What's New and Important in Pediatric Ophthalmology and Strabismus in 2023 – ALL STARS

Review of literature Feb 2022- Feb 2023 inclusive

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1. AMBLYOPIA

Multivariable Analyses of Amblyopia Treatment Outcomes from a Clinical Data Registry.
Repka MX, Li C, Lum F.
Ophthalmology. 2023 Feb;130(2):164-166. doi: 10.1016/j.ophtha.2022.09.005. Epub 2022 Sep 11. PMID: 36100075.
This is a retrospective database study presenting a multivariable analysis of factors associated with amblyopia treatment success. Subjects included patients between 3-12 years of age enrolled in the AAO's IRIS registry from 2013-2019. Success was assessed using IRIS-50. The IRIS-50 is an outcome measure for amblyopia treatment developed by the AAAO for use with data in the IRIS registry for children specifically for children 3-7 years old, but a secondary analysis was performed for children 8-12 years old. Treatment success was determined by passing at least 1 of the following criteria: Corrected interocular (or if not reported, uncorrected) visual acuity difference of less than 0.23 logMAR 3 to 12 months after first diagnosis of amblyopia, or improvement in the corrected visual acuity of the amblyopic eye of 3 or more Snellen lines (0.30 logMAR) 3 to 12 months after first diagnosis of amblyopia, or final visual acuity in the amblyopic eye of 20/30 or better (0.18 logMAR) 3 to 12 months after first diagnosis of amblyopia. Note that the method of treatment is not available in the IRIS registry. The reported success rates for children 3-7 years old was 77% and for children 8-12 was 55%. For the 3-7 yo group the odds ratio for success in treatment in black children vs. white children (0.71) and for Medicaid vs private insurance (0.65) were statistically significant. For the 8-12yo group, the odds ratios for treatment success in black children vs. white children (0.81), hispanic/latino vs white children (1.16), and Medicaid vs private insurance (0.84) were statistically significant. This study highlights the healthcare outcome disparities associated with race and with insurance coverage, which affects a broad proportion of children in the US (nearly 50% of children have Medicaid). Limitations of this study include lack of data on treatment modality and compliance, loss of follow up, and inadequate documentation
Binocular amblyopia treatment improves manual dexterity
Birch EE, Morale SE, Jost RM, Cheng-Patel CS, Kelly KR

2. VISION SCREENING

Effectiveness of the Spot Vision Screener using updated 2021 AAPOS guidelines
Peterseim MMW, Trivedi RH, Monahan SR,Smith SS, Bowsher JD, Alex A, Wilson ME, Wolf BJ
J AAPOS 2023; 27:24.e1-7
Spot Vision screener was evaluated for vision screen validation using the updated 2021 AAPOS vision screening Committee guidelines. Spot screening was successful in 1,036 of 1,090 children (95%). Forty-eight percent of participants were referred for further screening using the Spot manufacturer guidelines, and 40% of all children were found to have a 2021 amblyopia risk factor or visually significant refractive error by gold standard examination. The Spot recommendation compared reasonably well to the 2021 criteria, with an overall sensitivity of 0.88 and a specificity of 0.78. Applying updated guidelines to the Spot for hyperopia, anisometropia, and astigmatism yielded moderate-to-poor sensitivity (0.27-0.77) but excellent specificity (.0.9). The area under the curve of the receiver operating characteristic analysis demonstrates overall good prediction performance for the Spot for each diagnosis—myopia, hyperopia, astigmatism, anisometropia (range, 0.87-0.97). Results of our study suggest increasing the instrument referral criterion for astigmatism from 1.5 D (manufacturer thresholds of the screener used in this study) to 2 D in older children. Decreasing the anisometropia cutoff from 1 D to 0.75 D would improve sensitivity from 0.59 to .0.8. The overall predictive ability of the Spot is good, with a sensitivity of 0.88 and a specificity of 0.78. This study recommends applying specific device refractive referral criteria to maximize screening effectiveness using the updated AAPOS guidelines.

Web-based visual acuity testing for children.
Eileen E. Birch, PhD, Lindsey A. Hudgins, BA, Reed M. Jost, MS, Christina S. Cheng-Patel, CCRP, CCRC, Sarah E. Morale, BS, and Krista R. Kelly, PhD.
J AAPOS 2022;26:61.e1-5.
Despite the covid-19 pandemic leading to a growing acceptance/need for telemedicine, at-home visual acuity testing remains challenging. This is an issue as inaccurate visual acuities can lead to alterations in clinical decision making. This study evaluated two new at-home visual acuity tests (ATS-HOTV for 3–6-

year-olds and E-ETDRS for 7–12-year-olds) to see if visual acuity measured at home yielded results similar to those collected during an office visit using the same test. A total of 65 children were enrolled (34 preschoolers and 31 school aged children). Each child had their visual acuity tested in the office and again at home. Parents were given detailed instructions on how to accurately measure vision. On the ATS-HOTV test, 14 of 68 eyes (21%) had abnormal vision on the in-office test and 12 of 68 eyes (18%) had abnormal vision on the at-home test. The concordance was 97%. On the E-ETDRS test, 22 of 62 eyes (35%) had abnormal vision on the in-office test and 21 of 62 eyes (34%) had abnormal vision on the at-home test. The concordance was 98%. This study is important as it highlights a type of home visual acuity testing that is overall quite accurate. Advantages of these tests are compliance with AAO recommendations, simple calibration, efficient testing, good reliability, ability to test from 20/800 to 20/12, and immediate availability of results. Disadvantages are need for a computer, internet access, and a 3-meter testing distance. Having a more accurate way to test visual acuity at home will allow for great utilization of telemedicine in ophthalmology. It also may allow for greater enrollment into studies for families that would otherwise be unable to travel to the study site for multiple exams.

3. REFRACTIVE ERROR

Myopia Control Effect of Repeated Low-Level Red-Light Therapy in Chinese Children: A Randomized, Double-Blind, Controlled Clinical Trial.
Dong J, Zhu Z, Xu H, He M.
Ophthalmology. 2023 Feb;130(2):198-204. doi: 10.1016/j.ophtha.2022.08.024. Epub 2022 Aug 29. PMID: 36049646.
This is a randomized, double-blind, controlled clinical trial assessing the efficacy and safety of repeated low-level red-light therapy and single vision spectacles vs. sham and single vision spectacles. in controlling myopia progression. The study included 112 Chinese children aged 7 to 12 years with myopia of at least e0.50 diopter (D), astigmatism of 1.50 D or less, and anisometropia of 1.50 D or less. The RLRL group was exposed to desktop red-light therapy device twice daily for 3 minutes, with at least 4 hours between sessions for 6 months. The sham device control group received the same intervention with 10% of the original device's power. At the end of 6-months, the spherical equivalent refraction change was 0.06 for treatment group vs -0.11 for sham group, which was statistically significant. Mean axial length change at 6 months was greater for the sham groups vs treatment group (0.13mm vs 0.02mm) and was statistically significant. Changes in AL progressed more slowly for treatment vs sham. Distance visual loss was significantly greater in the sham group compared to treatment group (0.076 logMAR vs. -0.002 logMAR). There were no adverse events reported that were deemed related to the light therapy by the data safety monitoring committee. These results provide new evidence that RLRL treatment may be an effective and safe intervention against myopia progression. Additional investigation on RLRL vs sham vs no treatment would be ideal to better determine if the 10% level light had any treatment affect. A longer duration, past 6-months of follow-up would also shed light on myopia control past this period.

Spectacle Lenses with Aspherical Lenslets for Myopia Control vs Single Vision Spectacle Lenses: A Randomized Clinical Trial
Jinhua Bao PhD, Yingying Huang MD, Xue Li PhD
JAMA Ophthalmol. April 2022; 140(5):472-478
The goal of this study was to evaluate the efficacy of spectacle lenses with highly aspherical lenslets and slightly aspherical lenslets compared with conventional single-vision spectacle lenses in controlling myopia progression throughout 2 years. This was a double-masked randomized control study of 157 children who were randomly assigned in a 1:1:1 ratio to receive spectacle lenses with highly aspherical lenslets (HAL), spectacle lenses with slightly aspherical lenslets (SAL), or single-vision spectacle lenses (SVL). The main outcomes were the two year changes in cycloplegic spherical equivalent refraction (SER), axial length, and their differences between the three groups. They found that at two years children who wore SAL and HAL had reduced rates of myopic progression and axial elongation compared with children in SVL at two years. There was also a dose-dependent effect demonstrated, with children who wore HAL full time demonstrating increased myopic control efficacy. Differences in myopia control efficacy could be linked to differences in lens designs, namely, the concentric ring configuration with

aspherical lenslets (this study) and to lens design features such as the amount and area of lens addition or peripheral defocus.

4. Visual Impairment

Li D, Chan VF, Virgili G, Piyasena P, Negash H, Whitestone N, O'Connor S, Xiao B, Clarke M, Cherwek DH, Singh MK, She X, Wang H, Boswell M, Prakalapakorn SG, Patnaik JL, Congdon N. Impact of Vision Impairment and Ocular Morbidity and Their Treatment on Depression and Anxiety in Children: A Systematic Review. Ophthalmology. 2022 Oct;129(10):1152-1170. doi: 10.1016/j.ophtha.2022.05.020. Epub 2022 May 31. PMID: 35660416.

This is a systemic review and meta-analysis summarizing existing evidence to establish whether vision impairment, ocular morbidity, and their treatment are associated with anxiety and depression in children. The analysis included 36 studies, 58% of which were observational studies concerning vision impairment, 22% were observational studies concerning strabismus, and 19% were interventional studies. The studies that reported scores for depression, anxiety and those that included strabismus surgery were included in a meta-analysis. The meta-analysis showed that children with vision impairment have higher depression and anxiety scores than normally sighted children. Studies in which myopia was the cause of vision impairment showed significantly higher depression scores than children with normal vision. There was no difference in anxiety scores between children with myopia and those with other causes of vision impairment. The meta-analysis also showed that strabismus surgery significantly improved symptoms of depression and anxiety. The authors note that the main limitation was the heterogeneity of the studies included. The quality of most included studies was low to moderate, as most studies did not clearly describe sampling methods, did not report the definition of vision impairment, and used various tools to measure depression and anxiety. Despite these limitations, this study does help to emphasize the mental health impact of visual impairment and importance of treatment in strabismus patients.

Prevalence and Factors Related to Visual Impairments in Children With Bilateral Cataract Following Surgery and the Potential Need for Education and Rehabilitation Services

Claudia Yahalom, Moria Medezinsky Kochavi, Hadas Mechoulam, Evelyne Cohen, Irene Anteby

Journal of Visual Impairment & Blindness v116(1) pp61-69 2022

Pediatric cataract is a major cause for childhood visual impairment. The authors analyzed the prevalence of children with impaired vision (6/15 or worse) after surgery for bilateral cataract to evaluate factors associated with it and to emphasize the importance for visual rehabilitation including the use of visual aids, education, and social services. This retrospective study reviewed medical records from 55 children who underwent cataract surgery up to age 6 with follow-up of at least 4 years (median 6.8 years). Clinical characteristics studied included visual acuity, presence of nystagmus and/or strabismus, age at surgery, IOL implantation and others. Visual impairment was found in 62.5% of children operated on before 6 months of age and 22.5% in those operated after 6 months of age. Thirty-eight of 55 children had a primary IOL implantation. Nystagmus and microphthalmos were associated with higher rates of visual impairment. The authors conclude that despite early and modern surgery, long term visual outcomes remain poor in children undergoing bilateral cataract surgery at a young age. Discussions with parents regarding visual prognosis should recognize factors associated with visual impairment, such as need for surgery before six months, nystagmus and microphthalmos, and the importance for early visual rehabilitation services. Early referral for visual rehabilitation will optimize quality of life and may allow for a wider range of opportunities as adults.

Clinical Spectrum of Ocular and Visual Dysfunction in Children with Periventricular Leukomalacia: A Need for an Interdisciplinary Approach

Zeynep Kayaarasi Ozturker, Sezin Akca Bayar, Sibel Oto, Sibel Aksoy, Imren Akkoyun, Taner Sezer

Journal of Pediatric Neurology 2022; 20:97-102

This retrospective study evaluated the ocular motility and visual and optic disc abnormalities on children diagnosed with periventricular leukomalacia (PVL). Analysis of 51 consecutive children under 12 years old between 2008 and 2020 who had ophthalmic symptoms and were diagnosed with PVL by MRI was performed. The children were assessed for visual function, strabismus, cycloplegic refraction, fundus exam, and if appropriate, spectral domain OCT and visual field testing. Primary outcome measures were the prevalence and visual and ocular motility dysfunctions. Mean age was 5.72 years, median birth weight

was 2740 grams, and median gestational age was 34 weeks. Twenty-one patients (39.6%) had neurological deficit, 11 (21.5%) had intellectual disability, and 19 (37.2%) had no neurological symptoms. Manifest strabismus was present in 35 patients (68.6%; 12 had esotropia, 16 had exotropia, 6 had vertical deviation). Manifest or latent nystagmus was detected in 14 patients (27.4%). Twenty-eight patients had optic nerve abnormality (54.9%; 2 had hypoplastic disc, 14 had optic disc pallor, 7 had large cupping, 5 had total optic atrophy. Ten patients had ≥3.0D myopia, 15 had ≥3.0D hyperopia, and 8 had ≥2.5D astigmatism. Thirteen (25.4%) children had best-corrected vision (Snellen card) between 20/40 and 20/20, 9 (17.6%) had strabismic amblyopia and 6 (11.7%) had anisometropic amblyopia. Subjects able to perform visual field testing (6/51) all had abnormal visual fields with inferior fields being most affected. The authors conclude that 1) children born with PVL are at high risk for developing CVI; 2) strabismus, nystagmus, optic nerve abnormalities, and visual disturbances are the common clinical features of PVL and may sometimes be the only presenting sign; 3) routine ophthalmological screening should be beneficial for children with PVL.

5. NEURO-OPHTHALMOLOGY

The visual morbidity of optic nerve head drusen: a longitudinal review
Gise R, Heidary G
J AAPOS 2023;27:30.e1-5
A retrospective review of medical records of pediatric patients diagnosed with optic nerve head drusen (ONHD) at a single, tertiary care ophthalmology department from January 1, 2010 to July,1 2018 was conducted for causes of visual morbidity. A total of 213 patients met inclusion criteria. Mean age at diagnosis was 10.13 years, and mean follow-up was 2.76 years. Formal visual fields were available for 208 eyes. Repeatable visual field defects were noted in 24 eyes(11.5%). The most common defect was a nasal step, which occurred in 11 eyes (45.8%). Fifteen eyes had visual field defects at presentation, and 9 eyes developed field loss within 1.39 years of diagnosis. There was no correlation found between intraocular pressure and degree of visual field loss. Choroidal neovascular membranes (CNVM) were clinically apparent in 5 eyes and treatment was required in 3 eyes. Nonarteritic ischemic optic neuropathy developed in 2 eyes. The limitation of the study is that each patient was not followed in the same manner. It is important to note patients with ONHD may be associated with visual morbidity and follow up is warranted to counsel patients and to monitor for treatable disease such as CNVM.

Comparative analysis of immunosuppressive therapies for myelin oligodendrocyte glycoprotein antibody-associated optic neuritis: a cohort study.
Xie L, Zhou H, Song H, Sun M, Yang M, Lai YM, Xu Q, Wei S.
Br J Ophthalmol. 2022 Nov;106(11):1587-1595. doi: 10.1136/bjophthalmol-2020-318769.
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a newly recognized auto-antibody-mediated CNS inflammatory disorder, distinct from multiple sclerosis and aquaporin-4 antibody NMO spectrum disorder. There are no standardized attack-prevention regimens, so the authors sought to evaluate the therapeutic action of different immunosuppressants in a bidirectional cohort of 121 patients with MOG optic neuritis. Immunosuppressive therapy (IST) was defined as taking at least one of the following: low-dosage prednisone, azathioprine (AZA), mycophenolate mofetil (MMF), rituximab (RTX) infusion or regular intravenous immunoglobulins (IVIG). About half the cohort were women, and mean age was 17.5 years with median disease duration 34.8 months. Among the 61 children < age 18, 39% received IST at some point. The median age in the adult group was 31 years, and while there was no significant difference in number of relapses between the 2 groups, more adults were prescribed IST (38 vs 24). Pediatric patients were more commonly treated with rituximab, while adult patients were more likely to be treated with mycophenolate mofetil. Patients with IST for at least 6 months were associated with a lower risk of relapse both in the pediatric and adult group. Notably, however, only 46.0% of patients in the no-IST group suffered a relapse attack at a median follow-up of 33.5 months, so the authors suggest that observation after a single attack remains a rational option.

Visual outcomes in idiopathic intracranial hypertension in children.
Chiu HH, Reginald YA, Moharir M, Wan MJ.
Can J Ophthalmol. Dec 2022;57(6):376-380. doi:10.1016/j.jcjo.2021.06.009

This is a retrospective cohort study of consecutive children who met the diagnostic criteria for IIH between 2009 and 2020. The goal is to report the visual outcomes. One hundred ten patients were included. Patients were divided into three groups by age. Prolonged papilledema was defined as papilledema greater than 12 months while on treatment. Recurrence was defined as signs or symptoms of elevated ICP that required re-initiation of treatment. The primary outcome measure was long-term visual outcomes – mild was defined as 20/40-20/80, and severe as 20/100 or worse. Mild visual field loss as -3 to -7 dB on 24-2 and severe ・ 7 dB. Only children with a detailed visual exam after completion of treatment with resolution of papilledema. Younger patients were less likely to present with headaches and more likely to present with no symptoms of high ICP (both significant). The BMI was normal in children, high-normal in early adolescents, and in the obesity range in later adolescents. Visual outcomes were available for 90 patients. 91% retained normal vision, while the rest had mild visual impairment. OCT data were available for 62 patients; however, the difference between OCT at presentation and after the resolution of papilledema was not statistically significant. The only risk factor for long-term visual impairment was greater severity of papilledema at presentation.

Visual Outcomes of Optic Pathway Glioma Treated With Chemotherapy in Neurofibromatosis Type 1.
José P, Couceiro R, Passos J, Jorge Teixeira F.
J Pediatr Ophthalmol Strabismus. 2022;59(2):128-135. doi:10.3928/01913913-20210720-02
This two-center retrospective cohort study of 58 children with NF1-associated OPG sought to analyze visual outcomes following chemotherapy w/ vincristine and carboplatin (2003-2016) and/or vinblastine (2017 onwards). Of the 58 children, 24 (41%) received chemotherapy. The median age at diagnosis was 3 years, and 61% of the children were female. From the first visit to the last follow-up visit, there was a statistically significant difference in mean BCVA in eyes in the no treatment group (P = .034) but not in eyes in the chemotherapy group (P = .824). A moderate and weak positive correlation was found (r = 0.58 and r = 0.29, respectively). At the last follow-up visit, BCVA remained stable in 73% and improved in 27% of eyes in the no treatment group, and BCVA worsened in 25%, remained stable in 62%, and improved in 13% of eyes in the chemotherapy group. At the last follow-up visit, BCVA and Dodge stage had a weak negative correlation (r = -0.06 and r = -0.17, respectively). A negative moderate correlation was identified between RNFL thickness and BCVA at the last follow-up visit (r = -0.48 in the no treatment group and r = -0.46 in the chemotherapy group). The authors concluded that children treated with chemotherapy had worse BCVA, although the treatment arrested the decline or improved BCVA in 75% of patients with no major side effects. The authors concede a number of limitations, including: retrospective design, lack of baseline ophthalmic data on some patients, and non-randomized intervention. For these reasons, the results lack generalizability and would benefit from further validation.

Ophthalmological Findings in Youths with a Newly Diagnosed Brain Tumor
Myrthe A. Nuijts, MD; Inge Stegemean, PhD; Tom va Seeters, MD, PhD; et al
JAMA Ophthalmology, October 2022; 140(10):982-993.
This is a cohort study of 170 Dutch patients aged 0 to 18 years with a newly diagnosed brain tumor, enrolled from 4 hospitals in the Netherlands. Children underwent a comprehensive ophthalmology exam within 4 weeks of brain tumor diagnosis, including an orthoptic evaluation. Visual fields were performed on all patients, which were interpreted by two ophthalmologists who were blinded to patient details. Ophthalmologic examination revealed abnormal findings in 134 of 170 patients (78.7%). At the time of diagnosis, 69 patients did not report visual symptoms. Of the patients without symptoms, 45 (65.2%) had abnormal ophthalmologic findings. The most prevalent ophthalmological abnormalities in youths at brain tumor diagnosis were papilledema (52.4%), gaze deficits (33.5%), visual field defects (28.1%), nystagmus (24.8%), strabismus (19.9%), and decreased VA (8.6%). These findings emphasize the importance of standardized ophthalmological evaluation at brain tumor diagnosis regardless of tumor location because timely detection of vision loss and subsequent early referral for visual rehabilitation therapy may be associated with improvement in regaining mobility, activities of daily living, and quality of life among youths with visual impairment.

6. NYSTAGMUS
Demographic and Clinical Characteristics of 600 Children With Nystagmus

Hertle RW, Evliyaoglu F, McRitchie B.
J Pediatr Ophthalmol Strabismus. 2022;1-5. doi:10.3928/01913913-20221026-02
This single-center, prospectively developed database sought to characterize nystagmus in a large, international cohort of 600 patients from 38 states and 30 countries aged from birth to 18 years. The authors found that: 58% were female, 55% were race other than White, 75% had infantile nystagmus syndrome, 17% had neurologically significant nystagmus, 7% had fusion maldevelopment nystagmus syndrome, 64% had strabismus, 56% had an anomalous head posture, 94% had a significant refractive error, 64% had an associated ophthalmic abnormality (excluding ametropia), and 45% had an associated systemic condition. Special testing showed abnormalities in 67% and 95% had treatment directed at their nystagmus. The authors concluded that infantile nystagmus syndrome was most common, and that eye movement recordings should be used to aid in accurate diagnosis and classification. provide a path toward accurate diagnosis and classification. One limitation was the absence of genetic testing.

7. Prematurity - none

8. Retinopathy of Prematurity

Structural and refractive outcomes of intravitreal ranibizumab followed by laser photocoagulation for type 1 retinopathy of prematurity.
Hoppe C, Holt DG, Arnold BF, Thinda S, Padmanabhan SP, Oatts JT.
J AAPOS. 2022 Dec;26(6):305.e1-305.e6.
Treatment for retinopathy of prematurity (ROP) has a long history of evolution which continues today. Cryotherapy, laser photocoagulation and now anti-vascular endothelial growth factor (anti-VEGF) have all been identified by studies as effective treatments. Current therapy includes early laser photocoagulation and/or anti-VEGF injections. Some studies show a higher prevalence and severity of myopia in infants treated with laser compared to anti-VEGF. This fact, as well as the thought that laser may be more stressful to the infant leads some to advocate for anti-VEGF injection over laser photocoagulation especially for posterior disease. There is still controversy concerning details surrounding ideal anti-VEGF treatment use (dosing, timing, systemic consequences, and risk of recurrence and reactivation, etc). The authors use retrospective review to evaluate refractive and structural outcomes for patients with Type 1 ROP treated with anti-VEGF and delayed laser defined as any laser treatment administered at least 2 weeks and less than 1 year after the initial anti-VEGF treatment of ranibizumab. All patients were initially treated with intravitreal ranibizumab for Type 1 ROP. The timing of delayed laser treatment was scheduled after any reactivation was identified. The authors demonstrate that combined anti-VEGF ranibizumab and delayed laser therapy resulted in satisfactory refractive and structural outcomes for their cohort at 2 years of age. Authors postulate that initial anti-VEGF treatment allows for additional retinal vascularization while subsequent delayed laser photocoagulation provides for definitive treatment truncating the period of observation monitoring for late reactivation. Refractive outcomes in this cohort gave a mean spherical equivalent (SE) of -1.09 D. Prevalence of strabismus in this cohort was 32% consistent with previously reported outcomes. Prevalence of amblyopia in previous studies after ROP laser is reported as 5-10%. The authors note a 19% frequency for amblyopia in their cohort and postulate it is related to extremely low birth weight compared with other studies. Limitations of the study include small sample size and 2-year follow-up. Larger randomized trials are still necessary to evaluate monotherapy vs combination therapy.

G-ROP criteria for predicting retinopathy of prematurity among neonates with different birth weight percentiles
Asli Okbay Gunes, Sevilay Topcuoglu, Gokhan Celik, Osman Kizilay, Muhammed Ali Recai, Akyurekli, Nilgun Karadag, Elif Ozalkaya, Guner Karatekin
J AAPOS.2022 Dec;26(6):309.e1-309.e5.
The Postnatal Growth and Retinopathy of Prematurity (G-ROP) Study showed that adding postnatal weight gain to birth weight and gestational age detected 100% of cases with type 1 retinopathy of prematurity (ROP) while reducing the ROP examinations by 30%. Current ROP screening guidelines have high sensitivity for detection of ROP but poor specificity for treatment-requiring ROP (TR-ROP). In order to reduce the number of exams for infants and make better use of resources, the addition of suboptimal weight gain has been suggested to be added to predictive models. Small for gestational age infants are at greater risk for suboptimal postnatal growth factor. The authors sought to determine if SGA

status affected the sensitivity and specificity of the G-ROP model. The authors found sensitivity of G-ROP for predicting any stage of ROP was lower for their cohort but the sensitivity for predicting TR-ROP was excellent (100%). Authors postulate this may be explained by epidemiologic factors. The number of exams was reduced by 25%. Several perinatal morbidities are significantly associated with TR-ROP. When these were added to the model, sensitivity increased as well as the number of infants to be examined. Care must be taken to not generalize these results to low-income countries where TR-ROP incidence is higher and ROP occurs in more preterm infants until more research is conducted to test the G-ROP model in these countries.

Ketamine Analgesia as an Alternative to General Anesthesia During Laser Treatment for Retinopathy of Prematurity.
Sanatkar M, Dastjani Farahani A, Bazvand F.
J Pediatr Ophthalmol Strabismus. 2022;59(6):416-421. doi:10.3928/01913913-20220225-01
This small study sought to determine the safety and efficacy of ketamine analgesia as an alternative to general anesthesia during laser treatment for retinopathy of prematurity (ROP). 18 premature neonates undergoing laser treatment were administered 1 mg/kg of ketamine. If the neonate exhibited movement or distress during the procedure, incremental doses of ketamine were administered. Perioperative ventilation status, severity of pain during the procedure, surgeon satisfaction, and perioperative events were recorded. 16/18 patients tolerated sedation without events. The Premature Infant Pain Profile (PIPP) scores during the procedure were 5 or less in 12 neonates (44.4%), 5 to 10 in 4 neonates (22.2%), and greater than 10 in 2 (11.1%) neonates. Three neonates had perioperative events, which resolved completely with minimal intervention. None of the neonates needed intubation perioperatively, and hemodynamic instability, hypotension, and bradycardia were not recorded in any of the neonates during or after the procedure. The authors concluded that ROP laser treatment could be performed under ketamine sedation with few perioperative complications, and perhaps even in the NICU. Albeit small, this was an interesting study raising the possibility of shorter procedure times in more convenient clinical environments.

Characterization of Errors in Retinopathy of Prematurity Diagnosis by Ophthalmologists-in-Training in the United States and Canada
Al-Khaled T, Patel SN, Valikodath NG, et al.
J Pediatr Ophthalmol Strabismus. 2022;1-7. doi:10.3928/01913913-20220609-01
This prospective cohort study of 32 ophthalmologists-in-training at 6 training centers in the US and Canada sought to identify factors that lead to misdiagnosis of ROP. They were presented 20 web-based cases of ROP using wide-field retinal images, and they were asked to diagnose plus disease, zone, stage, and category for each eye. Responses were compared to a consensus reference standard diagnosis for accuracy. The authors found that the category of ROP was misdiagnosed at a rate of 48%, and that classification of plus disease was most commonly associated with misdiagnosis of treatment-requiring and type 2 or pre-plus disease. The diagnostic error rate of postgraduate year (PGY)-2 trainees was significantly higher than PGY-3 trainees. The authors concluded that integration of structured learning for ROP in residency education may improve diagnostic competency - a point which reinforces the need for fellowship training in diagnosis and management of ROP.

Association of Optical Coherence Tomography-Measured Fibrovascular Ridge Thickness and Clinical Disease Stage in Retinopathy of Prematurity.
Thanh-Tin P. Nguyen, MD; Shuibin Ni, MS; Susan Ostmo, BS; et al.
JAMA Ophthalmol. 2022; 140(11):1121-1127.
This is a cross-sectional longitudinal study which compared OCT-based ridge thickness calculated from OCT B-scans by a masked examiner to the clinical diagnosis of 2 masked examiners using traditional ROP stage classifications. The goal was to evaluate whether optical coherence tomography (OCT)–derived retinal thickness measurements at the vascular-avascular junction are associated with clinical diagnosis of ROP stage. A total of 128 separate OCT examinations from 50 eyes of 25 patients were analyzed. Higher disease classification was associated with higher axial ridge thickness on OCT, with mean (SD) thickness measurements of 264.2 (11.2) μm ($P < .001$), 334.2 (11.4) μm ($P < .001$), and 495.0 (32.2) μm ($P < .001$) for stages 1, 2, and 3, respectively. They also fond a decrease in ridge thickness following treatment with bevacizumab. These results suggest that OCT-based quantification of peripheral

stage in ROP may be an objective and quantitative biomarker that may be useful for clinical diagnosis and longitudinal monitoring and may have implications for disease classification in the future. Despite the presence of standard photographs for instruction and comparison, there is inter observer variability for all components of the ICROP classifications due to a variety of factors (difficulty of examination, training differences). While not yet widely available, these results suggest that OCT may one day be used for ultra-widefield anatomic staging of ROP, more precisely characterizing the degree and extent of peripheral pathology. OCT is also superior to the ophthalmoscopic examination for identifying early vitreoretinal traction, which means surgical intervention could be timed early to prevent retinal detachments.

Rate of and time to complete retinal vascularization in premature infants and associated factors
Lai TT, Yang CM, Hsieh YT, Yeh PT, Huang CW, Tsai CY. Retina 43(1):p 102-110, January 2023. | DOI: 10.1097/IAE.0000000000003627
There is ongoing debate regarding management of babies with persistent avascular retina (PAR) after retinopathy of prematurity, and the authors argue that more longitudinal data is needed on vascular growth and time to complete vascularization in order to further clarify growth patterns and define PAR. They retrospectively reviewed the eye exams of all babies screened for ROP at the National Taiwan University Hospital over a 3-year period and documented time of complete vascularization. A total of 490 babies had complete records of retinal vascularization outcomes, of whom 439 (89.6%) achieved complete vascularization at an average age of 45.39 weeks gestational age. In babies who fully vascularized, 95% had vascularized by 64 weeks gestational age. ROP developed in 118 infants (22.6%), 33 of whom (6.10%) received anti-VEGF injections. Of the 51 babies who did not fully vascularize, 25 had received anti-VEGF injections (representing 83% of their anti-VEGF treated eyes), 25 had developed ROP that did not require treatment, and 1 had no history of ROP. No infant with incomplete vascularization required surgical intervention during the study period. Lower birthweight and history of anti-VEGF injection were the only two predictors of incomplete vascularization.

The time and financial ramifications of providing services for retinopathy of prematurity at a single inner-city institution in the United States: a pilot study.
Hawn VS, Muhtadi R, Oliviera J, Suman P, Quinn G, Mian U.
J AAPOS. 2022 Jun;26(3):135.e1-135.e4.
As the survival of premature infants increases, the demand for ROP screening and treatment will increase accordingly. ROP may result in blindness and requires a regimented schedule and timing to prevent vision loss. Inpatient reimbursement rates, time away from outpatient clinic and surgery, travel time, inadequate assistance by NICU staff, unpredictability of time in NICU and travel, as well as liability and malpractice are all “costs” to those limited and decreasing numbers of pediatric ophthalmologists that screen for ROP. The authors of this study sought to evaluate the time required for ROP services and to approximate compensation to better understand the implications of providing the necessary ROP screening and treatment. The data presented by the authors shows a substantially negative profit margin for both screening and treatments using average annual costs and margins for inpatient ROP activity despite ROP screening being a highly cost-effective way to significantly decrease ocular morbidity and blindness for this population. With the ever-increasing population of premature infants who will need to be screened, it is imperative to structure reimbursement in a more transparent and equitable method to incentivize providers to perform this necessary work. The importance of this article goes beyond pediatric ophthalmology and should be shared with our neonatology colleagues as well as hospital administrators to help them understand the true “work” associated with providing ROP services.

Artificial Intelligence for Retinopathy of Prematurity: Validation of a Vascular Severity Scale against International Expert Diagnosis.
Campbell JP, Chiang MF, Chen JS Collaborative Community in Ophthalmic Imaging Executive Committee and the Collaborative Community in Ophthalmic Imaging Retinopathy of Prematurity Workgroup. Ophthalmology. 2022 Jul;129(7):e69-e76. doi: 10.1016/j.ophtha.2022.02.008. Epub 2022 Feb 12. PMID: 35157950; PMCID: PMC9232863.

The purpose of this study was to compare the validity of the vascular severity score as an output of the ROP AI software as a medical device(SAMD) compared to an expert group of clinicians. The goal was to determine whether the current algorithm which was based on a reference standard diagnosis of a small group of experts reflects the broader community of ROP assessment of plus disease and overall severity. The study compared clinical diagnostic labels for stage 1 to 3 and plus disease assigned by the ICROP3 committee with the output of the i-ROP to investigate the clinical validity, of the vascular severity score. Images were classified by the ICROP3 clinicians for a score of 1-9 for plus datasets and similar classification for stage classification. The images were also labeled with deep learning-derived scores from the i-ROP DL algorithm and automated vascular severity scores from 1-9 were assigned. In the ICROP group there was variability on agreement of plus except at the extremes of the spectrum and for the stage dataset there was more variability in stage 1 and 2 ROP. Key findings were that the deep-learning derived quantitative vascular severity score correlated well with the expert labels of plus disease and diagnosis of peripheral stage. In addition, although ROP stages and plus were represented ordinally, it was found that most experts diagnosed on a continuum which may suggest that a quantitative vascular severity score(VSS) may be appropriate output for ROP SaMD. The ICROP data acknowledges that preplus and plus disease run a spectrum and clinical judgment needs to be applied to treatment decisions. It is important that minimal acceptable criteria have not yet been established such as improved clinical diagnostic performance with an assistive device compared with the reference standard. These criteria need to be higher in autonomous devices given the potential morbidity of missed diagnosis. The authors conclude that the study demonstrates that both plus and stage are a continuum and can be quantified using deep learning. This is one potential application to move from qualitative vs quantitative diagnosis. The use of ROP SaMD for treatment decisions will need validation in a clinical trial setting. If this can be accomplished it could have a significant impact on blindness secondary to ROP in the future especially in developing countries.

9. Strabismus

Application of Soft Directional Prismatic Contact Lenses to Correct Diplopia [published online ahead of print, 2022 Sep 14].
Parolini B, Penzani R, Pascotto P.
J Pediatr Ophthalmol Strabismus. 2022;1-5. doi:10.3928/01913913-20220727-01
This small prospective study sought to verify whether diplopia d/t strabismus <8PD could be corrected with soft contact lenses containing directional prismatic correction. The authors enrolled patients with vertical and/or horizontal diplopia. The patients underwent a complete examination and then had custom contacts made of Benz G5X material - developed for this study. All patients were first corrected with prismatic glasses, and then they were asked to wear custom-made directional prismatic contact lenses. Only 8 patients, but the soft directional prismatic contact lenses resolved diplopia in 100% of patients and all patients reported greater comfort and quality of vision with directional prismatic contact lenses. The authors concluded that strabismus within 8 PD could be corrected through the use of soft directional prismatic contact lenses, obtaining greater quality of vision free of aberrations, though the maximum deviation corrected was 6 PD in total, and up to 3.5 PD in one eye. If repeatable in a larger cohort, this is an exciting development in the management of microstrabismus amounts patients who cannot or will not wear glasses.

Vertical Comitance of Hypertropia in Congenital and Acquired Superior Oblique Palsy
Demer JL
J Neuroophthalmol. 2022;42(1):e240-e247
Differentiating congenital from acquired superior oblique (SO) palsy is an important clinical distinction that is not always obvious. Recently, some have posited that hypertropia (HT) greater in upgaze (compared to downgaze) is characteristic of decompensated, congenital SO palsy and is never present in acquired (e.g., ischemic, traumatic, or tumorous) SO palsy. This study seeks to test the validity of this assertion. The author begins by rigorously defining a “SO palsy,” a label he suggests has been used too broadly to describe all manner of vertical deviations. To accomplish this, the study defines a SO palsy as a “disorder of the trochlear nerve causing contractile deficiency of the SO muscle,” as demonstrated by subnormal

ipsilesional SO size on MRI. In this manner, the paper attempts to avoid the confounding data that would come with the inclusion of vertical deviations that mimic – but are not truly – SO palsies.
Using this criterion, the author identifies cases of cyclovertical strabismus in which of unilateral atrophy of the SO belly was confirmed on MRI. After exclusion criteria are applied, we are left with 9 patients with unequivocal history of congenital onset SO palsy ("congenital"), 7 with unequivocal acquired onset ("definite acquired"), and 14 with new SO palsy but no obvious etiology or inciting event ("progressive acquired").
On average, HT was 8.4D less in upgaze than downgaze in congenital and 3.7D less in the pooled group of acquired SO palsy. Only 3 of 9 (33%) cases of congenital SO palsy met the proposed criterion of HT greater in upgaze than downgaze; however, 9 of 22 cases (41%) of acquired SO palsy met this criterion, including 2 of 7 definite acquired cases.
Thus, in this group of patients with SO palsy confirmed by atrophy of the ipsilesional SO belly on MRI, HT was not characteristically greater in upgaze than downgaze in congenital SO palsy. This refutes the previously proposed statement that HT greater in upgaze than downgaze is characteristic of congenital SO palsy. It is suggested that ophthalmologists not rely solely on this exam finding to differentiate congenital and acquired SO palsy.

Association between near viewing and acute acquired esotropia in children during tablet and smartphone use Esther Van Hoolst, Liesbet Beelen, Ivo De Clerck, Louise Petit, Irina Balikova, Ingele Casteels, Maria Dieltiëns & Catherine Cassiman. Department of Ophthalmology, University Hospitals Leuven, Leuven. Strabismus 30:2. 59-64
In this study, they investigated a possible association between the acute onset of esotropia and tablet or smartphone use in children. They characterized the clinical aspects of esotropia associated with tablet or smartphone use. The medical records of 10 children aged between 5 and 15 years old with presumably tablet or smartphone associated esotropia were reviewed regarding orthoptic examination and cycloplegic refraction. Legal guardians of the children were asked to fill in a questionnaire regarding tablet and smartphone use of their child. This questionnaire was also conducted in a control group of age-matched children. The results of this questionnaire were compared to search for possible determinants of tablet or smartphone associated esotropia. All 10 patients presented with a comitant esotropia ranging from 8 to 45 prism diopters with no significant difference between near and far. The mean age of onset was 9.8 years. Cycloplegic refraction showed a mild hyperopia in eight patients, a mild myopia in one patient and emmetropia in the other patient. All patients had near full refractive correction at the onset of esotropia. Diplopia was reduced after visual hygiene recommendations, however in six patients, strabismus surgery was needed. The working distance was significantly shorter in the 10 cases compared to the controls. In children with acute acquired esotropia, They found a statistically significant association with a smaller working distance during tablet or smartphone use compared to age-matched controls. They hypothesize that intensive near viewing can be a precipitating factor in this type of esotropia.
Limitations of our study are the small heterogeneous case group of ten AACE patients with a known excessive smartphone or tablet history, and the fact that the questionnaire for the control group was conducted with children visiting the ophthalmology department at University Hospital Leuven. These results thus do not entirely represent tablet and smartphone use in the normal population, although it can be assumed that this is only a limited bias. Further, the working distance was not measured by the investigators and depended on the assumption of the parents. It is important to note that the statistical analysis demonstrates an association between working distance and esotropia, however this does not prove a causal relationship. The control group is larger than needed given that no power calculation was performed before onset of the study. However, in studies where cases are limited, a larger control-to case ratio might increase statistical power and does not affect further statistical analysis.

Utilising Virtual Clinics and Orthoptists to Aid COVID-19 Service Recovery in Adult Strabismus.
Francis JE, Rhodes M, Simmons J, Choi J. Utilising Virtual Clinics and Orthoptists to Aid COVID-19 Service Recovery in Adult Strabismus. Br Ir Orthopt J. 2022 Nov 7;18(1):144-151. doi: 10.22599/bioj.273. PMID: 36420120; PMCID: PMC9650973.
This prospective data analysis utilized data from virtual strabismus clinics from January 2015 to November 2021 to assess how effective strabismus services involving orthoptists as the first consultant was during the pandemic. The care pathway involving all new referrals to adult strabismus being seen

first by orthoptist and then being triaged to either an orthoptic clinic for non-surgical management, doctor for test results and surgical management, or discharge. During the pandemic, this pathway was adapted to involve telephone consultation with the orthoptist prior to in person evaluation with orthoptist. The following orthoptist visits or doctor's clinic visit were either in person or telephone consultation. With this adapted workflow, mean wait times during pandemic was 10.9 weeks compared to 21 weeks when service re-opened in July 2020. In person consultation for non-surgical cases dropped from 47.7% to 16.3%. With this modified pathway, 24.6% of patients were signed up for procedures after only the first visit. This study highlights how modifications made during COVID in many clinical pathways has improved efficiency and accessibility to care in the NHS. The limitation of this study is that it may not be applicable in the United States or other countries depending on the infrastructure of healthcare and payor systems.

Factors associated with the effectiveness of part-time patching for intermittent exotropia in children.
Choi H, Kim SJ, Jung J, Lee JE, Kim SY, Lee SU.
Eur J Ophthalmol. 2022 Jul;32(4):2026-2033.
This is a prospective observational study, in which 186 patients diagnosed with IXT were enrolled. Outcome measures included office-based control scales, magnitude of exo-deviation, and stereoacuity at near and distance after daily patching for 2 hours. We analyzed the clinical data and demographic factors association with improvement of IXT. The study was completed by 152 subjects of total enrolled patients who were followed for 1 year. Decrease in the magnitude of exo-deviation, improvement of control, and or gain of stereoacuity were observed in 31.6% patients of the recruited subjects after part-time patching. Multivariate analyses showed that prognostic factors determining improvement to part-time patching included convergence insufficiency (CI) type IXT ($p = 0.016$), poor distance stereopsis ($p = 0.044$), and large exotropic deviation at distance ($p = 0.025$). The authors conclude that CI-type exotropia, large distance magnitude of exo-deviation, and poor distance stereopsis may be associated with a better response to part-time patching, which can be a useful non-surgical treatment alternative to delay surgery in these cases.

10. Strabismus surgery

Diclofenac Versus Corticosteroids Following Strabismus Surgery: Systematic Review and Meta-analysis.
Karam M, Alsaif A, Al-Naseem A, et al.
J Pediatr Ophthalmol Strabismus. 2022;1-11. doi:10.3928/01913913-20221011-01
This meta-analysis reported outcomes of diclofenac vs corticosteroids following strabismus surgery, specifically: discomfort, chemosis, inflammation, conjunctival gap, intraocular pressure, and conjunctival injection and, secondarily, conjunctival congestion, discharge, and drop intolerance. They found 8 studies with a total sample of 469 eyes. At weeks 1 and 4 postoperatively, there were no statistically significant differences between the diclofenac and corticosteroid groups, except for conjunctival injection at week 1 favoring diclofenac. At week 2, all primary outcomes favored diclofenac. Conjunctival congestion was significantly improved for dexamethasone, whereas discharge and drop intolerance was not statistically different. The authors concluded that diclofenac is comparable to various corticosteroids when used following strabismus surgery and that it yielded significant improvements in discomfort, conjunctival chemosis, inflammation, conjunctival gap, intraocular pressure, and conjunctival injection, mainly at 2 weeks postoperatively. Although this meta-analysis, its results are worth studying in a prospective, controlled manner given potential implications for practice change across the field.

Effect of Modified Vertical Rectus Belly Transposition vs Augmented Superior Rectus Transposition Plus Medial Rectus Recession for Chronic Sixth Nerve Palsy: A Randomized Clinical Trial
Jing Yao MD, Chao Jiang MD, Xiying Wang MD
JAMA Ophthalmol. Published online August 4, 2022
The goal of this was to examine if modified vertical rectus belly transposition plus medial rectus recession (mVRBT-MRc) is more effective than augmented superior rectus transposition plus medial rectus recession (aSRT-MRc) for Chinese patients with chronic sixth nerve palsy. The main outcome was the change of horizontal deviation in primary position from baseline to 6 months. 25 patients were enrolled in this parallel design, double-masked, single-center randomized control study from January 2018 to May 2021 and randomly assigned to the VRBT group or the SRT group. The baseline main horizontal

deviation was 65.7 PD in the VRBT group and 60.5 PD in the SRT group. Similar amounts of MRc were performed in each group. At 6 months, more esotropia was corrected in the VRBT group than in the SRT group, favoring the VRBT procedure. Four times as many participants in the VRBT group than in the SRT group had more than 60Δ of esotropia corrected. Correspondingly, no VRBT participant was undercorrected, whereas 5 SRT participants (45%) had residual esotropia of more than 10Δ and needed additional treatments. Of these undercorrected participants, 4 had a preoperative esotropia of more than 60Δ. Based on these results, mVRBT-MRc was found to be superior to aSRT-MRc in patients with large esotropia of more than 60Δ.

Comparison of Unilateral and Bilateral Surgical Approaches for the Treatment of Age-Related Divergence Insufficiency Esotropia.
Bunyavee C, Archer SM, Wu CY, Del Monte MA.
J Binocul Vis Ocul Motil. 2022 Oct-Dec;72(4):205-211. Epub 2022 Aug 29. PMID: 36037434.
This retrospective study was conducted at the Kellogg Eye Center at the University of Michigan and involved 62 cases of involutional divergence insufficiency esotropia to compare unilateral medial rectus recessions (n=24), unilateral recession-resection with adjustable suture (n=18) and bilateral medial rectus recession with fixed sutures (n=20). Between the first and the last group, postoperative distance deviations were not statistically different for those with distance esodeviation<15PD. If deviation was greater , 15-20PD, postoperative distance deviations in all groups were statistically different. The second group of patients had the highest overall success rate. The study group concluded that unilateral medial rectus recession with or without lateral rectus resection and bilateral medial rectus recessions produced similar results. The limitation of this study was that it was retrospective, and multiple surgeons were involved. Decision to pursue one surgical approach to another could have affected outcome.

Non-absorbable versus Absorbable Sutures for Medial Rectus Advancement in Consecutive Exotropia, a Pilot Randomized Clinical Trial.
Akbari MR, Veisi A, Mirmohammadsadeghi A.
J Binocul Vis Ocul Motil. 2022 Jul-Sep;72(3):139-146.
This was a pilot randomized clinical trial of 40 subjects with consecutive exotropia who underwent unilateral medial rectus advancement with or without resection to compare non-absorbable and absorbable sutures. Thirty-three patients (18 in the non-absorbable and 15 in the absorbable group) had completed the study. The amount of the final correction of the distance and near deviation was not statistically different between the groups (P = .80 and P = .99, respectively). At the final examination, the exoshifts for distance and near were not statistically different between 2 groups (p = .61 and 0.54, respectively). At the final examination, the success was obtained in 12 patients (66.7%) and 8 patients (53.3%) in the non-absorbable and absorbable group, respectively (p = .73). The results of this study confirms the suspicion of many surgeons that absorbable sutures which are less prone to causing inflammation can be used instead of non-absorbable sutures when advancing muscles for consecutive strabismus.

Postoperative diplopia test—repeatability and prediction of surgical outcomes.
Laura Catherine Jane Jarwick, BMedSci, MMedSci, Kate Taylor, BSc, Alan John Connor, FRCOphth, and Caroline Sarah Fieldsend, BMedSci.
JAAPOS 2022;26:252.e1-5.
The postoperative diplopia test (PODT) is a preoperative test used to investigate the risk of diplopia developing after surgery. It is used in patients without the potential for binocular single vision considering nonfunctional strabismus surgery. The first purpose of this study was to evaluate the test-retest and interobserver reliability of the PODT method. The second purpose was to investigate the predictive value of the test for assessing risk for postoperative diplopia. More than half of the patients showed consistent results with repeated PODT testing; however, some patients showed substantial variability between tests, including some who reported diplopia on one instance of PODT but had no diplopia on the other PODT. As for post-operative diplopia, among patients who reported no diplopia over the range tested on PODT, none had persistent diplopia after surgery. Among 14 patients who experienced diplopia during PODT, 2 had persistent diplopia at 3 months post-op. Four patients with diplopia on PODT were within their suppression zone postoperatively, and 3 of these (75%) experienced no persistent diplopia, as predicted; 5 were predicted to be outside of their suppression zone postoperatively, yet 4 of these (80%)

experienced no persistent diplopia. Thus, the additional predictive value of suppression zones in the presence of any diplopia on PODT appears questionable. The study suggests that further testing with PAT or botulinum toxin injection could be used to better stratify risk in patients who do have diplopia on PODT. I think the most important thing this study points out is that the risk of intractable diplopia after nonfuctional strabismus surgery is rare but possible. It is very important to adequately counsel patients about the risk, especially if they have any diplopia on PODT.

11. Anterior Segment - none

12. Cataract - none

13. Cataract surgery - none

14. Glaucoma

Agreement of iCare IC200 tonometry with Perkins applanation tonometry in healthy children.
Theo Stoddard-Bennett, BS, Nicholas J. Jackson, MPH, PhD, Laura Robbins, OD, Phillip Villanueva, CO, Soh Youn Suh, MS, MD, Joseph L. Demer, MD, PhD, Stacy L. Pineles, MS, MD, and Simon S. M. Fung, MD, FRCOphth.
JAAPOS 2022;26:235.e1-5.
The purpose of this study was to assess the interdevice agreement between the iCare and Perkins applanation tonometry in pediatric patients. Forty-two children were included in the study. Each participant underwent IOP measurement using both the iCare and Perkins tonometers. The order of tonometers was randomized. After IOP was obtained using both devices, the central corneal thickness was measured. The mean difference between the iCare and Perkins tonometers was +0.72 mmHg. The iCare-Perkins difference was >2 mmHg in 35.7% and <2 mmHg in 9.52%. Absolute agreement between the tonometers was 0.63. The study found no significant correlation between CCT and the mean IOP measured by iCare or Perkins tonometry. CCT was also not associated with differences in IOP between the two tonometers. This study is important given the advantages to using rebound tonometry in a pediatric population. Given that the mean absolute difference between the tonometers was <1 mmHg in healthy children, the authors recommend the use of iCare in nonglaucomatous children. They caution that IOP readings that suggest glaucoma should be rechecked with Perkins tonometry.

Pediatric glaucoma suspects: characteristics and outcomes.
Stephanie N. Kletke, MD, FRCSC, Monte D. Mills, MD, Lauren A. Tomlinson, BS, Yinxi Yu, MS, Gui-shuang Ying, PhD, and Gil Binenbaum, MD, MSCE.JAAPOS 2022;26:236.e1-6.
The purpose of this study was to determine the characteristics and outcomes of pediatric glaucoma suspects (GS) and to evaluate the risk factors for progression to glaucoma. While GS status is well studied in the adult literature, there is a dearth of knowledge in the pediatric literature. This study aims to fill that gap. A retrospective sequential cohort study was conducted at the Children's Hospital of Philadelphia. Children were considered glaucoma suspects based on at least one and no more than 3 of the following criteria: optic nerve appearance, ocular hypertension, family history of glaucoma/GS, periocular lesion associated with glaucoma, systemic or genetic association, history of blunt ocular trauma, or other ocular anomalies. A total of 887 children met the criteria and were included in the study. For children who had at least one follow-up exam, 14 (2.9%) converted to a diagnosis of glaucoma, 324 (67%) kept their status as a glaucoma suspect, 148 (30%) were considered to have pseudoglaucomatous or physiologic cupping, and 1 (0.2%) developed treatment-requiring ocular hypertension. Baseline IOP > 24 mmHg and presence of a periocular lesion were associated with a higher risk for progression to glaucoma; however, baseline CDR and family history of glaucoma were not. This is an important study as it looks to identify potential risk factors for glaucomatous progression in pediatric GS. As this makes up a big part of a pediatric ophthalmologist's practice, future studies looking to help develop guidelines for management of these patients would be very helpful.

Topical netarsudil 0.02% as adjunctive therapy in refractory pediatric glaucoma

Abdelrahman M Elhusseiny, Javaneh Abbasian
J AAPOS. 2022 Dec;26(6):300.e1-300.e5.
The authors used retrospective review to evaluate the efficacy of topical netarsudil 0.02% as adjunctive therapy in children with refractory pediatric glaucoma. Pediatric glaucoma is most often treated surgically. Glaucoma medications are necessary to temporize until surgical intervention can occur or when intraocular pressure (IOP) cannot be controlled. The mechanism of action is inhibition of the Rho kinase signaling pathway improving aqueous outflow through trabecular meshwork. A total of 21 eyes of 16 patients were included in cohort with a history of previous glaucoma surgery and multiple medications prior to starting netarsudil. The IOP was significantly reduced from 26.3 ± 6.2 mm Hg before topical netarsudil to 19.6 ± 6.02 mm Hg at 1 month in 15 eyes ($P < 0.01$), 18.2 ± 6.9 mm Hg at 3-months in 18 eyes ($P < 0.01$), 18.3 ± 7.3 mm Hg at 6 months in 13 eyes ($P = 0.01$), 17.6 ± 5.07 mm Hg at 9 months in 14 eyes ($P = 0.002$), and 17.4 ± 3.1 mm Hg at 12 months in 13 eyes ($P = 0.002$). Additional glaucoma surgery was required in 43% of eyes due to failure of topical netarsudil to reduce IOP despite initial decrease. One eye had persistent elevation despite addition of topical netarsudil. Common adverse ocular events included congested conjunctival vessels and subconjunctival hemorrhage. No serious adverse events were reported in this cohort. The authors conclude that in this cohort of patients with refractory glaucoma, adding topical netarsudil reduced IOP which may delay further surgery. Limitations of this study are: retrospective review, small sample size, short variable follow-up, differences in age, type of pediatric glaucoma, variability between patients in IOP measurement instrument and various treatment regimens. Further research is needed to evaluate the safety and efficacy of netarsudil in children with glaucoma.

Risk Factors for Glaucoma Drainage Device Exposure in Children: A Case-Control Study.
Jomar DE, Al-Shahwan S, Al-Beishri AS, Freidi A, Malik R.
American Journal of Ophthalmology. 2023 Jan 1;245:174-83.
Glaucoma drainage device (GDD) exposure is a serious concern in children with glaucoma, as it can lead to endophthalmitis and poor visual outcomes. The aim of this retrospective case-control study was to evaluate patient characteristics associated with GDD exposure in children. This single center study included 21 eyes of 21 children with glaucoma and GDD exposure and 115 eyes of 115 children with glaucoma without GDD exposure. The authors estimated an overall incidence of 4.25% of GDD exposure based on their cohort. The risk factors that they found associated with GDD exposure included multiple previous ocular surgeries, longer follow-up duration, combined procedure at the time of primary implantation, and a younger age at the time of primary implantation. The mean time between implantation and exposure was 20 months. Age at implantation was 6 years (exposure group) compared to 12 years (control group). One limitation of this case-control study is that it did not include matching. Despite this, the study provides useful information with regards to risk factors and may be useful for surgeons in planning the risks and benefits discussion with parents prior to proceeding with GDD implantation.

Diagnostic yield of next generation sequencing gene panel assays for early-onset glaucoma in an ethnically diverse population
Maria Fernanda Villalba, Alana L Grajewski, Mustafa Tekin, Guney Bademci, Ta C Chang
J AAPOS. 2022 Dec;26(6):302.e1-302.e6.
Early-onset glaucoma, defined as glaucoma onset before age 40, is a potentially sight-threatening condition with high heritability. Next generation sequencing is a cost-effective alternative to individual gene screening
that could expedite its diagnosis. The diagnostic yield of multigene panel assays for early-onset glaucoma varies according to the tested population. In this study, the authors examined diagnostic yield of next generation sequencing panels in their cohort, and aimed to identify population characteristics that increase such yield. A retrospective review of the medical records of consecutive patients evaluated for early-onset glaucoma at a single institution over a 5 year period was performed. All patients had undergone next generation sequencing panels for molecular diagnosis. A total of 118 patients were included, in 22 of whom (19%) a causative variant was identified. Both in-house and third-party early-onset glaucoma gene panels were used. The in-house panel was performed in 82 patients, and a molecular diagnosis was identified in 13%. The remaining 36 patients underwent the third-party panels

31% identified a molecular diagnosis. However, when adjusted for early onset before age 3, both in-house and third-party panels identified molecular diagnosis in 32% of patients. In contrast, for patients with onset age after 3, total diagnostic yield was only 5%. Additionally, diagnostic yield varied significantly with ethnicity. It has been reported that populations identifying as Black are disproportionally affected by glaucoma. In this cohort, 42% of the patients identified as Black, yet most remain without a molecular diagnosis. This suggests either that there remain genes to be discovered for monogenic glaucoma or that the pattern of inheritance is complex and different approaches such as increasing the diversity of genome-wide association studies are needed. This study highlights the importance of gene panels in helping achieve molecular diagnosis, and identifies areas where additional research are much needed for better understanding of disease etiology, particularly in patients with older age of onset, and in patients who identify as non-White.

15. Refractive surgery - none

16.Genetics

Stickler syndrome - lessons from a national cohort.
Snead MP, Richards AJ, McNinch AM, Alexander P, Martin H, Nixon TRW, Bale P, Shenker N, Brown S, Blackwell AM, Poulson AV.
Eye (Lond). 2022 Oct;36(10):1966-1972. doi: 10.1038/s41433-021-01776-8. Epub 2021 Oct 5. PMID: 34611315; PMCID: PMC8491173.
The Stickler syndrome is part of the spectrum of inherited vitreoretinopathies. It is the most common cause of retinal detachment in childhood and the most common cause of familial retinal detachment. The Stickler Highly Specialised Service (HSS) has assessed 1673 patients from 785 families over 10 years. Using a combination of accurate phenotyping and molecular genetic analysis, the underlying genetic mutation wa identified in over 95% of cases, including those with deep intronic mutations likely to be missed by conventional exome panel analysis and which require whole gene sequencing and supplementary functional analysis to confirm pathogenicity. This article summarises ten selected briefcase histories from the national dataset with key learning points from each, including risk of retinal detachment and recommendation for prophylactic treatment. In contrast to many other blinding retinal conditions, blindness through giant retinal tear detachment, particularly in children, is largely preventable provided these high-risk groups are identified and appropriate evidence-based prophylaxis is offered.

Diagnostic yield of next generation sequencing gene panel assays for early-onset glaucoma in an ethnically diverse population
Maria Fernanda Villalba, Alana L Grajewski, Mustafa Tekin, Guney Bademci, Ta C Chang
J AAPOS. 2022 Dec;26(6):302.e1-302.e6.
Childhood glaucoma is a heterogeneous group of disorders with an extensive classification including primary, secondary and associated with systemic syndromes. Many variants as well as recessive and dominant inheritance patterns have been described that are associated with early onset glaucoma. Next-generation sequencing panels for a specific type of disease has become a valuable tool when investigating eye diseases. Multiple tools have been developed for early onset glaucoma with varying reported results. The authors used retrospective review to evaluate their own early-onset glaucoma panel as well as similar panels from third party labs for diagnostic yield and to identify patient traits associated with increased diagnostic yield. The authors specified estimated age of onset as before or after 3 years of age. The authors included 118 patients which was ethnically diverse: Black 42%, White 25%, Hispanic 29%, and 5% as other or did not disclose. A causative agent in the group with onset prior to age 3 had an overall diagnostic yield of 32% as contrasted with the onset after age 3 where only 5% had variants identified. Patients who identified as White had a statistically significant higher diagnostic yield than those who identified as non-White. The yield was also statistically higher in patients with ocular anomalies while co-existing systemic disease did not improve the diagnostic yield. With respect to in-house testing, the diagnostic yield was 13% while patients tested with third-party panels had a diagnostic yield of 31%. The authors attribute this difference to a higher number of patients with onset before age 3 and had additional ocular anomalies. For patients with onset prior to age 3 years, the diagnostic yield for in-house and third-party panels was the same. It is important to note that a molecular diagnosis was not obtained in 81% of patients. The importance of improving the diagnostic yield is several fold: improved counseling for patients, possible better prognostic predictions, and possible precision medicine treatments. Limitations of

the study include a wide spectrum of glaucoma phenotypes in this study resulting in a smaller sample size for each genetic condition. The high number of identified variants of uncertain diagnostic yield and lack of a specific molecular diagnosis reminds pediatric ophthalmologists to prepare patients for the fact that although genetic panel testing is an important new tool, it may result in ambiguous or no answers. There is more work to be done.

Three-year results of phase I retinal gene therapy trial for CNGA3-mutated achromatopsia: results of a non randomised controlled trial.
Reichel FF, Michalakis S, Wilhelm B, Zobor D, Muehlfriedel R, Kohl S, Weisschuh N, Sothilingam V, Kuehlewein L, Kahle N, Seitz I. British Journal of Ophthalmology. 2022 Nov 1;106(11):1567-72.
Achromatopsia (ACHM) is a well-characterized form of IRD affecting the cone photoreceptors and daylight vision. Mutations in CNGA3 and CNGB3 account for around 80% of all ACHM cases and cause disease following an autosomal recessive inheritance pattern, making it good targets for gene replacement strategies. The aim of this study is to determine long-term safety and efficacy outcomes of a subretinal gene therapy for CNGA3-associated achromatopsia. We present data from an open-label, nonrandomised controlled trial (NCT02610582). Nine patients were treated in three escalating dose groups with subretinal AAV8.CNGA3 gene therapy between November 2015 and October 2016. After the first year, patients were seen on a yearly basis. Safety assessment constituted the primary endpoint. On a secondary level, multiple functional tests were carried out to determine efficacy of the therapy. No adverse or serious adverse events deemed related to the study drug occurred after year 1. Safety of the therapy, as the primary endpoint of this trial, can, therefore, be confirmed. The functional benefits that were noted in the treated eye at year 1 were persistent throughout the following visits at years 2 and 3. While functional improvement in the treated eye reached statistical significance for some secondary endpoints, for most endpoints, this was not the case when the treated eye was compared with the untreated fellow eye. The results demonstrate a very good safety profile of the therapy even at the highest dose administered. The small sample size limits the statistical power of efficacy analyses. However, trial results inform on the most promising design and endpoints for future clinical trials. Such trials have to determine whether treatment of younger patients results in greater functional gains by avoiding amblyopia as a potential limiting factor.

17.Trauma

Evidence-Based Screening to Optimize the Yield of Positive Ophthalmologic Examinations in Children Evaluated for Suspected Child Abuse.
Su M, Taylor K, Stoutin J, Shaver C, Recko M.
J Pediatr Ophthalmol Strabismus. 2022;59(5):310-319. doi:10.3928/01913913-20220216-01
This single-center retrospective review sought to determine non-ocular findings associated with significant retinal hemorrhages in cases of suspected child abuse. The authors collected data on 274 children 36mo or younger in whom there was concern for child abuse and who underwent an ophthalmology consultation. They found that the presence of one or more abnormal neuroimaging findings had the strongest association with a univariate OR 170. Multivariate analysis found relationships among: abnormal neuroimaging, Glasgow Coma Scale score less than 15, altered mental status on examination, seizure activity, vomiting, bruising, scalp hematoma/swelling, and skull fractures. The authors propose an evidence-based screening algorithm to increase the yield of positive dilated examinations and decrease the burden of potentially unnecessary child abuse ophthalmologic examinations. This is a valuable contribution to the literature on ophthalmic evaluation in suspected child abuse. Perhaps with more broad adaptation, the proposed algorithm might be implemented broadly.

18.Retina

Laser prophylaxis in Stickler syndrome: the Manchester protocol
Linton E, Jalil A, Sergouniotis P, et al. Retina. 43(1):88-93, January 2023.
Patients with Stickler syndrome have high risk of giant retinal tears and retinal detachment, but there is presently no consensus about the optimal prophylactic approach. The authors retrospectively reviewed

the records of all patients treated for Stickler syndrome at their institution, excluding patients who presented with retinal detachment. They divided patients into two groups: those who underwent prophylactic 360° retinal laser, and those who didn't. Overall, 113 eyes of 63 patients met criteria. 82 of those eyes (72.6%) received prophylactic laser at an average age of 14.6 years, while the remaining 31 did not. Of the patients who received prophylactic laser, 7 (9%) eyes went on to develop retinal detachment at an average age of 19.7 years and none developed giant retinal tears. Of the 31 eyes that did not receive prophylaxis, 7 (23%) eventually developed retinal detachment at an average age of 21.9 years and 3 developed giant retinal tears. Though the study was limited by its retrospective nature, lack of randomization, and lack of matching patient characteristics between the two groups, the authors conclude that 360° retinal laser prophylaxis is a safe and effective approach for people with Stickler syndrome.

Analysis of optical coherence tomography angiographic findings of prematurely born children and its relationship with macular edema of prematurity.
Ersan Cetinkaya, MD, Mehmet Fatih K€uc€uk, MD, Elcin S€uren, MD, Mustafa Kalayci, MD, Muhammet Kazim Erol, MD, Fulya Duman, MD, Berna Dogan, MD, and Ozdemir Ozdemir, MD.
J AAPOS 2022; 26:73.e1-6.
In addition to having the vascular changes commonly associated with ROP, 30-60% of premature infants have cystoid macular edema (CME) that can be seen on portable spectral domain optical coherence tomography (SD-OCT). This edema disappears spontaneously by postmenstrual age (PMA) of 52 weeks; however, little is known about the long-term effects of this edema. This paper aims to compare foveal characteristics in pre- and full-term children and to evaluate their relationship with CME in the prematurity period using SD-OCT angiography (SD-OCTA). OCTA was performed on 70 children aged 4-6 years old (45 premature, 25 term) who were split into 3 groups: premature with CME (group 1), premature without CME (group 2), and term (group 3). Foveal avascular zone (FAZ), foveal vascular density (VD), and foveal thickness (FT) were compared amongst the 3 groups. This is the first study to evaluate these variables. The most notable finding was that the FAZ area was significantly large in group 3 compared to groups 1 and 2. FAZ area also correlated with gestational age and birth weight. Interestingly, there was no correlation between FAZ area and visual acuity or axial length. There were no significant differences in any of the parameters between groups 1 and 2. This study is important as it gives additional prognostic information that can be shared with the parents of premature infants. It is limited by the cross-sectional study design and small sample size.

Foveal hypoplasia grading in 95 cases of congenital aniridia: correlation to phenotype and PAX6 genotype.
Daruich A, Robert MP, Leroy C, de Vergnes N, Beugnet C, Malan V, Valleix S, Bremond-Gignac D.
American Journal of Ophthalmology. 2022 May 1;237:122-9.
A well-established manifestation of aniridia is foveal hypoplasia, though data about genotype-phenotype correlation in this condition is limited. The goal of this retrospective study was to characterize foveal hypoplasia in children with congenital aniridia and assess for a genotype-phenotype correlation. This was a retrospective single center study of 95 children with aniridia. All children underwent optical coherence tomography of the macula and foveal hypoplasia was graded using a standardized scale. The authors report several interesting findings. First, they found that foveal hypoplasia was more severe in those with PAX6 genetic changes. Among the genetic changes in PAX6, nonsense variants were associated with higher degrees of foveal hypoplasia. Deletions in the 3' regulatory regions flanking PAX6 were associated with less severe foveal hypoplasia and better vision. Additionally, the extent of the iris defects correlated to the severity of the foveal hypoplasia. As expected, visual acuity was better in children with thicker outer retinal layers. A specific genetic change (deletions in the 3' regulatory regions flanking PAX6) was associated with best outcomes in terms of foveal hypoplasia and visual acuity. This has implications for visual prognosis counseling for children with aniridia and genetic testing.

19.Retinoblastoma / Intraocular tumors
Tomar AS, Finger PT, Gallie B, Kivelä T, et al. American Joint Committee on Cancer Ophthalmic Oncology Task Force. Retinoblastoma seeds: impact on American Joint Committee on Cancer clinical staging. Br J Ophthalmol. 2023 Jan;107(1):127-132. doi: 10.1136/bjophthalmol-2021-318892.

Since the last update on RB staging by the American Joint Committee on Cancer Ophthalmic Oncology Task Force in 2017, new evidence has emerged on the topic of focal vs diffuse seeding. The committee therefore sought to examine if clinical characteristics and intraocular distribution of RB seeds at presentation can be used to predict local treatment failure and improve RB staging. 18 RB centers from 13 countries contributed data from RB patients diagnosed between January 2001 and December 2013. 2190 total patients were included in the registry, 2085 of which had sufficient data for study purposes. This study specifically analyzed 1054 eyes with clinically visible seeds assigned as category cT2b. Of these, 40% underwent primary enucleation. Of the remaining 59% who had an attempt at eye salvage, 40% were successfully salvaged. RB eyes with diffuse seeds were more commonly treated with primary enucleation. By far the most common treatment strategy for eye salvage was systemic chemotherapy (93%) vs IAC in 6% and EBRT in 0.5%. intravitreal chemotherapy was used in 5% and periocular chemotherapy in 6% of eyes. The distribution of seeds among globe salvage eyes was focal in 143 (24.2%) and diffuse in 449 (75.8%) eyes. Diffuse seeds, and specifically spherical seed types, were associated with an increased risk of local treatment failure. Subclassification of AJCC RB category cT2b into focal vs diffuse seeds can improve prognostication for eye salvage.

Tomar AS, Finger PT, Gallie B, Kivelä TT, Mallipatna A, Zhang C, Zhao J, Wilson MW, Brennan RC, Burges M, Kim J, Berry JL, Jubran R, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Volodin D, 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-Mora J, Correa-Llano G, Carreras E; American Joint Committee on Cancer Ophthalmic Oncology Task Force. Metastatic Death Based on Presenting Features and Treatment for Advanced Intraocular Retinoblastoma: A Multicenter Registry-Based Study. Ophthalmology. 2022 Aug;129(8):933-945. doi: 10.1016/j.ophtha.2022.04.022. Epub 2022 Apr 30. PMID: 35500608; PMCID: PMC9329221.
This is a multicenter registry-based case series, investigating the risk of metastatic mortality in patients with advanced retinoblastoma based on presenting clinical features, intraocular tumor size, and treatment modalities. Advanced RB was defined as 8th edition American Joint Committee on Cancer (AJCC) stage cT2 or cT3 categories. The study included 1841 patients from a pooled registry data base across 18 RB centers from 13 countries. High-risk clinical features for advanced RB were stratified in cT2 and cT3 subcategories: retinal detachment with risk of subretinal tumor cells (cT2a); seeding (cT2b); phthisis bulbi (cT3a); anterior segment tumor invasion (cT3b); rubeosis iridis with neovascular glaucoma (cT3c); hyphema, massive vitreous hemorrhage, or both (cT3d); and aseptic orbital cellulitis (cT3e). Tumor size was divided into 4 groups: 1= <50% of globe volume, 2= >50% but <2/3 globe volume, 3= >2/3 globe volume, and 4= diffuse infiltrating RB. Five and 10-year cumulative probabilities of survival by clinical AJCC categories were 98% for cT2a (subretinal fluid), 96% for cT2b (RB seeds), 88% for cT3a (phthisis), 95% for cT3b (anterior chamber involvement), 92% for cT3c (glaucoma), 84% for cT3d (intraocular hemorrhage), and 75% for cT3e (orbital cellulitis). In general, increasing subcategory translated to an increased risk of metastasis releated death. By treatment modality, the 5-year cumulative probability of survival was 96% for primary enucleation, 89% for systemic chemotherapy followed by secondary enucleation, and 90% for systemic chemotherapy with eye salvage. In terms of the size groups, 5-year cumulative probability of survival decreased with larger size: 99%, 96%, 94%, and 83% for Size Groups 1, 2, 3, and 4, respectively. In summary, this study found that higher AJCC stage, treatment attempts at eye salvage with systemic chemotherapy, and larger tumor size increase the risk of mortality by metastasis in patients with advanced RB. The 8th edition AJCC staging seems to be an effective tool to assess the risk of metastatic death in these patients.

Tomar AS, Finger PT, Gallie B, Kivelä TT, Mallipatna A, Zhang C, Zhao J, Wilson MW, Brennan RC, Burges M, Kim J, Berry JL, Jubran R, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Volodin D, 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-Mora J, Correa-Llano G, Carreras E; American Joint Committee on Cancer Ophthalmic Oncology Task Force. High-risk Pathologic Features Based on Presenting Findings in Advanced Intraocular Retinoblastoma: A Multicenter, International Data-Sharing American Joint Committee on Cancer Study.

Ophthalmology. 2022 Aug;129(8):923-932. doi: 10.1016/j.ophtha.2022.04.006. Epub 2022 Apr 15. PMID: 35436535; PMCID: PMC9329269.
This is a multicenter registry-based case series, investigating the strength of the association of high-risk clinical features of advanced retinoblastoma with high-risk pathologic features in eyes after primary enucleation. The 8th edition American Joint Committee on Cancer (AJCC) staging criteria were used to stratify the advanced RB by clinical features: retinal detachment with risk of subretinal tumor cells (cT2a); seeding (cT2b); phthisis bulbi (cT3a); anterior segment tumor invasion (cT3b); rubeosis iridis with neovascular glaucoma (cT3c); hyphema, massive vitreous hemorrhage, or both (cT3d); and aseptic orbital cellulitis (cT3e). The AJCC Ophthalmic Oncology Task Force also developed a size group stratification: 1= <50% of globe volume, 2= >50% but <2/3 globe volume, 3= >2/3 globe volume, and 4= diffuse infiltrating RB. The AJCC high-risk pathologic features corresponding to the pT3 category were defined as histopathologic evidence of massive choroidal invasion, post-laminar invasion of the optic nerve head with or without a positive margin, and scleral invasion, and those corresponding to the pT4 category were defined as extraocular extension. High-risk pathologic features were evaluated in only eyes classified as cT2 or cT3. The study included 942 primarily enucleated eyes with from a pooled registry data base across 18 RB centers from 13 countries. cT3c, cT3d, and cT3e were predictive factors for high-risk pathologic features when compared with cT2a with an odds ratio of 2.3 (P = 0.002), 2.5 (P = 0.002), and 3.3 (P = 0.019), respectively. Size Group 3 and 4 were the best predictive factors with an odds ratio of 3.3 and 4.1 (P < 0.001 for both), respectively, for high-risk pathologic features when compared with Size Groups 1. This data shows that elevated intraocular pressure from iris neovascularization, hyphema, massive vitreous hemorrhage, tumor size >2/3 of the globe or diffuse infiltrating tumors are important predictive factors for high-risk pathologic factors in RB. The AJCC retinoblastoma cT stratification and Size Groups appear to be an effective tool to stratify clinical risk factors that can be used to predict the presence of high-risk pathologic factors in advanced RB, which may help with treatment decision.

20. Orbit - none

21. Oculoplastics

Hendricks TM, Griepentrog GJ, Hodge DO, Mohney BG. Psychosocial and mental health disorders among a population-based, case-control cohort of patients with congenital upper eyelid ptosis. Br J Ophthalmol. 2023 Jan;107(1):12-16. doi: 10.1136/bjophthalmol-2021-319276.
This is population-based cohort study of 81 children diagnosed with simple congenital ptosis over a 40-year period and their sex- and age-matched controls. All subjects were <19 years of age and residents of Olmsted County, Minnesota. The authors sought to describe the prevalence and types of psychiatric and psychosocial abnormalities diagnosed by early adulthood. The medical records of both cases and their controls were reviewed for psychosocial and mental health parameters. An adverse psychosocial development was diagnosed in 41 (51%) patients with simple congenital ptosis compared with 26 (33%) controls (p=0.02), and mental illness was diagnosed in 38% of ptosis patients compared to 20% of controls (p=0.02). Children with ptosis were 2.5 times more likely than controls to develop a mental illness and 2 times more likely to develop a psychosocial maladjustment. Patients with ptosis were also significantly more likely to have a greater number of mental health disorders (p=0.02) and a longer duration of psychotropic medication use (p=0.007). Generalized anxiety, mood disorders and alcoholism were the most common types of disorders among children with ptosis. Social deficits or anxiety, anger issues, developmental delay, behavior problems at home, poor self-esteem and lack of motivation were significantly more prevalent among children with ptosis compared with controls. Neither the relative asymmetry between the height of the two upper eyelids nor the amount of ptosis measured by the MRD correlated positively with the rate of mental illness or psychosocial difficulty. Interestingly, neither having ptosis surgery nor the age at which surgery occurred influenced the rate of mental illness or psychosocial burden. However, among the 34 children who underwent ptosis repair, those displaying a greater change in fissure height had less mental illness or psychosocial burden. Maybe we should be fixing ptosis even if not amblyogenic? Or maybe we should refer our ptosis patients for early psychosocial intervention?

Evereklioglu C. Frontalis suspension by a minimally invasive "harvesting-stripping technique" for congenital blepharoptosis in children under 3-years-old.
Eur J Ophthalmol. 2023 Jan;33(1):161-170.
The authors describe a minimally invasive "harvesting-stripping technique" on a small segment of autogenous fascia lata (AFL) in small children with severe blepharoptosis under 3-years-old. A single-surgeon, uncontrolled surgical trial was designed for 25 eyelids of 18 small children (5 girls, 13 boys) with severe blepharoptosis. Single- and short-skin incisions (2-cm) were made on the thigh and a final 3X0.6-cm or 3.5X1-cm AFL segment was excised according to the ptosis laterality. The surface area of the harvested AFL was calculated and dissected for a final 9-cmX2-mm-long fascial strip for each eye. Functional and aesthetic outcomes of the upper eyelids were evaluated and the feasibility, effectiveness, and advantages of this novel approach in younger patients were assessed. The mean age was 28.3 months (17-35) with a mean follow-up of 34.3 months (6-96). All eyelids achieved good or excellent functional and aesthetic results (except one), with no peri- or post-operative severe complications such as hemorrhage, wound infection, hypertrophied thigh scar, muscle prolapses, eyelid contour abnormalities, ptosis recurrence or overcorrection. The authors conclude that the "harvesting-stripping technique" with the AFL may be an alternative approach to correct severe upper blepharoptosis in small children under 3-years-old, which offers various benefits over conventional methods with non-autogenous materials.

Parent-provided photographs as an outcome measure for childhood chalazia.
S. Ayse Erzurum, MD, Rui Wu, MS, B. Michele Melia, ScM, Zhuokai Li, PhD, Robert W. Arnold, MD, David I. Silbert, MD, John W. Erickson, OD, Nicholas A. Sala, DO, Raymond T. Kraker, MSPH, Jonathan M. Holmes, BM, BCh, and Susan A. Cotter, OD, MS, on behalf of the Pediatric Eye Disease Investigator Group.
J AAPOS 2022; 26:60.e1-5.
Monitoring of chalazia is traditionally done over several visits in the outpatient setting. This study sets out to determine if smartphone photos taken by parents could be used as an alternative to these in person examinations. Children were evaluated in person to determine if they had at least one chalazion measuring 2 mm or larger in diameter. Parents then took 4 photographs of their child’s eyelids that were evaluated by a masked eyecare professional to look for the presence of a chalazion. No clinical history was given to the masked readers. A total of 240 eyelid photographs were available; 85 with at least one chalazion, 155 without a chalazion. The masked reader correctly identified 68 of 85 eyelids with a chalazion (sensitivity 80%) and 151 of 155 eyelids without a chalazion (specificity 97%). Sensitivity increased to 89% for lesions >5 mm in diameter and to 94% for superficial lesions. This paper is important as it demonstrates a possible excellent use for tele-ophthalmic care. Parent submitted photographs could help increase care in underserved areas and decrease wait times for clinical visits. They may be particularly useful for monitoring resolution in clinical practice and future clinical trials looking at the treatment of chalazia.

Teprotumumab reduces extraocular muscle and orbital fat volume in thyroid eye disease
Jain AP, Gellada N, Ugradar S, Kumar A, Kahaly G, Douglas R.
Br J Ophthalmol. 2022 Feb;106(2):165-171.
This is a retrospective review of 6 patients enrolled in the phase III teprotumumab clinical trial (OPTIC, NCT03298867) with active TED who received 24 weeks of teprotumumab and had pre- and post-treatment orbital imaging (CT or MRI). Twelve non-TED patients (24 orbits) were analyzed as a comparative control group. Three-dimensional volumetric analyses of four orbital rectus muscles, orbital fat and the orbital cavity were performed using the previously validated 3D image analysis software. The hypothesis was that inhibition of the IGF-1R pathway with teprotumumab results in decreased orbital soft tissue volumes of EOM and orbital fat, correlating with the clinical findings of a reduction in the CAS, diplopia and proptosis. A single orbit was designated as the study orbit, which was based on the more severely affected orbit, in accordance with previous clinical trial protocols. The study orbit demonstrated a 36% mean decrease in total EOM volume (range 17%–45%) over the 24 week period ($p<0.01$). The inferior rectus demonstrated the greatest reduction in muscle size in 4/6 patients with a 48% mean reduction in muscle volume (range 29%–68%; study orbit). The mean fat volume (FV) in the study orbit prior to therapy was 12,391 mm3. Post-therapy, there was a reduction of 4387 mm3 to a mean of 8004 mm3 ($p<0.03$), resulting in a 30% average FV reduction in the study orbit (range−12% to 44%). There

was a mean proptosis reduction as measured by Hertel exophthalmometry of 5 mm (range 3–7 mm) in the study eye. At baseline, 8/12 orbits had a CAS of 5 or 6. At the end of the clinical trial (week 24), the CAS reduced to 0 or 1 in all 6 patients. The difference between the total EOM volume in post-therapy patients and non-TED controls was not significant (p=0.09), demonstrating that post-treatment EOM volume returned to normal volumes. However, there was a statistically significant difference between post-therapy patients and controls regarding orbital FV measurements ($p<0.05$), indicating that post-treatment orbital FV was reduced, but did not return to a normal when compared to controls. This study is limited in Its small number of participants and retrospective nature, but it helps demonstrate the soft tissue changes resulting from teprotumumab therapy and the associated clinical benefits.

Tenzel PA, Brown K, Zhou B, Itani KM, Mancini R.
Facial Asymmetry in Children With Unilateral Congenital Ptosis.
Ophthalmic Plast Reconstr Surg. 2022 Mar 30. Epub ahead of print. PMID: 35353779.
Unilateral congenital ptosis is a disease of both functional and cosmetic importance. Patients can develop amblyopia and vision impairment depending on the degree of ptosis. Surgical treatment is often considered to minimize amblyopia and improve cosmetics. Studies have shown that pre-existing facial asymmetry may contribute to patient dissatisfaction with surgical outcome. The purpose of this study is to analyze facial asymmetry in children with unilateral congenital ptosis. This is a retrospective review of pediatric patients undergoing unilateral ptosis repair at a single center. Gender, age, lateraling, MRD1, LF, and surgical intervention were analyzed. Preoperative photos were asssessed using ImageJ software. Measurements from this software were used in symmetry analysis. 44 patients were included in this study. 20% of patients had mullerectomy, 34% had levator resection, and 46% had frontalis suspension. The side of the face with blepharoptosis had smaller MRD1, smaller horizontal palpebral fissure, shorter mid face height and a more inferiorly displaced lateral canthus. There are limitations to this study including retrospective nature, use of only one photograph at one point in time per patient, and incomplete standardization of photograph. Further studies should include further imaging analysis such as MRI/CT and postoperative photos. A larger cohort of patients and a standardization of patients without ptosis would be helpful. This is however important for surgeons to know to help patients have realistic expectations of surgical outcome.

22. Infections - none

23. Pediatrics / Infantile Disease/ Syndromes
Association of Mood Disorders, Substance Abuse, and Anxiety Disorders in Children and Teens With Serious Structural Eye Diseases.
Meer EA, Lee YH, Repka MX, Borlik MF, Velez FG, Perez C, Yu F, Coleman AL, Pineles SL.
American journal of ophthalmology. 2022 Aug 1;240:135-42.
Decreased visual acuity and visual impairment can affect quality of life as well as wellness and mental health. This cross-sectional study using a commercial insurance claims database aimed to describe the association between mental illnesses and 5 eye diseases (glaucoma, cataract, congenital optic nerve disease, congenital retinal disease, and blindness/low vision). Over the 11 year study period, the authors identified over 11.8 million children, of which over 180,000 had at least one of the ocular conditions of interest..The authors found that after adjusting for confounding variables such as age, sex, race and ethnicity, education, family net worth, and geographic region, there was a significant association between the eye conditions and schizophrenia, anxiety, depression, and bioplar disorders. Due to the nature of this study and data, it is not possible to establish a causal relationship. Additionally, the insurance database excludes Medicaid patients, ultimately limiting its generalizability outside of the study population. Despite these limitations, the findings of this study do demonstrate the importance of the overlap between ocular disease and mental health. The authors encourage consideration of multidisciplinary approaches to support children with eye conditions at risk for mental illness.

Ophthalmic involvement in PHACES syndrome: prevalence, spectrum of anomalies, and outcomes.
Soliman SE, Wan MJ, Pennal A, Pope E, Mireskandari K.
J AAPOS. 2022 Jun;26(3):129.e1-129.e7.

The authors used retrospective, noncomparative, single institution observational case series of 43 children with PHACES syndrome (posterior fossa malformations, infantile hemangiomas, arterial, cardiac, eye, and sternal anomalies) to highlight prevalence, spectrum of anomalies, and outcome of ophthalmic involvement. Prevalence of ocular involvement of 6-7% is based on case reports and case series of 8 patients. Vision may also be affected by periocular obstruction of the visual axis with amblyopia as well as intracranial anomalies causing cranial nerve palsies and papilledema. The authors report 12% of the cohort in their study had PHACES-specific ocular criteria which is almost double prevalence reported in a consensus statement on PHACES and other published reports. They suggest population differences and referral center bias may explain these differences. Some studies relied on imaging studies alone to diagnosis ocular involvement without an ophthalmologic exam which could have detected abnormalities that could not be detected on MRI imaging. Five children had PHACES-specific ocular abnormalities meeting diagnostic criteria. Posterior segment anomalies included peripapillary staphyloma, retinal vascular anomalies, and optic nerve hypoplasia. Anterior segment anomalies included cataract and corneal opacity. Four children had non-PHACES specific ocular anomalies. These included a dysmorphic optic nerve and anterior segment anomalies that did not meet criteria including Peters anomaly and persistent pupillary membrane. Ocular anomalies were ipsilateral to the facial hemangioma. All eyes with posterior involvement with major criteria had intracranial vascular anomalies. Periocular involvement of the eyelids by hemangioma was seen in 29 children (67%). Severe infantile hemangioma-related ophthalmic involvement was seen in 21/29 patients consisting of severe ptosis, proptosis, and strabismus. Amblyopia occurred in 67% of the children with severe ocular involvement at presentation. Poor vision was associated with a diagnostic structural anomaly. The authors propose that the term anterior segment dysgenesis be considered in the future as a minor diagnostic criterion. The authors emphasize that it is important to recognize and manage amblyopia as early as possible. They suggest ophthalmologic examination soon after diagnosis to detect ocular anomalies as well as risk factors for amblyopia. Ophthalmic follow-up is guided by risk factors for amblyopia needing intervention. One limitation of the study is that the treatment protocol changed halfway through the study period from steroids to beta-blockers. Another limitation was small cohort size. Longer-term follow up may also be important in understanding outcome of ocular presentations. This study is important to pediatric ophthalmologists in highlighting the spectrum of disease seen in PHACES syndrome and as a reminder for the need to be ever vigilant about the detection and treatment of amblyopia.

Vision and Concussion: Symptoms, Signs, Evaluation, and Treatment (already presented)
Christina L. Master, MD, FAAP;Darron Bacal, MD, FAAP;Matthew F. Grady, MD, FAAP;Richard Hertle, MD, FAAP;Ankoor S. Shah, MD, PhD;Mitchell Strominger, MD, FAAP;Sarah Whitecross, MMedSci, CO;Geoffrey E. Bradford, MD, MS, FAAP;Flora Lum, MD;Sean P. Donahue, MD, PhD;
AAP SECTION ON OPHTHALMOLOGY; AMERICAN ACADEMY OF OPHTHALMOLOGY; AMERICAN ASSOCIATION FOR PEDIATRIC OPHTHALMOLOGY AND STRABISMUS; and AMERICAN ASSOCIATION OF CERTIFIED ORTHOPTISTS
Pediatrics (2022) 150 (2): e2021056047. https://doi.org/10.1542/peds.2021-056047
Concussion is a common injury in childhood, affecting an estimated 1.4 million children and adolescents annually in the United States. Blurred vision, light sensitivity, and double vision have been reported to occur in up to 40% of children and adolescents immediately after concussion. Additional symptoms may include complaints of losing one's place or ocular fatigue while reading. Another consideration is that children are frequently unable to recognize or articulate specific visual complaints; thus, clinicians may need to have an appropriately elevated index of suspicion to identify vision-specific issues. Although concussion symptoms generally spontaneously resolve over the course of 4 weeks after injury in children and adolescents, up to one-third may have prolonged symptoms. Of those with prolong symptoms, 69% had at least one associated vision disorder. This article summarizes ocular related findings associated with concussion. Tests necessary for evaluation include: Pursuits, Saccades, VOR (vestibular ocular reflex), Near point of convergence, accommodative amplitudes, strabismus. In general, treatment of the visual complications of concussion can be divided into 2 categories: symptom management with task modification and referral to specialists for targeted treatment of the observed oculomotor abnormalities. A summary of strategies to manage concussion-related vision disorders is provided.

24. Uveitis - none

25. Practice Management / Health Care Systems / Education

Carbon footprint of the 2021 and 2022 AAPOS annual meetings.
Constance E. West, MD, and David G. Hunter, MD, PhD.
JAAPOS 2022;26:255-257.
This paper endeavored to study the impact of converting the AAPOS meeting from an in-person format to a virtual format on carbon dioxide emissions. The cities and countries of origin were obtained for the 2021 AAPOS Annual Meeting (scheduled for Boston, MA) and the 2022 AAPOS Annual Meeting (Scottsdale, AZ). Driving emissions were calculated for those deemed close enough to drive to the meeting site and flight emissions were calculated for all other attendees. There was a total savings of 1,282 tonnes of CO2 emissions due to the conversion of the 2021 AAPOS meeting to a virtual format. For the 2022 meeting in Scottsdale, US attendees incurred 19% greater CO2 emissions than if they had attended the 2021 meeting in Boston due to the meeting location relative to the population of attendees. This study likely underestimates the overall environmental impact of switching to virtual meetings as it only considers the CO2 emissions associated with travel to the venues. It points out other benefits to a virtual format including gained time from lack of travel, ability to reach a more diverse group of attendees, and increased flexibility for participants with clinical or familial demands. At the same time, the benefits of in person meetings are also mentioned, including the ability to do hands-on courses and to foster comradery. Overall, I think this is an insightful paper and an important topic to consider. Likely the best arrangement for meetings will be a hybrid format or switching to every other year in person/every other year virtual. At the least, a conversation should be had on an organizational level discussing the environmental and inclusivity benefits that can come from a virtual format.

Income Disparities in Outcomes of Horizontal Strabismus Surgery in a Pediatric Population.
Zdonczyk AN, Gupte G, Schroeder A, Sathappan V, Lee AR, Culican SM.
J Pediatr Ophthalmol Strabismus. 2022;59(3):156-163. doi:10.3928/01913913-20210824-02
This single-center retrospective review sought to examine the potential impact of SES on pediatric patients undergoing horizontal strabismus surgery, using PEDIG surgical failure criteria: undercorrection w/ misalignment >10PD at near or distance, overcorrection with misalignment >6PD at near or distance, or undergoing a reoperation. The authors reported the outcomes of 284 subjects and found that there was no difference in failure rates between patients with Medicaid and patients with private insurance 24 months postoperatively (45.9% vs 50.5%, respectively, P = .46). Patients with Medicaid were more likely to not follow up postoperatively (28.2% vs 9.6%, respectively, P < .01), whereas patients with private insurance were more likely to complete more than three follow-up appointments in 24 months (21.5% vs 39.0%, respectively, P < .01). Postoperative attendance was linked to Medicaid status (P < .01) but not travel time, neighborhood income levels, or social deprivation index factors. The authors concluded that although there was no difference in failure rates between patients with Medicaid and patients with private insurance, Medicaid status was significantly predictive of loss to follow-up. The authors cited retrospective design and unequal group distributions as limitations, and although they addressed rationale for choosing 11 months as the minimum follow-up period for inclusion, they noted that only 62% of patients who ended up meeting failure criteria by 24 months did so by 11 months.

Comparing the diagnostic accuracy of telemedicine utilization versus in-person clinical examination for retinopathy of prematurity in premature infants: a systematic review.
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J AAPOS 2022; 26:58.e1-7.
ROP screening is important to limit visual impairment in premature infants; however, there are logistical challenges to in person screening. This study aimed to compare the accuracy of telemedicine to ophthalmic examination for ROP detection. Over 500 studies were identified and screened, 14 studies were deemed eligible and were included in the final qualitative review. Virtually every study found that telemedicine compared favorably with in-person examination in detecting ROP. Sensitivity and specificity ranged from 70-100%. The sensitivity for treatment-requiring disease was particularly high with several studies showing 100% sensitivity. This paper is important as it shows that telemedicine can be incorporated into ROP screening while still maintaining a high level of care.