital blepharoptosis were included (dystrophic, blepharophimosis, Marcus-Gunn syndrome, other). Patients who did not have either Snellen or tumbling E visual acuity assessments were excluded. The study sought to evaluate all causes of visual function loss in this patient population. Of the initial cohort, 143 eyes of 123 patients met inclusion criteria and 28.5% had vision loss. The leading cause was amblyopia at 24.4% while 4.1% had vision loss related to structural eye pathology. Derivational amblyopia was the most common cause of amblyopia followed by refractive and strabismic amblyopia. Structural eye pathology was variable and included microphthalmos, aniridia, secondary glaucoma, bilateral iris coloboma, and optic atrophy among other causes. All eyes with derivational amblyopia had severe blepharoptosis was complete obstruction of the visual axis. The authors conclude that recognition and timely treatment for severe blepharoptosis as well as structural eye pathology will improve final vision and the level of ophthalmic care in this patient population.

An Unusual Presentation of a Dermoid Cyst Mimicking a Chalazion
Wadhwani M, Kursange S, Singh L, Khanam S.
J Pediatr Ophthalmol Strabismus. 2020 Jun 23;57

Dermoid cysts typically occur in suture lines during embryologic development such as the relatively common superolateral anterior dermoid overlying the frontozygomatic suture. Dermoid cysts near the tarsus are rare, this case is the third reported. The authors excised the dermoid en-bloc and histopathologic analysis found a cyst wall lined by stratified squamous epithelium with adnexal structures. Dermoids presenting in this location could be confused with chalazia and create diagnostic confusion leading to incorrect surgical treatment.

Congenital Eyelid Imbrication Syndrome Mimicking Ophthalmia Neonatorum.
Vempuluru SV, Tripathy D.
J Pediatr Ophthalmol Strabismus. 2020 Jul 1;57(4):272.

Congenital imbrication syndrome is a rare condition characterized by eyelid laxity, over-riding upper eyelid and tarsal conjunctival hyperemia. In this case, one upper eyelid was everted and the conjunctiva very swollen raising the possibility of ophthalmia neonatorum. The microbiologic work up was negative, and the patient’s dramatic conjunctival swelling and eyelid eversion slowly resolved with a pressure patch. The appearance of the eye had normalized by 8 weeks and he had mild residual eyelid laxity bilaterally. This case highlights a rare presentation, of a rare condition. Additionally, examination of the seemingly uninvolved involved eye, which demonstrated lid laxity and an over-riding upper eyelid, helped secure the diagnosis.

Management of a Case of Congenital Dacryocystocele
de Beaufort, Heather; Dumitrescu, Alina V; Kipp, Michael A; Wagner, Rudolph S.
J Pediatr Ophthalmol Strabismus. 2020 Jul;57(4):208-209.

In this round table discussion the authors describe their experience with congenital dacryocystocele. The importance of early recognition of breathing problems in bilateral cases, nasal endoscopy to identify and treat intranasal cysts and timing of surgery were discussed. Additionally one author noted an increase in prenatal consults for this problem.

Congenital nasolacrimal duct obstruction continues trend for spontaneous resolution beyond first year of life
Nakayama T, Watanabe A, Rajak S, Yamanaka Y, Sotozono C
Br J Ophthalmol 2020 Aug;104:1161-1163.

This study conducted in Japan analyzed the rate of spontaneous resolution of congenital nasolacrimal duct obstruction (CNDLO) in children over age 12 months. They conducted a retrospective, observation case study at a single institution. Patients were included when diagnosed with CNDLO after 12 months of age, and were offered intervention. 133 children (155 cases) were included, and were divided into 62 patients (70 cases) in whom spontaneous resolution occurred and 71 patients (85 cases) who underwent dacryoendoscopic guided probing and stenting. The mean age of resolution was 17.8 months. Probing and stenting was successful in 83/85 cases (97.6%). The results found that resolution of CNDLO after 12 months of age occurred in 45% of infants. Of the patients who accepted intervention, the spontaneous resolution rate could not be estimated, but the authors suggest the true rate of resolution is above 45%. The authors conclude that either approach could be proposed in this patient group.

Frontalis Linkage Without Intraoperative Eyelid Elevation for the Management of Myopathic Ptosis
Diniz S, Akaishi P, Cruz A
Ophthalmic Plast Reconstr Surg May/June 2020;36:258–262

The paper aimed to report the effect of frontalis linkage without intraoperative eyelid elevation for the management of myopathic ptosis. This was a retrospective analysis of 21 (42 eyelids) myopathic patients with bilateral ptosis who were operated between 1999 and 2017. All patients had orbicularis weakness and poor or absent Bell's phenomenon. Surgery consisted of using an autogenous fascia sling to link the tarsal plate to the frontalis muscle without any degree of intraoperative eyelid elevation. The main outcome measures were margin reflex distance, brow height and degree of brow excursion and degree of lagophthalmos, and exposure keratitis. After surgery, there were significant changes ($p < 0.0001$. Postoperative lagophthalmos was not detected in 31 (74%) eyes. In the remaining 11 eyes (26%), lagophthalmos ranged from 1.2 to 5.2mm (mean = 1.7mm ± 0.74 DP). Mild inferior superficial keratitis was detected in 14 eyes (33.3%) of 7 patients only 3 of which had lagophthalmos. One patient needed additional surgery to correct unilateral eyelid retraction. Overall, 81.81% of the patients were pleased with the procedure. The authors concluded that myopathic ptosis can be alleviated with a minimal amount of lagophthalmos by just linking the tarsal plate to the frontalis muscle without lifting the eyelid margin intraoperatively. Children were included as part of this study. Although the sample size was small, it is important to consider other approaches to ptosis repair.

The Use of Anterograde Percutaneous Transluminal Coronary Angioplasty Balloons in Congenital Nasolacrimal Duct Obstruction: A Cost-Effective Alternative to the Traditional Dacryoplasty Balloons
Bothra N, Gupta N, Nowak R, Ali M
Ophthalmic Plast Reconstr Surg May/June 2020;36:302–304

The paper aimed to assess the efficacy of commonly available coronary angioplasty balloon catheters as a low-cost alternative to the traditional dacryoplasty catheters in select patients of congenital nasolacrimal duct obstruction. This was a prospective, interventional study was performed between July 2018 and December 2018 in children with congenital nasolacrimal duct obstruction, who underwent balloon dacryoplasty using the coronary angioplasty balloon catheters (2.75×10mm, SPALNO, Cardiomac, Haryana, India). The inclusion criteria were children ≥4 years of age, and/or previously failed probing and/or previous failed intubation. Parameters documented were demographics, techniques, costs, complications, and postoperative outcomes. Twenty-three eyes of 22 children underwent balloon dacryoplasty using coronary angioplasty balloon catheters. The mean age of the patients was 4.33 years (range 1.5–10 years). The procedure was performed in 8 patients (8 eyes, 35%) as the primary procedure. The remaining 14 patients (15 eyes, 65%) had a history of probing, of which 4 eyes had it twice earlier. All eyes underwent balloon dacryoplasty as per standard protocols. The insertion profile and trackability of the coronary catheters were good. At a mean follow up of 6.17 months (range 1.5–9 months), anatomical and functional success was obtained in 87% cases (n = 20/23). No lacrimal passage trauma or injuries were noted during the procedure. The cost of coronary balloon catheter was approximately $60. The present pilot study has shown that outcomes of balloon dacryoplasty in patients with congenital nasolacrimal duct obstruction with coronary balloon catheters is comparable to that of traditional balloons and offers significant economic advantage for developing nations. The study is a

good example of the ongoing discussion of proper treatment of CNLDO and provides another method to keep in mind for difficult to treat cases.

Unilateral Frontalis Suspension With Silicone Sling Without Levator Extirpation in Congenital Ptosis With Marcus Gunn Jaw Winking Synkinesis
Shah G., Khurana D, Das S
Ophthalmic Plast Reconstr Surg July/Aug 2020;36:390–394

The study aimed to evaluate the efficacy of unilateral tarso-frontalis silicone sling without levator extirpation or disinsertion in dampening the jaw wink in patients with congenital ptosis associated with Marcus Gunn Jaw Winking synkinesis phenomenon. This was a retrospective review of all patients of congenital ptosis with moderate to severe Marcus Gunn jaw winking synkinesis who underwent the said procedure. Data were collected about the pre- and the postoperative severity of the ptosis and the amount of Marcus Gunn jaw winking excursion. Twenty-three patients were included in the study. Mean postoperative follow up duration was 31.2 (range 6–208) weeks. The severity of the preoperative jaw wink was mild (5mm eyelid excursion) in 8 (35%) patients. Postoperatively, 20 (87%) patients had mild residual jaw wink, 3 (13%) patients had moderate jaw wink and none of the patient had severe residual jaw wink. Although the sample size was small, the authors felt that unilateral tarsofrontal silicone sling without disinsertion or extirpation of the levator can reduce the severity of the jaw wink excursion in patients with congenital ptosis with moderate to severe preoperative Marcus Gunn jaw winking synkinesis.

Surgical Intervention of Periocular Infantile Hemangiomas in the Era of β-Blockers
Clara J. Men, Lilangi S. Ediriwickrema, Ji Sun Paik, Jennifer Murdock, Michael T. Yen, John D. Ng, Catherine Y. Liu, Bobby S. Korn and Don O. Kikkawa
Ophthalmic Plast Reconstr Surg Nov/Dec 2020;36:70–73

This multicentred retrospective study aimed to examine the role of adjuvant surgical resection of infantile hemangiomas after systemic β-blocker therapy. A standard protocol for oral propranolol was employed by the referring physicians. Ocular indications for surgery included ptosis obstructing the visual axis, high degrees of astigmatism causing amblyopia, or disfigurement from residual tumor. Patients underwent complete excision or debulking. Eleven girls and 4 boys were surgically treated with mean operative age of 34.4 months. Patients were followed for a mean of 19.6 months after surgery. Four patients required surgical treatment due to an inability to tolerate medical therapy secondary to drug-related side effects (including bradycardia). The other 11 patients proceeded to surgery due to residual eyelid and orbital lesions despite medical treatment. All 15 patients underwent orbitotomy for residual hemangioma excision. Four patients also underwent simultaneous levator advancement at the time of excision. In all cases, there was resolution of ptosis with clearing of the visual axis. No complications were incurred during the surgical treatment and there were no hemangioma recurrences. This is the first study to report surgical management of periocular infantile hemangiomas recalcitrant to standard therapy in the β-blocker era. In patients with infantile hemangioma who have failed medical therapy, adjuvant surgical treatment still plays an important role. For patients with persistent tumor causing ocular sequelae, surgical intervention aimed at soft tissue debulking and ptosis repair can be successful in achieving excellent functional and aesthetic outcomes with minimal side effects.

A Modified Levator Resection to Improve Postoperative Lagophthalmos and Eyelid Lag
Yasser H. Al-Faky, Mohamed A. Abu El-Eneen, Khaled M. Selim, and Hassan A. Ali
Ophthalmic Plast Reconstr Surg Nov/Dec 2020;36:38–44

This was a retrospective case-control study that looked to assess the effect of releasing the central attachment between the Whitnall's ligament (WL) and the levator palpebrae superioris muscle on the postoperative levator function (LF), eyelid lag, and degree of lagophthalmos. The study included patients with moderate and severe simple congenital ptosis who underwent skin approach levator aponeurosis resection (LR) as a primary procedure with a minimum of 6-month follow up. Patients were divided into 2

groups; the first group underwent LR without WL release (control group) while the second group underwent LR with WL release. Preoperative demographics and clinical data were reviewed. Postoperative LF, eyelid lag, and degree of lagophthalmos as well as surgical outcomes were compared and analyzed in both groups. There were a total of 81 patients (88 eyelids) included in this study. 50 were males (61.7%) and the mean age was ±SD 12.0±9.5 years. The first group included 43 eyelids while the second had 45 eyelids. There was no statistical difference in demographics and preoperative data between both groups. The postoperative LF was higher in the second group (10.7±2.1mm) with less consecutive eyelid lag compared with the control group (7.8±1.9mm) ($p < 0.001$). The control group had acquired more postoperative lagophthalmos compared with the second group ($p < 0.001$). Complete surgical success was achieved in 82.2% in the second group compared with 60.5% in the control group ($p = 0.024$). The authors felt that releasing the central attachment between WL and levator palpebrae superioris muscle has achieved an improvement in LF with minimal postoperative eyelid lag, lagophthalmos, and corneal complications.

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approximately $60. The present pilot study has shown that outcomes of balloon dacryoplasty in patients with congenital nasolacrimal duct obstruction with coronary balloon catheters is comparable to that of traditional balloons and offers significant economic advantage for developing nations. The study is a good example of the ongoing discussion of proper treatment of CNLDO and provides another method to keep in mind for difficult to treat cases.

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22. INFECTIONS

Congenital Zika Syndrome: Surgical and Visual Outcomes After Surgery for Infantile Strabismus
Ventura, Liana O; Travassos, Simone; Ventura Filho, Marcelo C; Marinho, Polyana; Lawrence, Linda; et al.
J Pediatr Ophthalmol Strabismus 2020 May 1;57(3):169-175.

In this case series, the motor, visual field and behavioral results of five patients with congenital Zika syndrome and horizontal strabismus who underwent surgery are reported. All of the children had at least moderate vision loss. The cause vision loss was multifactorial and included various structural eye abnormalities (80%) such as optic nerve hypoplasia, chorioretinal scarring and nerve pallor as well as neurologic disease including microcephaly, seizures and hydrocephalus. Additionally all of the patients has significant refractive error and could have had amblyopia. Four patients were esotropic and one exotropic. Motor success (alignment within 10PD) was achieved in 80% after six months of follow up. Improved visual fields were noted in 4/7 temporal visual fields, and the parents of all patients noted improved peripheral vision and social skills. The authors discussed strabismus surgery in patients with neurodevelopmental delay and performed less surgery than suggested by the standard tables to avoid over correction in this patient population. The series is limited by lack of masking and the difficulty of accurately measuring vision and visual fields in patients with developmental delay and vision loss.

Review of maternal COVID-19 infection: considerations for the pediatric ophthalmologist.
DiSciullo A, Mokhtari N, Fries M.
J AAPOS. 2020 Aug;24(4):209-211.

The purpose of this report is to summarize data regarding pregnancy and the postpartum period for mothers and neonates in the setting of the COVID-19 pandemic. The specific focus of this paper is to elucidate potential transmission risks for pediatric ophthalmologists. The report discusses that pregnant women are at higher risk to contract viral illnesses due to their relative immunosuppressed state and review considerations from a labor and delivery, pediatric, and ophthalmic perspective. The authors discuss standard contact precautions and also special considerations for examining infants with unknown COVID status.

Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report.
Valente P, Iarossi G, Federici M, Petroni S, Palma P, Cotugno N, De Ioris MA, Campana A, Buzzonetti L.
J AAPOS. 2020 Aug;24(4):212-215.

Much remains to be learned about the novel coronavirus (SARS-CoV-2) responsible for the 2020 COVID-19 pandemic and this preliminary report described the ocular manifestations and viral shedding in tears of 27 COVID-19 positive pediatric patients. Of these patients, 15% were asymptomatic, 56% had respiratory symptoms, and 30% had gastrointestinal symptoms. 15% of the patients showed signs of viral conjunctivitis and 11% of patients demonstrated conjunctival swabs positive for SARS-CoV-2 (1 asymptomatic patient and 2 symptomatic patients). The authors conclude that similar to other studies, children often have a milder phenotype of COVID-19 infection when compared to adults. They also discuss the implications for pediatric ophthalmologists that viral shedding can occur in tears of asymptomatic patients.

Ocular Manifestations and Clinical Characteristics of Children with Laboratory-Confirmed COVID-19 in Wuhan, China.
Ma N, Li P, Wang X, Yu Y, Tan X, Chen P, Li S, Jiang F.

JAMA Ophthalmol. 2020 Oct 1;138(10):1079-1086.

This was a retrospective clinical study on the clinical and ocular characteristics of pediatric patients with laboratory-confirmed COVID-19 from Wuhan Children's Hospital in Wuhan, China. The study was conducted and the specimens collected between January 26 and March 18, 2020. A total of 216 pediatric patients were included and 134 (62%) were boys. Overall, median age was 7.25 years (range 2.6-11.6 years). For the 49 children (22.7%) with ocular manifestations, median age was 4.1 years (range 1.1-10.2 years) and of these, 9 had ocular complaints as the initial manifestation of COVID-19. The most common ocular manifestations were conjunctival discharge, eye rubbing, conjunctival congestion. The most common systemic symptoms of symptomatic children were fever [81 (37.5%)] and cough [79 (36.6%)]. Of note, the authors divided the pediatric children in 4 age groups: < 1 year, 1 to < 5 years, 5 to < 10 years, 10 to < 16 years. With the exception of the 1 to < 5 year group, the most common ocular symptom in the different age groups was conjunctival secretion. For the 1 to < 5 year group, the most common ocular symptom was eye rubbing. Differences between the age groups also reported eyelid swelling only in the 10 to < 16 year group and reported tearing only in the 1 to < 5 year group. Although the authors reported patients' systemic symptoms associated with ocular symptoms, limitations of this study is that no slit lamp equipment was used with any of the patients, due to the limitations of equipment usage in the COVID-19 isolation unit of the Wuhan Children's Hospital. A second study limitation is the results of the 3 younger age groups to describe their ocular symptoms; it is especially challenging for a child < 10 years to accurately describe their ocular symtpoms during a hospital visit in a COVID-19 isolation unit. In summary, this retrospective study is helpful because, to date, there are few studies addressing the relationship with ocular manifestations of COVID-19 in children. The good news is that the authors reported mild ocular symptoms in all COVID-19 pediatric patients with full recovery and improvement.

Visual Outcomes in Presumed Congenital Foveal Toxoplasmosis.
Reynolds MMM, Chisolm SAM, Schroeder R, et al.
Am J Ophthalmol. June 2020; 214:9-13.

This retrospective observational case series of 10 patients from a single center with congenital macular lesions presumed to be from congenital foveal toxoplasmosis aims to describe the visual outcomes and the benefits of amblyopia therapy in this specialized patient population. The authors found the median age at presentation to be 2.8 years old. Amblyopia therapy was undertaken in 9 of the 10 patients and 6 of those patients showed improvement with this therapy – an average of 4.6 lines with a final acuity from 20/25 to 20/250. The authors concluded that despite the striking appearance of the lesions in these patients, that visual acuity potential is better than one would anticipate and recommend a trial of occlusion therapy. This paper is limited by its small numbers of this rare disorder, the retrospective nature, and very variable amblyopia therapy regimens. However, this is an important paper to remind the pediatric ophthalmologist not to disregard amblyopia therapy in this specific setting as outcomes may be better than predicted.

Post-antibiotic Ocular Surface Microbiome in Children: A Cluster-Randomized Trial
Thuy Doan, Armin Hinterwirth, Lee Worden, Ahmed M.Arzika, Ramatou Maliki, Cindi Chen, Lina Zhong, Nisha R Acharya, Travis C Porco, Jeremy D Keenan, Thomas M Lietman
Ophthalmology. Aug 2020(8);127:1127-30.

In Africa, biannual mass oral administration of azithromycin to children has been shown to decrease childhood mortality. The authors studied the effect of this treatment on the microbiome on the conjunctival surface. The predominant bacterial species were Haemophilus, Moraxella, Lactobacillus, and Streptococcus. Twenty-four months after treatment, there was a greater diversity of species detected in the azithromycin group compared with the placebo. There was no difference in the small viral load detected. The significance of these findings to the overall health of the eye is unknown, but even intermittent dosage with azithromycin caused a persistent change in the microbiome of the conjunctiva.

Longitudinal visual acuity development in ZIKV-exposed children
Da Silva Lima D. Baran LCP, Hamer RD, da Costa MF, Vidal KS, Damico FM, Barboni MTS, de Matos Franca VCR, Martins CMG, Tabares HS, Dias SL, Silva LA, Decleva D, Zatz M, Bertozzi APAP, Gazeta RE, Passos SD, Venura DF,
J AAPOS; 2020 Feb;24(1):23.e1-23.e6

Ocular manifestations due to Zika virus (ZIKV) infection during pregnancy are recognized among congenital Zika syndrome (CZS) patients. This is a prospective study measuring visual acuity via Teller Acuity Cards in children with (1) confirmed exposure to ZIKV (ZE) through the mother only (22 children), (2) with confirmed infection (ZI) (11 children) and (3) unaffected controls (27 children). The Visual acuity was measured 2 to 4 times in each child during the first 30 months of life. Among children who did not present clinical outcomes, there were no significant difference in visual acuity compared to the control group. Among the few children with CZS effects, only one presented with choriorteinal atrophy and had a visua acuity loss below the normative value. The main limitation of the study is the small sample sizeof typical CZS cases and inferences about visual acuity in children with neurological impairment without retinal abnormalities cannot be made. Another limitation is all patients did not have all 4 planned evaluations.

23. PEDIATRICS / SYNDROMES / SYSTEMIC DISEASE

Prevalence of Ophthalmologic Diagnoses in Children With Autism Spectrum Disorder Using the Optum Dataset: A Population-Based Study.
Melinda Y. Chang, Danielle Doppee, Fei Yu, Claudia Perez, Anne L. Coleman and Stacy L. Pineles.
American Journal of Ophthalmology, 2021 Jan; 221:147-153.

This population-based retrospective cohort study of over 10 million claims was designed to understand the relationships between ophthalmic disorders and autism spectrum disorder (ASD). The authors used a de-identified data asset to look at children less than or equal to 19 between 2007 and 2013 who had a diagnosis of ASD or pervasive developmental disorder (PDD) who also had amblyopia, strabismus, optic neuropathy, nystagmus, or retinopathy of prematurity. There was an increased risk of all the ophthalmic disorders in patients who carried a diagnosis of ASD. These results are not surprising because there are increased medical disorders in this population as a whole. The main limitation of the study was the methods since claim reports can limit the information you can obtain. The authors concluded that more work needed to be done to understand this relationship since the mechanisms of why this would occur are not understood. Nonetheless this is an important article because it reminds the pediatric ophthalmologist of the importance of a full eye exam in patients with ASD.

Optical coherence tomography findings in Cohen syndrome.
Huang LC, Kelly JP, Cabrera MT, Olmos de Koo LC, Weiss AH, Herlihy EP.
J AAPOS. 2020 Oct;24(5):306-309.

This is a report of cases of Cohen syndrome, a rare disease that causes myopia and retinal degeneration in the setting of developmental delay and characteristic craniofacial features. Optical coherence tomography (OCT) abnormalities in 4 patients with Cohen syndrome, 2 of whom have longitudinal follow-up are reported. All subjects had schisis-like changes, with cystoid spaces in the inner retina as well as diffuse outer retinal atrophy sparing the subfoveal region. Ophthalmologic findings in 1 patient led to the work-up that resulted in a diagnosis of Cohen syndrome, suggesting that characteristic retinal abnormalities visualized by fundus examination and OCT may represent distinguishing features of this syndrome.

Functional Vision Analysis in Patients with CHARGE Syndrome.
Martin GC, Robert MP, Challe G, Trinh NTH, Attié-Bitach T, Brémond-Gignac D, Bodaghi B, Abadie V.
J Pediatr Ophthalmol Strabismus. 2020 Mar 1;57(2):120-128.

Few prior studies have evaluated vision in patients with CHARGE syndrome, and these reports are limited by the difficulty of obtaining Snellen or similar acuity measurements in this patient population. This study sought to better characterize the functional vision of patients with CHARGE syndrome using both visual acuity and a questionnaire called VISIONCHARGE developed by the authors. Additionally, the study reported the patients' ocular findings and some developmental features. The VISIONCHARGE questionnaire was completed by 36 patients, a large series for CHARGE syndrome. Of the 36 patients, 89% had at least one ocular coloboma and 56% had visual acuity data available. As expected, distance and near vision scores and visual acuity were better in patients with peripheral colobomas compared to patients with colobomas involving the optic nerve and/or macula. However, the authors found no difference in overall ability score or parental evaluation of global vision between the severely and mildly effected groups. While this could be a result of the VISIONCHARGE questions failing to detect a difference between these groups, the general impression of parents and caregivers that patients adapt and compensate for severe disease to a surprising extent is supported by these results. The authors recommend against giving a poor functional visual prognosis to parents of a newborn with bilateral optic nerve and/or macular colobomas. Learning to walk and educational level appeared to be associated with

visual function, independent of other manifestations of CHARGE syndrome. Therefore, regular eye care and early visual stimulation to foster development of the social brain and visual cortex are recommended.

Influence of prenatal environment and birth parameters on amblyopia, strabismus, and anisometropia.
Lingham G, Mackey DA, Sanfilippo PG, Mountain J, Hewitt AW, Newnham JP, Yazar S.
J AAPOS. 2020 Mar;24:74.e1-7.

The authors present prevalence of amblyopia, strabismus, and anisometropia in young adults from a single center in Perth, Austrailia and to evaluate the prenatal and early-life risk factors. The participants are in the Raine Study, a randomized clinical trial which is an ongoing multigenerational epidemiological study in Perth, Australia. Of note, participants in the Raine Study have been followed from mid-gestation (n=2868 newborns) to young adulthood. Risk factors during pregnancy were determined from medical records and questionnaires completed by mothers at 18 weeks' gestation. At 20 years old follow-up, 1344 participants had a complete eye examination at Lions Eye Institute in Perth. From the 1344 participants examined, 1128 (83.9%) were of Northern European ancestry. Three patients with nystagmus were excluded and analysis was completed on 1125 participants; 551 (49%) were female. Of homogenous racial background of 1125 participants, 12 (1.1%) had amblyopia, 39 (3.5%) had strabismus, and 33 (2.9%) had anisometropia. Analysis of risk factors during pregnancy showed associations rather than statistical significance: (1) amblyopia associated with maternal history of pregancy-induced hypertension, (2) esotropia associated with lower gestational age and a heavier placenta, (3) exotropia associated with maternal history of previously treated hypertension and maternal use of recreational drugs during early pregnancy, (4) anisometropia associated with older maternal age and an abnormal umbilical cord. Findings in this cohort is similar to other studies in preterm childrens regarding the prevalence of amblyopia, strabismus, and anisometropia. Limitations of the study include the homogenous racial and ethnic cohort and the analysis of risk factors during pregnant mothers from questionnaires at 18 weeks' gestation. In summary, this large study finds similar prevalence levels of amblyopia, strabismus, anisometropia in Perth, Australia in preterm children at evaluation at 20 years old.

Ocular alignment, media, and eyelid disorders in Down syndrome.
Makateb A, Hashemi H, Farahi A, Mehravaran S, Khabazkhoob M, Asgari S.
Strabismus. 2020 Mar;28(1):42-48.

The authors sought to determine the prevalence of ocular pathology in children and young adults with Down syndrome. They performed a cross-sectional study in which Down syndrome patients between 10-30 years old underwent an eye examination by a general ophthalmologist (and confirmed by a sub-specialist where needed). Of the 226 patients who met the inclusion criteria, the mean age was 16.05 years old and nearly equal gender distribution (53% male). Refractive errors were common (myopia - 33.6%, hyperopia – 45.6%, astigmatism – 20.3%). Strabismus was found in 23.4% (most often esotropia) and nystagmus in 11.7%. Blepharitis was the most common eyelid disorder (81.9%), followed by floppy eyelid (19.9%). Posterior embryotoxon and corneal vascularization were found in 17.7% of patients and congenital lens opacity in 37.8%. The authors then compare their findings with other published articles in patients with Down syndrome and found fairly similar findings, apart from slightly higher prevalence of eyelid abnormalities. This manuscript highlights the importance of a complete eye exam in this subgroup of patients.

Relationship between motor skills, balance, and physical activity in children with CHARGE syndrome.
Perreault M, Hailback-Beach P, Lieberman L, Foster E.
J Vis Imp Blin 2020 Vol 114(4) 315-324

Children with CHARGE syndrome show delays in balance and motor skills due to multisensory impairments and also have fewer opportunities to engage in physical activity. The purpose of this study was to examine the relationship of these factors. Thirty-seven children (17 males, 20 females) with CHARGE syndrome aged 3-16 years (average 9.64 years) who could walk independently without

assistive devices were enrolled in the study. The children completed the Mini-BEST balance test and five motor skills (run, jump, slide, kick, and throw) form the Test of Gross Motor Development II. Parents of these children also completed the Physical Activity Questionnaire for Children or Adolescents. The study demonstrated that anticipatory control had significant positive correlation with all five of the tested motor skills, sensory orientation with three motor skills, and reactive postural control and dynamic gait with two motors skills. The study recommends parents and physical education teachers should work with students with CHARGE syndrome on increasing balance and motor skill performance to improve competence and confidence in physical activity.

Ocular Complications in School-Age Children and Adolescents after Allogeneic Bone Marrow Transplantation.
Hoehn ME, Vestal R, Calderwood J, et al.
Am J Ophthalmol. May 2020; 213:153-160.

The goal of this retrospective cohort study of 162 patients was to describe the ocular complications in school aged and adolescent patients after allogeneic bone marrow transplantation (BMT). The authors looked at patients aged 7-18 years old who survived at least 1 year after BMT and had a long follow up period ranging from 13 months to 12 years (mean 4 years). The patients were followed at one institution over fifteen years. The authors found that cataract formation was noted in 57 of the 162 patients, (97 eyes – 6 of these eyes needed surgery) and that this was associated with total body irradiation. Fifty-one of the patients developed dry eyes and this was associated with systemic graft vs. host disease. The authors concluded that due to the high incidence of treatable and vision threatening diseases associated with BMT, continued surveillance by a pediatric or general ophthalmologist should occur at least yearly. This study is important because of the increased long-term survival in post BMT pediatric patients. Other studies have looked at these complications in adults and in small children, but this is the only study to look at the outcomes in this age group. The authors point out that the results of this study differ from those in adults in that the pediatric patients had a lower incidence of dry eyes. This paper is important to the pediatric ophthalmologist who is counseling the pre and post BMT pediatric patient and their parents since it has some solid statistics for this age group regarding complications. However, it probably overestimates some of the complications since there have been improvements in the radiation protocols and technology – the authors of the paper do point out these limitations.

Incidence and Prognostic Role of the Ocular Manifestations of Neuroblastoma in Children.
Graef S, Irwin MS and Wan MJ.
Am J Ophthalmol. May 2020; 213:145-152.

The authors of this retrospective cohort study aimed to describe the ocular manifestations of neuroblastoma in a cohort of 523 patients over 28 years at one institution. Median follow up was 4 years. Of the 523 patients, 86 patients (16.4%) had ocular manifestations – 58 at diagnosis and 29 during the disease course. The most common findings were orbital involvement, opsoclonus, and Horner syndrome. Importantly, in 16 patients (3.1%), there were only ocular findings at presentation – 9 with orbital involvement and 7 with Horner syndrome. Orbital involvement was associated with a worse prognosis. Interestingly Horner syndrome and opsoclonus was associated with a high rate of survival in this cohort. The authors have an interesting discussion about the utility of imaging in isolated anisocoria being likely unjustified and in Horner syndrome being of low utility but possibly associated with neuroblastoma. The limitations of this study were mainly related to its retrospective nature.

Ophthalmic Findings in Fetal Alcohol Spectrum Disorders – A Cohort Study from Childhood to Adulthood.
Gyllencreutz E, Aring E, Landgre V, et al.
Am J Ophthalmol. June 2020; 214:14-20.

Thirty patients who were adopted from eastern Europe to Sweden in the 1990s and diagnosed with fetal alcohol spectrum disorder (FASD) were recruited in this prospective cohort study. The goal of this study

was to investigate if the ophthalmic findings in childhood in these patients persisted into young adulthood. The patients were seen by a multidisciplinary team at the median age of 8 years and then seen by the same team 13-18 years later. The authors collected data including visual acuity, refraction, stereoacuity, strabismus, and structural eye data. They found that the presence of optic nerve hypoplasia and tortuosity of the retinal blood vessels that were detected in childhood persisted into early adulthood. Treatable disorders such as refractive error and strabismus are also frequent in this population both in childhood and early adulthood. This paper's strength is in its long follow up period, however it is a small study and does little to change the way that the pediatric ophthalmologist cares for their patient, but does remind us of the importance of the full ophthalmic evaluation in this at-risk group of patients.

24. UVEITIS

Oral phospholipidic curcumin in juvenile idiopathic arthritis-associated uveitis.
Miserocchi E, Giuffrè C, Cicinelli MV, Marchese A, Gattinara M, Modorati G, Bandello F.
Eur J Ophthalmol. 2020 Nov;30(6):1390-1396.

Juvenile idiopathic arthritis (JIA) is a disease of arthritides that can have chronic ocular inflammation. Current treatment modalities include glucocorticoids, DMARDS, and biologics. Curcumin is a natural pigment that has anti-inflammatory, anti-oxidant, antimicrobial, and anti-tumorigenic properties. There have been some beneficial effects of curcumin based products in different ocular inflammatory conditions such as uveitis, glaucoma, dry eye, diabetic retinopathy, and ARMD. The purpose of this study was to evaluate the safety and efficacy of adjunctive treatment with curcumin-phosphatidylcholinee tablets (NORFLO) in children with JIA. This was a retrospective longitudinal study of patients with JIA. The primary outcome measure was the efficacy in reducing AC flare level and inactivity/reduction of the flare. 27 patients were included in those study. Disease inactivity was achieved in 22 patients at the end of the follow up. The mean number of flare-up recurrence before starting this adjunctive treatment was 3 episodes per year and was reduced to one episode during the study period. The medication was well tolerated and safe in humans. There was no drop out due to side effects of this medication. This is interesting as anpotential adjunctive treatment, although the lack of a control group and limited follow up period are limitations to this study.

Pediatric Sympathetic Ophthalmia: 20 Years of Data From a Tertiary Eye Center in India
Parthopratim Dutta Majumder, Saurabh Mistry, Sudharshan Sridharan, Amala Elizabeth George, Vineeta Rao, Sudha K Ganesh, Jyotirmay Biswas
J Pediatr Ophthalmol Strabismus. 2020 May 1;57(3):154-158

In this study, a retrospective case series of 20 pediatric patients with sympathetic ophthalmia (SO), the authors evaluate their experience with this condition over a 20-year period. This is the largest series of pediatric SO reported. The patients were predominantly male (70%), the average age was 11 years and trauma alone was the most common inciting event (65%), followed by surgery (15%), and surgery following trauma (20%). In 65% of patients SO developed within 2 months of the inciting event, and 35% had a “delayed” presentation of greater than 6 months. Anterior chamber inflammation and vitritis were the most common clinical findings. The findings discussed thus far are similar to other SO case series. In contrast to other reports, this series reported a high rate of steroid-sparing immunosuppression use (85%) and azathioprine was the most commonly used agent. Additionally the authors report “good” vision of 6/12 or better (20/40) in 70% of patients in the sympathizing eye. The authors suggest the early use of steroid-sparing agents could improve visual outcomes. Furthermore, the authors recommend raising awareness about this condition among patients and families to facilitate earlier recognition and treatment; they reported one patient who developed SO 15 years after several vitreoretinal surgeries for ROP. The incidence of SO could increase as improved instrumentation and operative techniques have increased the number of vitreoretinal surgeries performed in pediatric patients.

Results 5 to 10 years after cataract surgery with primary IOL implantation in juvenile idiopathic arthritis-related uveitis.
Leinonen S, Kotaniemi KM, Kivelä TT, Krootila K.
J Cataract Refract Surg. 2020 Aug;46(8):1114-1118.

Summary: This retrospective case series performed in Helsinki, Finland, looked at results of cataract extraction with primary intraocular lens (IOL) implantation in patients with juvenile idiopathic arthritis (JIA) and uveitis-related cataract. All consecutive patients younger than 20 years with JIA-uveitis–related cataract undergoing cataract extraction with primary IOL implantation in 1 or both eyes from February

2000 to April 2012 were included. Twenty eligible patients with 26 operated eyes were identified; 14 were girls and 6 were boys. All patients had a follow-up of 5 years and 13 patients (16 eyes [65%]) reached 10 years of follow-up. The authors found that preoperative median corrected distance visual acuity (CDVA) was 0.05 in decimal notation. Median CDVA was 1.0 at 5 years and 0.9 at 10 years of follow-up. Two eyes did not reach CDVA 0.5 with the operation, and in 2 eyes, CDVA decreased below 0.5 over the period of 3 to 5 years after the operation. Active uveitis during 3 and 12 months preoperatively was a risk indicator for postoperative CDVA <0.5 at 5 years (P = .005 and P = .00, respectively). The study conclusion was that cataract extraction with primary IOL implantation provides long-standing good visual acuity for young patients with well-controlled JIA-related uveitis.

Importance: Best practices with regards to extraction of JIA-associated uveitic cataracts in pediatric patients have been controversial. Many patients have been left aphakic in this setting due to long-term visual acuities worse in this patient population than in patients with cataracts related to other types of uveitis. This paper indicates that primary IOL implantation using current techniques was well-tolerated in patients with well-controlled JIA-related uveitis. The main limitation of the study is the small number of eyes operated.

RETINAL FINDINGS IN PRESUMED INFECTIOUS POSTERIOR UVEITIS AND CORRELATION WITH POLYMERASE CHAIN REACTION RESULTS
ELYASHIV S, SAMSON M, JABS D
RETINA Mar 2020; 40:567–571.

The goal of the study was to correlate demographics, retinal lesion characteristics, and host immune status with the pathogen found on polymerase chain reaction analysis of aqueous fluid in patients with suspected infectious posterior uveitis. Medical records of patients who underwent anterior chamber paracentesis for suspected infectious posterior uveitis and had retinal photographs between 2014 and 2016 at a single institution were reviewed. Data collection included demographics, clinical appearance of the lesions, and polymerase chain reaction results. Fundus photographs were evaluated by two masked observers for the clinical features of the retinitis. Twenty-eight patients were included in the study. There was substantial to almost perfect agreement on retinitis location (k = 0.67) and number (k = 0.76) between the masked photograph graders. Polymerase chain reaction results were positive for herpes simplex virus or varicella zoster virus in 43%, cytomegalovirus in 11%, and toxoplasmosis in 3%; 43% had negative polymerase chain reaction results. Detection of herpes simplex virus or varicella zoster virus on polymerase chain reaction of the aqueous was associated with paucifocal lesions (82%, P = 0.021) and lesions involving the peripheral retina (91%, P = 0.023), consistent with the diagnosis of acute retinal necrosis. These data suggest that the diagnosis of acute retinal necrosis can be reasonably inferred on clinical examination, providing a guide for initial empiric therapy.

25. PRACTICE MANAGEMENT/ HEALTH CARE SYSTEMS / EDUCATION

Cost-effectiveness of Autonomous Point-of-Care Diabetic Retinopathy Screening for Pediatric Patients With Diabetes.
Wolf RM, Channa R, Abramoff MD, Lehmann HP.
JAMA Ophthalmol. 2020 Oct 1;138(10):1063-1069

This is an evaluation of the economic parameters for the screening of children with type 1 diabetes (T1D) and type 2 diabetes (T2D) from March 2019 to January 2020, the authors designed a decision analysis model in which the proportion of diabetic retinopathy was defined as 'effectiveness' and patient/family out-of-pocket cost was defined as 'cost.' The authors' goals were to develop a model to estimate the cost savings of using autonomous AI diabetic retinopathy (DR) screening in children versus a clinic-based ophthalmoscopy examination by an eye care professional (ECP). Of note, previous studies report the adherence to regular DR screening in children with T1D and T2D ranges from 35% to 72%.
The comparison between AI and ECP, results showed that the expected true-positive proportions for standard ophthalmologic screening by an ECP were 0.006 for T1D and 0.01 for T2D, and the expected true-positive proportions for autonomous AI were 0.03 for T1D and 0.04 for T2D. According to the calculations, if 20% of the children adhered to the DR screening, the use of autonomous AI screening would result in a higher mean patient payment ($8.52 for T1D and $10.85 for T2D) compared to ECP screening ($7.91 for T1D and $8.20 for T2D). However, the calculations by the authors indicate that when more than 23% of children adhered to the DR screening, autonomous AI screening is cost-saving and the preferred strategy for the patient and his/her family. Overall, with adherence of more than 23% of the children to DR screening, the cost-effectiveness ratio of $31 for T1D and $95 for T2D for each additional pediatric case of DR identified when compared to the standard practice of ECP. Limitations of this study is that it only focused on the DR screening and not on the long-term and potential downstream complication costs related to DR. Also, the 'cost' and 'effectiveness' definitions in the economic model were limited and did not include costs of equipment, personnel, technology implementation. Future studies for a broader comparison of AI and ECP should include more parameters. In summary, while autonomous AI is an innovative tool in detecting retinopathy, and DR in particular, it is too premature to conclude that AI is more cost effective than ECP for pediatric diabetic screening examinations, especially when only looking at economic parameters and not considering the accuracy and consistency of the pathologic findings of AI as compared to ECP.

The Pediatric Examination Assessment Rubric (PEAR) toolkit: reliability study.
Langue M, Scott IU, Ely AL, Soni A.
J AAPOS. 2020 Dec 2: Epub ahead of print.

The current standard in medical education stresses assessment tools to evaluate trainee competency in achieving a goal and providing specific objective feedback and eliminate bias in a formal tool rather than through informal general conversation. The ophthalmic clinical examination (OCEX) checklist is used to evaluate the ophthalmology resident's history taking, examination, communication, professionalism and case presentation skills. Examining children requires additional skills and the authors have introduced the Pediatric Examination Assessment Rubric (PEAR) and in this study sought to inter-rater reliability of the tool in the educational clinical setting. The majority of the examination skills showed moderate to almost perfect reliability. The authors conclude that the data supports the use of PEAR toolkit as a reliable educational toolkit in assessing and giving feedback to residents for clinical encounters involving pediatric eye examinations. Limitations of the study include small sample size: six residents in one residency program. The authors suggest that additional studies be performed to confirm the validity of the tool, This study is important to the pediatric ophthalmologist in order to stay current with current techniques of evaluating and giving feedback to trainees.

Pediatric Eye Care: We Cannot Lose Sight of Its Importance despite the COVID-19 Pandemic
Camhi SS, Shah K, Cavuoto KM.
J Binocul Vis Ocul Motil. 2020 Oct-Dec;70(4):147-149.

Visual impairment affects over 19 million children globally and, if left untreated, can result in significant ocular morbidity. Due to the treatable nature of many childhood visual disturbances, pediatric vision screening is essential for optimization of health and developmental outcomes. The coronavirus disease 2019 (COVID-19) pandemic has inevitably disrupted the provision of routine pediatric health care as evidenced by reduced adherence to vaccination schedules. Further, the home environment, which many children have now become confined to, is known to pose risk for eye trauma which may result in irreversible vision loss. Therefore, it is imperative for pediatricians and pediatric ophthalmologists to focus on eye health and safety, despite the backdrop of a global pandemic.

The effect of nonmodifiable physician demographics on Press Ganey patient satisfaction scores in ophthalmology.
Michalak SM, Bhullar PK, Enyedi LB.
J AAPOS. 2020 Oct;24(5):299-301.

A retrospective review of Press Ganey (PG) surveys received for physicians employed at Duke University Department of Ophthalmology over a 2 year-period (September 2017 to September 2019). 25,545 PG surveys were returned (17.8% response rate) for 61 ophthalmologists (44% female; 59% white). male; 59% white). The average physician top box score was 87.2, and neither physician gender, race, or age was significantly correlated with scores received. Ophthalmic subspecialty was independently correlated with patient satisfaction scores. Retina specialists received the highest patient satisfaction scores. This was significantly higher than either pediatric ophthalmology or neuro-ophthalmology. In the multivariate analysis, when considering age, race, gender, and subspecialty, subspecialty was the only factor significantly correlated with patient satisfaction scores ($P < 0.02$). There are several limitations to this study, including the low response rate (17.8%) and single institution and variables outside physician control that affect patient satisfaction scores.

Validation of a novel strabismus surgery 3D-printed silicone eye model for simulation training
Jagan L, Turk W, Petropolis C, Egan R, Cofie N, Wright K, Strube Y.
JAAPOS Feb 2020; 24:3.e1-6

There are biologic and non-biologic strabismus surgery simulators. This is a multicenter study that compares the fidelity of a 3D printed silicone model to the rabbit head for strabismus surgery training. A validated questionnaire was developed to assess fidelity of the model and rabbit head. The overall globe, conjunctiva, muscle and sclera fidelity was rated on a 5 point scale. The survey was disseminated at three strabismus instruction courses. Participants at 2 courses participated on the model and rabbit head prior to completing the questionnaire, the 3rd course used only the model. Repeated measures analysis of variance compared ratings. Pearson's or Spearman's correlation evaluated correlation between years of experience to participants' responses. A total of 47 participants completed the questionnaire. The model rated 18% higher than rabbit head for anatomical accuracy and 25% higher for position of eyes within the head. Most experienced participants were more likely to strongly agree that silicone conjunctiva and scleral tissue effectively mimics real conjunctiva and sclera. The limitations of the study are the sample size, the number of attempts with each model was not recorded and with which model they started with. The model lacked Tenon's capsule, oblique muscles and required lubrication. Overall, the 3D printed silicone model holds promising for strabismus surgery training.

Comparison of Strabismus Surgical Efficiency and Complications Between Attending Surgeon Versus Supervised Ophthalmology Residents
Alixandra Riddering, MD; Xihui Lin, MD; Kim Le, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):235-237.

The purpose of the study was to compare surgical operating times and complication rates in strabismus surgery undertaken by attending surgeons versus supervised residents.
A total of 36 surgeries were included: 19 were bilateral muscle surgeries and 17 were unilateral surgeries. Residents completed a microsurgical course prior to operating. One attending surgeon was present for all surgeries, but there were 10 different first year residents involved in the cases. Major complications were defined as any complication requiring return to the operating room within 90 days of initial operation. Minor complications were defined as additional steps required in surgery. Primary outcomes were attending surgeon and resident surgical times and complications. On average, residents took 35.5 minutes to operate on an eye muscle compared to 19.3 minutes for the attending surgeon ($P < .0001$). Of the resident surgeries, there was one complication, a suture granuloma, requiring a return to the operating room. There were six minor complications during resident surgeries and one minor complication during attending surgeon surgery ($p=0.054$).
As expected, resident operation times were nearly double attending surgeon surgical times. There was a trend toward more minor complications among residents. No complication was vision-threatening. The authors believe that the microsurgical course likely contributed to the low number of complications but the study was not designed to evaluate this, as there was no comparison group of residents performing surgery who did not take the microsurgical course. The authors recommend that physicians disclose resident involvement during the consenting process for pediatric strabismus surgeries.

Pediatric Publication Trends in Leading General Ophthalmology Journals for 20 Years
Leshno, Ari; Stolovitch, Chaim; Barak, Adiel; Loewenstein, Anat; Mezad-Koursh, Daphna
J Pediatr Ophthalmol Strabismus 2020 Mar;57(2):78-84.

The authors reviewed the publication rate of pediatric topics in five leading comprehensive ophthalmology journals. Over a 20 year period the rate of publication (%, pediatric articles/total) deceased while the absolute number of pediatric publications remained unchanged, owing to an annual increase in total publications. Subsequently three pediatric ophthalmology and strabismus subspecialty journals were included and underwent analysis. Similar to the comprehensive journals, the pediatric ophthalmology journals also were publishing more articles each year. When the comprehensive and pediatric ophthalmology journals were looked at together, there was no significant change in publication rates of pediatric topics over the last twenty years. This could indicate a shift in where pediatric ophthalmology research is published, and indicates a move away from comprehensive journals and towards pediatric specific subspecialty journals. One potential negative consequence of this is less exposure for residents and comprehensive ophthalmologists to pediatric topics.

Management of Pediatric Ophthalmology Patients During the COVID-19 Outbreak: Experience From an Italian Tertiary Eye Center
Aldo Vagge, MD, PhD; Lorenzo Ferro Desideri, MD; Michele Iester, MD, PhD; Chiara Del Noce, MD; Carlo Catti, MD; Maria Musolino, BSc; Carlo E. Traverso, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):213-216.

The authors describe the treatment of pediatric patients with ophthalmological problems during the COVID-19 pandemic in an Italian tertiary eye center. A flow chart of their protocol is provided. First, the patients underwent telephone triage. Nonurgent complaints were deferred to future post-pandemic visits. Complaints that were unclear re: urgency were first evaluated using telemedicine. Patients with urgent complaints were triaged as to whether the patient was likely to have COVID (symptoms, recent COVID exposure) or not. The patients unlikely to have COVID were seen in the ophthalmology clinic utilizing precautions such as temperature screening, ophthalmologist wearing gloves/surgical mask/goggles or visors, slit lamps with breath shields, patients older than age 2 wearing masks, minimizing the number of people in the clinic. The patients with possible COVID were sent to the emergency room, and were seen by the ophthalmologist in the emergency room in an isolation room and the ophthalmologist wearing full personal protective equipment including N95 mask. Of note, this manuscript was submitted for publication on April 30th 2020, and by that time, 151 Italian physicians had died to due COVID-19. The

protocols published in this manuscript are similar to those subsequently adopted by many ophthalmologists in the United States.

The impact of the COVID-19 shutdown on US pediatric ophthalmologists.
Robbins SL, Packwood EA, Siegel LM; AAPOS Socioeconomic Committee.
J AAPOS. 2020 Aug;24(4):189-194.

The COVID-19 pandemic has taken an economic toll on many sectors of the economy including many outpatient specialties such as pediatric ophthalmology. Specifically, many pediatric ophthalmology practices are at risk for serious economic impact. This report discusses the results of a survey sent to AAPOS members in April 2020 to assess the economic impacts of the COVID-19 pandemic on pediatric ophthalmology practices. 416 of 1047 physicians responded, resulting in a 40% response rate representing 46 states and Puerto Rico. Private practice physicians made up the majority of the respondents (68%). Nearly all respondents had a surgical revenue decrease >51% and 21% had no guaranteed income, with 78% generating 0-25% of normal revenue. Paycheck protection program loan recipients varied geographically, with East coast practices receiving the majority of these loans. Bankruptcy was considered by 10% of those surveyed. This report provides concrete data regarding the financial viability of pediatric ophthalmology practices in many settings.

Your eye doctor will virtually see you now: synchronous patient-to-provider virtual visits in pediatric tele-ophthalmology.
Areaux RG Jr, de Alba Campomanes AG, Indaram M, Shah AS; Pediatric Tele-Ophthalmology Consortium.
J AAPOS. 2020 Aug;24(4):197-203.

The 2020 COVID-19 pandemic presented pediatric ophthalmology practices with critical questions on how best to take care of their patients while protecting both patients and providers from a highly infectious pandemic. This report, on behalf of the pediatric tele-ophthalmology consortium, serves to compile the experience and expertise regarding best practices for pediatric ophthalmology telemedicine, or synchronous patient-to-provider virtual visits. This report describes workflows for scheduling these visits, technology available to assist in the visits themselves, specific examples of cases, and potential barriers to receiving care through this modality. This report serves as an excellent primer to the pediatric ophthalmologist considering incorporating telemedicine into their practice.

Experience of a non-pediatric-trained ophthalmic hospitalist at a children's hospital.
Khalili A, Hymowitz M, Gorski M, Schwartzstein HR, Kodsi S.
J AAPOS. 2020 Jun;24(3):165-167.

Inpatient and emergency room pediatric ophthalmology presents unique challenges in terms of patient pathology and ability to cooperate with ophthalmic examinations. This is a short report of a practice describing their experience with a non-pediatric-trained ophthalmic hospitalist at a children’s hospital. Over a 2-month period, the provider evaluated 61 pediatric patients, only 15 (25%) of which required specific pediatric ophthalmology consultation, which was performed via discussion in 2/3 of those with the other 1/3 requiring direct patient care. The highest yield consults were those for red eyes or abnormal eye movements. The authors discuss that an ophthalmic hospitalist provides a valuable role to the medical center while not drawing on the outpatient resources of the sub-specialists in the department. From both a patient and provider perspective, this report provides information on the value of a hospitalist in terms of increasing efficiency and quality of care at an academic hospital responsible for covering emergency and inpatient consultations.

The impact of an eye drop booklet on distress in children when receiving eye drops.
Pilon F, Veen H, Kef S, van Genderen MM.

Strabismus. 2020 Apr 30:1-6. Online ahead of print.

Authors identified that the instillation of dilating eye drops was a source of anxiety for children presenting to clinic. An eye drop booklet was developed for the child to indicate how he/she would like to have the drops administered. Children aged 4-12 years with refractive error or strabismus were enrolled and divided into groups that received or did not receive the eye drop booklet. Parents filled in a questionnaire and the child indicated the level of distress on a face/numerical scale. Children were subdivided by age group for further analysis (4-6 years, 7-9 years, 10-12 years). Of the 370 children enrolled, 2/3 had received drops previously. No significant differences in the results for gender and experience with eye drops. There was no statistically significant differences in distress scores between those who used the booklet and those who did not. Age groups 1 and 2 differed significantly in their distress scores ($p=0.019$) but there was no difference between groups 1 and 3 or 2 and 3. Most parents reported either a positive effect on the child (69%) or no effect but positive outlook (24%). The authors summarize that anxiety is highest in ages 7-9, which is consistent with childhood development, and that the book was not sufficient in alleviating distress due to the complex nature of distress as well as possibly increasing focus on drop instillation. Despite the lack of statistical different, the majority of parents appreciated the eye drop booklet and the authors encourage future projects with similar goals of providing children more control.

Rowe, F., Hepworth, L., Howard, C. and Lane, S., 2020. Orthoptic Services in the UK and Ireland During the COVID-19 Pandemic.
Rowe F, Hepworth L, Howard C, Lane S.
British and Irish Orthoptic Journal. Apr 2020;16(1):29-37.

COVID-19 has widely impacted hospital services. The purpose of this study was to determine the impact of COVID-19 on Orthoptists and their clinical practice in the UK, Ireland, and Channel Islands. The authors conducted a prospective survey-based cross-sectional study using an online survey aiming for coverage of orthoptic departments across the UK, Ireland, and Channel Islands. The study was an online survey which was distributed through the British and Irish Orthoptic Society that reached over 95% of UK and Irish orthoptic services, and through social media and orthoptic research networks. Questions addressed the impact to orthoptists personally in their working lives, changes to their working environment, changes to their working practice and how they consult with patients, and access by orthoptists to professional support and guidelines. The survey response rate was 79%. The survey was completed by orthoptic departments, on average about 10 days post lockdown. During this time, many orthoptic services were cancelled/paused with remaining services largely reserved for emergency cases and urgent care. A substantial rise in tele-consultations was reported by 94% of respondents. These consultations largely consisted of telephone and video calls and were regarded generally as working well. Barriers to tele-consultations were mainly IT related but there were concerns raised regarding ethical and confidentiality issues for the remote visits. Shortage of personal protective equipment (PPE) was reported by one third of departments that responded along with issues relating to conflicting information about the use of PPE. The authors have reported information on the changing face of orthoptic clinical practice during the COVID-19 pandemic. They hope to perform future research, exploring the validity of app testing remotely in self-administration mode by parents/patients and also plan a follow-up survey in the future to capture how orthoptic services and practice have changed since this initial response. The survey highlighted emerging tele-consultation practice and the importance of centralised profession-specific guidelines when implementing such measures in an orthoptic practice.

Does the EyeChart App for iPhones Give Comparable Measurements to Traditional Visual Acuity Charts?
Ansell K, Maconachie G, Bierre A.
British and Irish Orthoptic Journal. Apr 2020;16(1):19-24.

This study sought to investigate if the EyeChart app gives accurate visual acuity (VA) measurements that are comparable to those achieved using traditional VA charts. Twenty-four participants (aged 18–27 years, mean 20.13 ± 1.78 years) with VA of 6/60 Snellen or better regardless of any strabismus, amblyopia, or ocular pathology volunteered for this prospective study. The best-corrected monocular VA

of each participant's right eye was measured on the Snellen chart at 6 m, the ETDRS chart at 3 m, and the EyeChart app presented on an iPhone SE at 1.2 m (4ft). The mean VA scores obtained were: –0.13 ± 0.08 logMAR on the Snellen chart, –0.11 ± 0.08 logMAR on the ETDRS chart, and –0.09 ± 0.07 logMAR on the EyeChart app. After Bonferroni Correction adjustments were applied, a significant difference was found between the EyeChart app and the Snellen chart ($t = –3.756$, $p = 0.003$), however the difference between the EyeChart app and the ETDRS chart did not reach statistical significance ($t = –2.391$, $p = 0.076$). The EyeChart app had a strong correlation with both the Snellen ($r = 0.79$, $p < 0.01$) and ETDRS charts ($r = 0.88$, $p < 0.01$). The Coefficients of Agreement revealed a variation of less than one logMAR line between the EyeChart app and the traditional VA charts (Snellen: 0.09 logMAR; ETDRS: 0.08 logMAR). This study found that the EyeChart app gives accurate VA scores that are comparable to those achieved using the gold-standard ETDRS chart in a healthy young adult population. This study found that the EyeChart app can give accurate VA scores when participants are wearing their refractive correction. However, to ensure the closer testing distance does not adversely affect the results obtained when refractive errors are uncorrected, the EyeChart app must be shown to be equally sensitive at detecting reduced VA caused by both uncorrected myopia and hypermetropia. Furthermore, before it could be introduced as a clinical VA assessment tool, it would be important to establish both the intra- and inter-examiner repeatability of the EyeChart app in addition to a value for the test-retest variability in both normal and patient populations as these will help examiners to know if any change in VA detected using the EyeChart app is true.In summary, this study found that the VA scores achieved on the EyeChart app are comparable to those achieved using the gold-standard ETDRS chart in a healthy young adult population. This is a promising finding; however, it is necessary for further large-scale studies to investigate the EyeChart app when used on a variety of patient population groups. These types of studies could be used to delineate whether the EyeChart app should be used regularly in lieu of other methods and integrated into regular practice.

The "Crab" Memory Tool for the Actions of the Extraocular Muscles.
Kruger JM, Anteby I, Frenkel S.
J Binocul Vis Ocul Motil. Jul-Sept 2020;70(3):86-88.

Understanding the primary, secondary and tertiary actions of the vertical recti and oblique muscles is important in the diagnosis of various types of strabismus (superior oblique palsy, A- and V-patterns). Unfortunately, learning these actions can be very challenging. The authors designed a visual memory tool entitled the crab diagram, and assessed its usefulness for medical students. Medical students undergoing their rotation in ophthalmology were taught the actions of the extraocular muscles either without the memory aid (control group) or with it (test group). The crab diagram represents the actions of each of the oblique and vertical recti such that the actions of the muscles intersect to form the shape of a crab. 73 students participated in this study. The students were surveyed one week and one month later to determine their ability to recall the muscle actions and asked to subjectively rate the usefulness of the memory aid. Approximately 40% of the test group used the memory tool and the students who used the memory tool and expressed value in it performed the best in the after-test. Eighty-seven percent of the respondents recommended that the memory aid be taught in the future. Overall, there was no significant difference in the ability to recall the actions of the muscles between the control and test groups. However, those students who found the memory aid helpful had significantly better recall than those who did not. The authors note that there may have been limited interest in the memory tool by some students and this may have affected the results.
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