

What's New and Important in Pediatric Ophthalmology and Strabismus in 2022

ALL STARS – approximately top 10% of articles

Review of literature February 2021-January 2022 inclusive

AAPOS Meeting, Scottsdale Arizona

March 2022

Presented by the AAPOS Professional Education Committee

Emily McCourt MD - Chair

Carolina Adams, MD

Austin E Bach, DO

Smith Anne M. Chisholm

Robert A Clark MD

Alina Dumitrescu, MD

Gena Heidary MD PhD

Prashanthi Giridhar, MD

Laryssa A. Hurn, MD

Alexander J Khammar MD

Eunice Maya Kohara, DO

Euna Koo, MD

Sharon S Lehman MD

Phoebe Dean Lenhart, MD – vice chair

Lauren Mehner, MD

Julius Oatts, MD

Michael Puente, MD

Lance Siegel, MD

Jasleen K Singh, MD

Hersh Varma, MD

Grace M. Wang MD, PhD

TABLE OF CONTENTS

1. Amblyopia
2. Vision Screening
3. Refractive error & Myopia control
4. Visual Impairment
5. Neuro-Ophthalmology
6. Nystagmus
7. Prematurity
8. ROP
9. Strabismus
10. Strabismus surgery
11. Anterior Segment
12. Cataract
13. Cataract surgery
14. Glaucoma
15. Refractive surgery
16. Genetics
17. Trauma
18. Retina
19. Retinoblastoma / Intraocular tumors
20. Orbit
21. Oculoplastics
22. Infections
23. Pediatrics / Infantile Disease/ Syndromes
24. Uveitis
25. Practice management / Health care systems / Education

1. AMBLYOPIA

Randomized controlled trial of a dichoptic digital therapeutic for amblyopia.

Xiao S, Angjeli E, Wu HC, Gaier ED, Gomez S, Travers DA, et al. for the Luminopia Pivotal Trial Group. *Ophthalmology* 2022;129:77-85. *with commentary by Dr. John Sloper in same issue p86, "Answers and questions about the digital dichoptic treatment of amblyopia"

Digital therapeutics are a new class of interventions that are software driven and are intended to treat various conditions. The authors developed and evaluated a dichoptic digital therapeutic for amblyopia, as it is a neurodevelopmental disorder for which current treatments may be limited by poor adherence and residual vision deficits. This was a 3-phase, randomized controlled trial in which 105 children ages 4-7 years of age with amblyopia were enrolled at 21 academic and community sites in the United States to evaluate the safety and efficacy of a dichoptic digital therapeutic for amblyopia. Participants were randomized 1:1 to the treatment or comparison group, stratified by site. Participants in the treatment group used the therapeutic at home for 1 hour per day, 6 days per week and wore glasses full-time. Participants in the comparison group continued wearing glasses full-time alone. The primary efficacy outcome was change in amblyopic eye visual acuity (VA) from baseline at 12 weeks, and VA was measured by masked examiners. Safety was evaluated using the frequency and severity of study-related adverse events. Primary analyses were conducted using the intention-to-treat population. Between January 16, 2019, and January 15, 2020, 105 participants were enrolled; 51 were randomized to the treatment group and 54 were randomized to the comparison group. At 12 weeks, amblyopic eye VA improved by 1.8 lines in the treatment group and by 0.8 lines in the comparison group. At the planned interim analysis, the difference between groups was significant (1.0 lines; $P=0.0011$) and the study was stopped early for success, according to the protocol. No serious adverse events were reported. This study is important because the findings support the value of the therapeutic in clinical practice as an effective treatment. However, 2 potential sources of bias are that the children were aware of whether they were in the control or intervention group and this could have influenced their effort and that the authors of the study all have a financial interest in the digital therapeutic. Future studies should evaluate the therapeutic compared with other methods (standard amblyopia treatments—patching, atropine) and in additional patient populations. Furthermore, it is unclear whether and how the dichoptic component of the treatment contributes to the therapeutic effect.

Identifying Characteristics Predictive of Lost-to-follow-up (LTFU) Status in Amblyopia.

Shoshany TN, Chinn RN, Staffa SJ, Bishop K, Michalak S, Hunter DG.

American journal of ophthalmology. 2021 May 13.

The treatment of amblyopia relies on parental compliance with both treatment and follow up, though loss to follow up remains a major issue and impediment to better outcomes in this condition. This retrospective study of over 2,000 children aged 2-12 at a single center with amblyopia aimed to assess factors associated with loss to follow up after an initial visit where amblyopia was diagnosed. In this cohort, almost a quarter of all patients were lost to follow up after their first visit. Factors associated with higher risk for loss to follow up included older age at presentation, longer interval of requested follow up time, African American race, lack of insurance, and diagnosis of mild or "sub-threshold" amblyopia. The authors propose a risk score based on their multivariate analysis which predicted probability of loss to follow up. This study and tool sheds light on factors which put patients at risk for poorer outcomes related to follow up and suggests that specific attention to these factors could improve compliance and potentially outcomes.

Effect of Sequential and Simultaneous Patching Regimens in Unilateral Amblyopia.

Chinn RN, Michalak SM, Shoshany TN, Bishop K, Staffa SJ, Hunter DG.

American journal of ophthalmology. 2021 Jul 22.

Children with unilateral amblyopia are often treated with either glasses alone followed by patching or glasses and patching at the same time. Given the unclear literature on difference in outcomes between these two approaches, this group conducted a retrospective study of 98 children aged 3-12 treated for unilateral amblyopia with presentation vision between 20/40 and 20/00 at a single institution. In this

group, around 40% were recommended to undergo simultaneous glasses and patching and the remainder were started in glasses at the first visit and patching at a later visit. The main outcome was visual acuity and stereopsis at the last visit on treatment. The main finding of this study is that there was no significant difference in treatment strategy between the two groups. Visual acuity improved around 4 lines in each group. Generally, for patients that did not have stereopsis on presentation, the sequential strategy led to better stereopsis outcomes. This study sheds light on the role of glasses versus glasses with patching and how stereopsis on presentation may determine treatment strategy.

2. VISION SCREENING

Analysis of vision screening failures in a school-based vision program (2016-19)

Milante RR, Guo X, Neitzel AJ, Kretz AM, Mukherjee MR, Friedman DS, Repka MX, Collins ME

J AAPOS 2021; 25: 29.e1 - 29.e7

Analysis of vision screenings failures in school-based program conducted in state-mandated grades (pre-kindergarten [pre-K] or kindergarten [K], 1st and 8th grade), and nonmandated grades (2nd to 7th) were evaluated during school years 2016-19, 51,593 pre-K to 8th grade students from 123 Baltimore City Public Schools. Assessments included distance visual acuity, Spot photoscreening, stereopsis, and cover testing. Screening failures were analyzed by grade using aggregate data. Failure rates for mandated and nonmandated grades were compared using a logistic regression model, and visual acuity distributions were analyzed using individual data. Over the 3-year period, 17,414 (34%) of students failed vision screening. Failure rates by grade ranged from 28% to 38%. Children in kindergarten and 3rd grade and higher were statistically more likely to fail screening than those in 1st grade. Reduced visual acuity was the most common reason for failure (91%). Failure rates were significantly higher in nonmandated grades than in state-mandated testing grades (34.7% vs 32.5%). Mean visual acuity of all students who failed vision screening was 20/50 in the worse-seeing eye and was 20/40 in the better-seeing eye. One-third of students failed vision screening. High screening failure rates across all grades suggest that screening in select grade levels, as currently mandated in Maryland schools, is inadequate for detecting vision problems in the low-income communities served by this program

Age Does Not Influence the Positive Predictive Value of Vision Screening to Detect Amblyopia Risk Factors

Raymond Zhou, Tyler Pfister, Yuhua Liu, Qingxia Chen, Sean P Donahue

Ophthalmology; 2022 Feb;129(2):230-1

This short report retrospectively compared the positive predictive value (PPV) of instrument-based vision screening in young children (< 3 years old) with direct testing of visual acuity in slightly older children (3-5 year olds). For the 3114 children referred after failing vision screening, the PPV of 60.5% for younger children was virtually identical to the PPV of 59.5% for slightly older children, with no differences found based on gender or ethnicity. Younger children had slightly higher rates of refractive errors, while older children had slightly higher rates of strabismus. The authors' conclusion that instrument-based testing is comparable to visual acuity testing adds additional data to support the current recommendation to routinely use instruments to screen for amblyopia risk factors in young children.

Reducing the Costs of an Eye Care Adherence Program for Underserved Children Referred Through Inner-City Vision Screenings.

Chung SA, Snitzer M, Prioli KM, Pizzi LT, Zhang Q, Levin AV.

American journal of ophthalmology. 2021 Jul 1;227:18-24.

Community based screening programs have been used to identify children at risk for vision issues. One specific program, the Children's Eye Care Adherence Program is a school-based social worker driven intervention in Philadelphia. The goal of this specific study was to evaluate the cost effectiveness of a revised version of this intervention. Changes in the newer version of the intervention included reducing the number of attempted phone calls to parents, focusing on schools within a closer geographic radius to the clinic, and sending email reminders instead of letters. Of the 16,000 children screening, 3% were identified as needing referral to a pediatric ophthalmologist. Their modifications led to a decrease in cost per patient from \$77 to \$32. This study sheds light on the importance of screening underserved populations while also emphasizing cost-related barriers and suggesting interventions available which could improve cost-effectiveness and increase adherence.

3. REFRACTIVE ERROR & MYOPIA CONTROL

The risks and benefits of myopia control.

Bullimore MA, Ritchey ER, Shah S, Leveziel N, Bourne RRA, Flitcroft DI.

Ophthalmology 2021;128:1561-1579.

The prevalence of myopia is increasing around the world, stimulating interest in methods to slow its progression. The primary justification for slowing myopia progression is to reduce the risk of vision loss through sight-threatening ocular pathologic features in later life. The goal of this study was to analyze whether the potential benefits of slowing myopia progression by 1 diopter (D) justify the potential risks associated with treatments. First, the known risks associated with various methods of myopia control are summarized, with emphasis on contact lens wear. Based on available data, the risk of visual impairment and predicted years of visual impairment are estimated for a range of incidence levels. Next, the increased risk of potentially sight-threatening conditions associated with different levels of myopia are reviewed. Finally, a model of the risk of visual impairment as a function of myopia level is developed, and the years of visual impairment associated with various levels of myopia and the years of visual impairment that could be prevented with achievable levels of myopia control are estimated. Results: Assuming an incidence of microbial keratitis between 1 and 25 per 10 000 patient-years and that 15% of cases result in vision loss leads to the conclusion that between 38 and 945 patients need to be exposed to 5 years of wear to produce 5 years of vision loss. Each additional 1 D of myopia is associated with a 58%, 20%, 21%, and 30% increase in the risk of myopic maculopathy, open-angle glaucoma, posterior subcapsular cataract, and retinal detachment, respectively. The predicted mean years of visual impairment ranges from 4.42 in a person with myopia of -3 D to 9.56 in a person with myopia of -8 D, and a 1-D reduction would lower these by 0.74 and 1.21 years, respectively. The authors conclude that the potential benefits of myopia control outweigh the risks: the number needed to treat to prevent 5 years of visual impairment is between 4.1 and 6.8, whereas fewer than 1 in 38 will experience a loss of vision as a result of myopia control.

Comparison of myopic progression before, during, and after COVID-19 lockdown.

Ophthalmology 2021;128:1655-1657.

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease against which lockdown has been applied widely as a policy to stop its spread. Although many people believe that myopic progression has accelerated during the COVID-19 pandemic lockdown, evidence to support this presumption is lacking. The Myopia Screening Survey of Children and Teenagers in Schools is a cohort study conducted in 46 primary and junior high schools in Hangzhou, China. The first participants were examined in early 2019, with examinations performed at approximately 6-month intervals thereafter. By now, 4 rounds of the survey have been completed, with 3 periods between them. The COVID-19 lockdown was implemented during period 2. The presenting visual acuity (VA) was defined as corrected VA in students with glasses and uncorrected VA in others. Refractive error was estimated by noncycloplegic autorefractometry. Of the 44,187 students at baseline, 29,719 (59 438 eyes) were included in the analyses. The proportions of myopia and high myopia at rounds 1 through 4 were 48.0%, 53.2%, 73.7%, and 67.9% and 1.3%, 1.9%, 2.8%, and 2.7% respectively. The mean rate of spherical refraction change during periods 1, 2, and 3 was -0.030 D/month, -0.074 D/month, and 0.016 D/month. Interestingly, this study indicates that there was accelerated myopic progression during the COVID-19 pandemic lockdown in children and teenagers. However, this myopic progression was reversed partially after lockdown, suggesting that both accommodative spasm and structural changes contributed to this accelerated rate. The authors maintain that myopic progression should be considered and managed when a lockdown is imposed in the future.

Smartphone Use Associated with Refractive Error in Teenagers: The Myopia App Study

Clair A. Enthoven, Jan Roelof Polling, Timo Verzijden, J. Willem L. Tideman, Nora Al-Jaffar, Pauline W.

Jansen, Hein Raat, Lauwerens Metz, Virginie J.M. Verhoeven, MD, Caroline C.W. Klaver

Ophthalmology; 2021 Dec;128(12):16081-8

This study used an app to monitor smart phone usage and face-to-screen distance objectively in a cohort of 525 Dutch teenagers over a period of 13 months. The key study variables were the hours per day of smart phone usage, the number of daily episodes of greater than 20 minutes of continuous smart phone usage per day, the average face-to-screen distance, and self-reported outdoor exposure times. The key outcome variables were the change in axial length-to-corneal radius ratio and the cycloplegic spherical equivalent refractive error. A secondary comparison was smart phone usage on school days versus weekend and holiday days. The average age of subjects was 13.7 ± 0.85 years and only 19% were myopic. Smart phone usage was similar between school days 3.7 ± 1.7 hours and non-school days 3.8 ± 2 hours, with 6.4 and 7.1 episodes of more than 20 minutes continuous use, respectively. More hours of smart phone usage, more continuous episodes of smart phone usage, and less outdoor time all correlated with higher levels of myopia, but the effect was very mild (<0.1 diopters). There was no correlation with distance to screen. Weaknesses include a fairly homogenous European population with a relatively low rate of myopia, suggesting this particular population may not be at great risk for higher levels of myopia. The overall conclusion that excess and continuous smart phone usage can increase the rate of myopic progression is probably correct, although the magnitude of the effect does not appear to be large.

Glasses versus Observation for Moderate Bilateral Astigmatism in 1-to <7-Year-Olds.

Wang JY, Hodge DO, Mohny BG.

American Journal of Ophthalmology. 2021 Jul 31.

Consensus around refractive thresholds for prescribing glasses in children can vary based on child age, refractive error, and physician preferences. This aim of this paper was to evaluate outcomes for over 1,200 children aged 1 to <7 who were diagnosed with moderate bilateral astigmatism ($+1.25$ to $+3.25$ diopters). Roughly two thirds of the children were prescribed glasses and the other third were observed without glasses. Generally, those that were prescribed glasses were younger. The rate of developing amblyopia after 4 years was similar between groups (10.3% in the glasses group and 8.3% in the observation group). Rates of strabismus were similar between groups as well (around 7% in each group). Using glasses did not provide a significant improvement in amblyopia prevention for those with higher or lower amounts of cylinder. Similarly, they did not provide significant improvement in amblyopia prevention for those younger or older at the time of treatment initiation. Overall, this study calls into question the practice of prescribing glasses for younger children with moderate astigmatism and that larger studies to confirm specific refractive thresholds by age may be useful.

Meridional aniseikonia—causes, symptoms, and therapies

Velez FG, Pineles SL, Rosello N, Nguyen A, Guyton DL

J AAPOS 2021; 25: 31.e1 - 31.e5

Meridional aniseikonia, different image sizes may occasionally cause significant distortion of the binocular spatial sense in perceptive patients. This is a retrospective study of medical records of 3 adult patients who complained of binocular spatial distortion consistent with meridional aniseikonia. Detailed descriptions of symptoms, ocular findings, and management are reported. Each patient had undergone a refraction-altering surgical procedure, and each complained of binocular spatial distortion characterized by a trapezoidal view of square or rectangular shapes. Each patient improved following management of the astigmatic spectacle correction. Following cataract or corneal surgery patients with complaint of binocular spatial distortion may be caused by meridional aniseikonia, which may be corrected by astigmatic correction.

4. VISUAL IMPAIRMENT

none

5. NEURO-OPHTHALMOLOGY

Interocular Difference in Retinal Nerve Fiber Layer Thickness Predicts Optic Neuritis in Pediatric-Onset Multiple Sclerosis

Waldman AT, Benson L, Sollee JR, Lavery AM, Liu GW, Green AJ, Waubant E, Heidary G, Conger D, Graves J, Greenberg B.

Journal of Neuro-Ophthalmology. 41(4):469-475, December 2021.

In this retrospective multicenter study, the authors explore the use of Heidelberg OCT rNFL thickness measurements in 157 patients to determine what features correlate with a remote diagnosis of optic neuritis from pediatric onset multiple sclerosis. Mean rNFL thickness was compared with healthy controls. A mean thickness of 104.0 microns (SD 9.0, range 86–130) was found in healthy subjects and an abnormal rNFL thickness of < 86 microns was defined as 2 standard deviations from the mean. This occurred in 50% of patients with known optic neuritis and in 11% of those patients in whom a remote diagnosis had not been made. Further, the authors found that an interocular difference of > 5 microns in thickness was also indicative of a remote history of optic neuritis. This interocular difference allowed diagnosis of a remote history of optic neuritis even when rNFL thickness in both eyes measured > 86 microns. Therefore the authors propose using this novel observation in addition to rNFL thickness of an individual eye towards establishing a history of remote optic neuritis.

Utility of Spectral-Domain Optical Coherence Tomography in Differentiating Papilledema From Pseudopapilledema: A Prospective Longitudinal Study

Jivraj I, Cruz CA, Maxwell P, Kohli AA, Liu GT, Shindler KS, Avery RA, Garvin MK, Wang J-K, Ross A, Tamhankar M.

Journal of Neuro-Ophthalmology. 41(4):509-515, December 2021.

Differentiating between papilledema and pseudopapilledema is critical for appropriate work up and management and therefore a diagnostic tool which may discriminate between these two entities is sought. In this study, 52 adults were prospectively evaluated with Cirrus OCT to assess the value of OCT in distinguishing between these two diagnoses. There was a significant difference in the delta between baseline and follow up of parameters including total retinal thickness, rNFL thickness, and optic nerve volume with higher measurements for papilledema compared with pseudopapilledema. This study expands on the utility of OCT in providing the longitudinal data to support how to accurately diagnose the two entities.

Utility of Ultrasound and Optical Coherence Tomography in Differentiating Between Papilledema and Pseudopapilledema in Children

Farazdaghi MK, Trimboli-Heidler C, Liu GT, Garcia A, Ying G-S, Avery RA.

Journal of Neuro-Ophthalmology. 41(4):488-495, December 2021.

Differentiating between papilledema and pseudopapilledema is critical for appropriate work up and management and therefore a diagnostic tool which may discriminate between these two entities is sought. In this study, the authors retrospectively evaluated data from 181 eyes with respect to characteristics on ultrasound and Heidelberg Spectralis OCT to determine the utility of these modalities in diagnosis. Authors were able to establish a threshold that optic nerve sheath widening of 4.5 mm or greater (measured 3 mm posterior to and perpendicular to the retina) or global rNFL thickness of 140 microns or greater were associated with papilledema. When both of these findings were present, the specificity for papilledema was 95% (95% CI, 88%–98%).

Variability Within Optic Nerve Optical Coherence Tomography Measurements Distinguishes Papilledema From Pseudopapilledema

Flowers AM, Longmuir RA, Liu Y, Chen Q, Donahue SP.

Journal of Neuro-Ophthalmology. 41(4):496-503, December 2021.

Differentiating between papilledema and pseudopapilledema is critical for appropriate work up and management and therefore a diagnostic tool which may discriminate between these two entities is sought. In this study, the authors performed a retrospective study of 116 eyes in patients > 18 years of age using Cirrus OCT rNFL thicknesses in patients with papilledema and pseudopapilledema to determine

whether there were distinguishing findings in these two cohorts. They found that the mean rifle thickness was higher in papilledema patients. Further, when comparing by clock hour, the variability in rifle thickness measurement was higher in those eyes with papilledema. The authors used these data to create an Optic nerve edema index risk score with high fidelity for diagnosis.

Brain MRI and Ophthalmic Biomarkers of Intracranial Pressure

D'Antona L, Asif H, Craven CL, McHugh JA, Vassiliou A, Thorne L, Matharu MS, Watkins LD, Bremner F, Toma AK.

Neurology. 2021 Apr 13;96(22):e2714-e2723.

In this retrospective study of 45 patients undergoing ICP monitoring, the authors evaluated 6 “brain and ophthalmic biomarkers” to determine their relationship with ICP. This effort would help to identify a profile of risk for the presence of elevated ICP using these non-invasive imaging and ophthalmic tools. The biomarkers assessed included assessment of the pituitary gland, optic nerve head protrusion on neuroimaging, tortuosity of the optic nerve, optic nerve sheath diameter/distension, the presence of papilledema, and evaluation of spontaneous venous pulsations. Protrusion of the optic nerve head was strongly reflective of elevated ICP. An empty sella turcica was associated with elevated ICP but not a marked elevation. The biomarkers with the strongest positive predictive value of elevated ICP were absence of spontaneous venous pulsations, optic nerve head protrusion and papilledema. If the pituitary shape was normal, this had a strong negative predictive value towards normal ICP. This study is important because it highlights non invasive details which may be gleaned from neuroimaging and the clinical ophthalmic examination which may help to identify patients at risk for elevated ICP and pursue further evaluation and treatment as indicated.

Prevalence of Optic Disc Drusen in Young Patients With Nonarteritic Anterior Ischemic Optic Neuropathy: A 10-Year Retrospective Study

Fraser JA, Rueløkke LL, Malmqvist L, Hamann S.

Journal of Neuro-Ophthalmology. 2021 June 41(2):200-205.

In this retrospective review of 37 adult patients with NAION, the prevalence of optic nerve head drusen was determined to evaluate whether optic nerve head drusen may be a risk factor for NAION. The prevalence of optic nerve head drusen among NAION patients was 56.7%. This is higher than published prevalence of up to 2.2% optic nerve head drusen in the general population. Optic nerve head drusen was buried and often bilateral. This study raises important implications for the potential contribution of the presence of optic nerve head drusen in an already vulnerable optic nerve towards the pathogenesis of NAION and warrants further investigation.

Role of Ocular Ultrasonography to Distinguish Papilledema From Pseudopapilledema

Kohli AA, Pistilli M, Alfaro C, Ross AG, Jivraj I, Bagchi S, Chan J, May D, Liu GT, Shindler KS, Tamhankar MA.

Journal of Neuro-Ophthalmology. 2021 June 41(2):206-211.

Distinguishing papilledema from pseudopapilledema may be difficult for providers and many ancillary modalities have been utilized to facilitate this process: OCT, FA, neuroimaging, and ultrasound. In this study, the authors evaluated ocular ultrasonography in 49 adult patients prospectively enrolled for diagnosis of papilledema versus pseudopapilledema. Ultrasound was 68% sensitive for papilledema and 54% specific for pseudopapilledema. The ability of ultrasound to detect true papilledema when disc edema was mild was somewhat limited. Further, the correlation between ultrasound results and rNFL longitudinally was less strong than anticipated. This study suggests that ultrasound alone should not be used as the only testing modality when the diagnosis of papilledema versus pseudopapilledema is being sought, but it may be a complementary modality in this context.

Use of En Face Optical Coherence Tomography to Monitor Papilledema in Idiopathic Intracranial Hypertension: A Pilot Study

Carey AR, Bosley TM, Miller NR, McCulley T, Henderson AD.

Journal of Neuro-Ophthalmology. 2021 June 41(2):212-216.

OCT has served as an important ancillary testing tool to assist in the management of patients with IIH. Use of rNFL thickness, optic nerve volume, and GCL thickness have all been evaluated in this setting with respect to diagnosis, treatment effectiveness, and visual prognosis. In this study, authors compared en face OCT features in two patients with papilledema longitudinally with peripapillary rNFL thickness to determine the utility of qualitative en face details including area of disc edema in monitoring papilledema in these patients. In this pilot study, the authors found strong agreement between ranking of degree of disc edema done by trained neuro ophthalmologists who were using en face OCT images and peripapillary rNFL thickness. Given the small sample size, further studies are warranted to determine the use of en face OCT images in clinical practice.

Accuracy of a Deep Learning System for Classification of Papilledema Severity on Ocular Fundus Photographs

Vasseneix C, Raymond P, Najjar RP, Xu X, Tang Z, Loo JL, Singhal S, Tow S, Milea L, Wei Ting DS, Liu Y, Wong TY, Newman NJ, Biousse V, Milea D, on behalf of the BONSAI Group
Neurology. 2021 Jul 27;97(4):e369-e377.

This study is a new publication from the BONSAI (Brain and Optic Nerve Study with Artificial Intelligence) group examining the performance of a deep learning system to grade papilledema severity. Prior publications focused on the performance of deep learning to discriminate papilledema from other forms of optic nerve swelling or abnormality. Papilledema severity grade is relevant as worse disc edema is associated with poorer visual outcomes, but grading according to the Frisen scale often is variable and inconsistent amongst providers. The deep learning system was trained on a dataset of 2103 fundus photos and then tested on a smaller dataset of 214 photos. Papilledema was graded in a binary fashion (mild/moderate Frisen 1-3 versus severe Frisen 4,5). The goals of the study were twofold: to determine whether deep learning was able to discriminate papilledema grade and to compare performance on this scoring versus three neuro-ophthalmologists. Deep learning was comparable to the the group of three neuro-ophthalmologists in severity scoring with a similar sensitivity of 91.8% and a slightly higher specificity of 82.6%. This study importantly expands the potential of utilizing AI to risk stratify patients who present with papilledema and complement the clinical examination. The utilization of AI in this setting may be particularly helpful to the non ophthalmologist in an emergency room or neurology setting.

Long-Term Follow-Up After Unilateral Intravitreal Gene Therapy for Leber Hereditary Optic Neuropathy: The RESTORE Study

Biousse V, Newman NJ, M YW, Carelli P, Carelli V, Moster M, Vignal-Clermont C, Klopstock T, Sadun AA, Sergott RC, Hage R, Esposti S, La Morgia C, Priglinger C, Karanja R, Blouin L, Tiel M, Sahel JA, for the LHON Study Group Less
Journal of Neuro-Ophthalmology. 2021 Sep 41(3):309-315.

Treatments for the mitochondrially inherited optic neuropathy LHON continue to be sought. This study the “RESTORE” study focused on the 3-year visual outcomes of two phase 3 clinical trials RESCUE and REVERSE for LHON utilizing unilateral intravitreal injection of an adenovector virus for the *ND4* gene which is mutated most frequently in LHON and is associated with poor visual prognosis. Primary outcome measure was visual acuity and secondary outcome was QOL in 61 patients. Visual acuity showed a sustained improvement with vision remaining “on chart” (final mean 1.26 logMAR) throughout the study both in treated and also in non-treated eyes. For QOL, there was a significant and meaningful improvement in patients treated. This study reflects a promising therapeutic approach to a potentially devastating condition and may ultimately transform the management of LHON.

6. NYSTAGMUS

none

7. PREMATURITY.

none

8. RETINOPATHY OF PREMATURITY

International Classification of Retinopathy of Prematurity, Third Edition

Michael F. Chiang, Graham E. Quinn, Alistair R. Fielder, Susan R. Ostmo, R.V. Paul Chan, Audina Berrocal, Gil Binenbaum, Michael Blair, J. Peter Campbell, Antonio Capone, Jr., Yi Chen, Shuan Dai, Anna Ells, Brian W. Fleck, William V. Good, M. Elizabeth Hartnett, Gerd Holmstrom, Shunji Kusaka, Andrés Kychenthal, Domenico Lepore, Birgit Lorenz, Maria Ana Martinez-Castellanos, Sengül Özdek, Dupe Ademola-Popoola, James D. Reynolds, Parag K. Shah, Michael Shapiro, Andreas Stahl, Cynthia Toth, Anand Vinekar, Linda Visser, David K. Wallace, Wei-Chi Wu, Peiquan Zhao, Andrea Zin
Ophthalmology; 2021 Oct;128(10):e51-68.

This study reports the work of an international expert committee of 14 pediatric ophthalmologists and 20 retinal specialists to revise the international classification for ROP. The previous revision was from 2005, pre-dating advances in imaging and anti-VEGF treatments. The key terms that were retained were the zones, stages, and circumferential extent of disease. Key new terms include: *posterior zone II* for the region 2 disk diameters peripheral to zone 1; *notch* for an incursion less than 2 clock hours in circumference into a more posterior zone; *aggressive ROP* for rapidly progressive ROP in Zone 1 or posterior zone 2; and *stages 5a, 5b, and 5c* for open funnel, closed funnel, and anterior segment changes, respectively in stage 5 total retinal detachments. New terms related to anti-VEGF treatments include persistent peripheral avascular retina (PAR) and reactivation. The report includes new standard photos to use to define preplus and plus disease. The new terminology is fundamental to documenting, treating, and researching ROP going forward and should be adopted by all practitioners who screen for ROP.

Xu LT, Levine DA, Hutchinson AK, Rao P, Hubbard GB 3rd. Clinical Features And Outcomes Of Infants With Retinopathy Of Prematurity Who Fail Antivascular Endothelial Growth Factor Therapy. Retina. 2021 Nov 1;41(11):2269-2277. PMID: 34190725; PMCID: PMC8542626.

AntiVEGF treatment has been used to treat ROP. It has advantages such as it can be performed without anesthesia, quicker than laser treatment, and lower rates of myopia. Reactivation of ROP has been reported in the literature. The purpose of this study is to describe the characteristics and outcomes of patients with ROP who fail intravitreal anti-VEGF. This is a retrospective case series of 211 eyes at Emory Healthcare and Children's Healthcare of Atlanta. Patients were included in the study if they had antiVEGF as initial therapy. Treatment failure was defined as recurrent plus, recurrent stage 3, onset of stage 4/5, or need for repeat treatment before 50 weeks PMA. 23 eyes of 15 patients failed antiVEGF therapy. The median time to failure was 10 weeks. Failure was presented as recurrent plus in 58% of patients, recurrent stage 3 in 54% of patients, and RD in 21% of patients. Failure was treated with laser, repeat injection or PPV. Initial failure occurred in 13% of patients after 50 weeks PMA. Most patients who failed initial antiVEGF injection had favorable outcomes after secondary treatment. This study adds to the growing literature of risk of reactivation following primary anti-VEGF treatment for ROP and outlines outcomes.

Fundus Pigmentation in the Diagnosis and Treatment of Retinopathy of Prematurity

Kenneth C. Fan, Sarah P. Read, Nimesh A. Patel, Elizabeth A. Vanner, Hasenin Al-Khersan, Diana M. Laura, Parastou Pakravan, Catherin I. Negron, Audina M. Berrocal
Ophthalmology; 2021 Aug;128(8):1242-3

This study attempted to correlate the degree of fundus pigmentation with the severity of ROP at a single university-based NICU. The fundus pigmentation was graded on a three level scale – light (visible choroidal vessels in the macula), medium (visible choroidal vessels only outside the macula), or dark (no choroidal vessels visible) by a single unmasked observer. The ROP was graded using standard international criteria regarding stage, zone and plus disease. More than 1200 infants were examined and placed into three pigmentation groups: 39% light, 58% medium, and only ~2% dark. The infants with a light fundus had 1.4 times the rate of any ROP and 2.7 times the rate of intravitreal anti-VEGF agents. The authors speculate that melanin pigments might perform an antioxidant role in the fundus, so their absence could contribute to more severe ROP. The study could have benefited from including skin pigmentation levels, given neonatologists an easy marker for borderline infants to refer for screening, and also eliminating the dark pigmentation group since so few infants qualified. Overall, however, the size of

the pigmentation effect was large enough to suggest that low fundus pigmentation is likely an independent risk for worse ROP.

Campbell JP, Kim SJ, Brown JM, Ostmo S, Chan RVP, Kalpathy-Cramer J, Chiang MF, on behalf of the Imaging and Informatics in Retinopathy of Prematurity Consortium. *Ophthalmology* 2021;128(7):1070-1076.

The goal of this very interesting study was to evaluate the clinical usefulness of a quantitative deep learning-derived vascular severity score for retinopathy of prematurity (ROP) by assessing its correlation with clinical ROP diagnosis and by measuring clinician agreement in applying a novel scale. The study consisted of analysis of an existing database of posterior pole fundus images (from clinical examinations of patients in the Imaging and Informatics in ROP Consortium) and corresponding ophthalmoscopic examinations by 4 Ophthalmologists and 1 study coordinator using 2 methods of assigning a quantitative scale to vascular severity. A quantitative vascular severity score (scale 1-9) was applied to each image using a deep learning algorithm. A database of 499 images was developed for assessment of interobserver agreement. Distribution of deep learning-derived vascular severity scores with the clinical assessment of zone (I, II, or III), stage (0, 1, 2, or 3), and extent (<3 clock hours, 3–6 clock hours, and >6 clock hours) of stage 3 evaluated using multivariate linear regression and weighted κ values and Pearson correlation coefficients for interobserver agreement on a 1-to-9 vascular severity scale. Results: For deep learning analysis, a total of 6344 clinical examinations were analyzed. A higher deep learning-derived vascular severity score was associated with more posterior disease, higher disease stage, and higher extent of stage 3 disease ($P < 0.001$ for all). For a given ROP stage, the vascular severity score was higher in zone I than zones II or III ($P < 0.001$). Multivariate regression found zone, stage, and extent all were associated independently with the severity score ($P < 0.001$ for all). For interobserver agreement, the mean \pm standard deviation weighted κ value was 0.67 ± 0.06 , and the Pearson correlation coefficient \pm standard deviation was 0.88 ± 0.04 on the use of a 1-to-9 vascular severity scale. The authors conclude that a vascular severity scale for ROP seems feasible for clinical adoption; corresponds with zone, stage, extent of stage 3, and plus disease; and facilitates the use of objective technology such as deep learning to improve the consistency of ROP diagnosis. Of note, there is a very interesting commentary on this article ("Reducing Blindness Resulting from Retinopathy of Prematurity Using Deep Learning" by Drs. Moshfeghi and Trese) in the same issue of *Ophthalmology* discussing the significance of deep learning for ROP.

9. Strabismus

Association between esodeviation and primary open-angle glaucoma: the 2010–2011 Korea National Health and Nutrition Examination Survey

Kim JS, Kim YK, Kim YW, Baek SU, Ha A, Lee J, Lee HJ, Kim DW, Jeoung JW, Kim SJ, Park KH. Br J Ophthalmol. 2021 Dec;105(12):1672-1677.

Recently, the hypothesis that traction of the optic nerve sheath can contribute to the development of glaucoma has been gaining attention. For example, OCT studies have shown that eyeball adduction temporally tilts and displaces the pre-laminar optic nerve head (ONH) and peripapillary tissues. If adduction really does play a role in the development of glaucoma, patients with esodeviation might be especially vulnerable. The authors sought to evaluate the association between strabismus and POAG in a representative Korean population. 11,114 participants aged 20 years or older in the Korea National Health and Nutrition Examination Survey (KNHANES) database over a 1 year period were reviewed. The control group included patients who were not classified into the POAG group, including those who had types of secondary glaucoma (non-POAG). The overall prevalence of POAG among the included participants was estimated to be 3.16%. The overall prevalence of clinically significant esodeviation and exodeviation among the participants were estimated to be 0.16% (95% CI 0.05% to 0.27%, 15 subjects) and 0.51% (95% CI 0.34% to 0.67%, 59 subjects) respectively. The overall prevalence of POAG among the subjects with exodeviation ≥ 15 PD was 3.80% (5 subjects), and that with esodeviation ≥ 10 was 12.32% (3 subjects). Subjects with esodeviation had a significantly higher prevalence of POAG for at least one eye than those without esodeviation ($p=0.016$ for esodeviation >10 PD). Presence of esodeviation was significantly associated with POAG (OR 8.33, $p<0.001$), whereas presence of exodeviation was not ($p=0.990$). After adjusting for age and IOP, esodeviation was significantly associated with POAG (OR 7.61, $p=0.002$). This study has several limitations, including the fact that KNHANES examinations are survey based and not necessarily the result of detailed evaluations by ophthalmologists. Secondly, the number of patients with strabismus was extremely small in the study. While an interesting hypothesis, I think more work needs to be done on this topic.

Home- and Office-Based Vergence and Accommodative Therapies for Treatment of Convergence Insufficiency in Children and Young Adults: A Report by the American Academy of Ophthalmology
Melinda Y. Chang, David G. Morrison, Gil Binenbaum, Gena Heidary, Rupal H. Trivedi, Jennifer A. Galvin, Stacy L. Pineles

Ophthalmology; 2021 Dec;128(12):1756-65

This study reports the results of a literature review on the effectiveness of vision therapy, either office- or home-based, for convergence insufficiency in children and young adults (<35 years old). The overall evidence was quite good, with 8 level 1 studies included. Among those studies, a consistent treatment effect was observed, with improved objective and subjective parameters, but the results were inconsistent when comparing the relative efficacy of office- versus home-based treatments. This inconsistency may have resulted from the wide variety of interventions employed under the umbrella term “vision therapy”. In addition, a substantial percentage of subjects remained symptomatic after treatment, suggesting a proportion of the population that may not respond to vision therapy. The results do support a role for vision therapy for convergence insufficiency, but further research is required to determine the type and intensity of vision therapy that might be most effective as well as the most cost effective.

Increasing incidence and risk factors for divergence insufficiency esotropia.

Xinyi Chen, BS, Justin D. Marsh, MD, Sidra Zafar, MBBS, Elizabeth E. Gerber, MD, PhD, and David L. Guyton, MD.

JAAPOS 2021;25:278.e1-6.

Primary divergence insufficiency (DI) esotropia is a gradually progressive esotropia that is worse at distance than near. The purpose of this study was to document the increasing incidence of this entity and to identify risk factors. A total of 646 patients with acquired esotropia were included in the study. In the cohort from 1978-1988, 11.8% had DI; however, in the cohort from 1999-2018, 29.4% had DI ($p<0.001$). DI was found to be more common amongst patients wearing PALs and amongst older patients. This study shows a clear increase in the incidence of DI from 1978 to 2019. A proposed etiology is as follows: Near work without sufficient spectacle lens power for comfortable near focusing leads to chronic activation of the near triad, which can cause unwanted increase in convergence tonus. Over time, this

convergence leads to shortening of the medial rectus muscles and lengthening of the lateral rectus muscles leading to the characteristic pattern of DI. PALs are thought to contribute to this as it can be difficult to use the full add power in these lenses. This article highlights the possible role of PALs in inadequate optical treatment of presbyopia and its possible role in DI esotropia. It may encourage ophthalmologists to consider lined bifocal/trifocal glasses or separate single vision reading glasses for their patients.

Factors leading to loss to follow-up after strabismus surgery in children.

Daly CM, Dembinski RL, Kraus CL.

J AAPOS. 2021 Jun;25(3):142.

The authors conducted a retrospective review to assess risk factors (LTFU) and identify obstacles to returning for necessary follow up care after strabismus surgery. Children were identified who had not returned for follow up care and a telephone survey was conducted. Demographic information for those not LTFU and those LTFU was compared and reasons given for LTFU were classified. There were significant socioeconomic differences found in these two groups consistent with the literature. Patients who were LTFU were more likely to be black, and have state or government issued insurance. The most common reason for missing postoperative visits were: perceived positive outcome making follow up care unnecessary, work conflicts, transportation issues, travel time, and forgotten appointment. Limitations to the study was the small number of families able to complete survey, ability to participate by telephone and possible spurious responses. Interest in telemedicine as an alternative was expressed by 68% of those participants who completed survey. Possible remedies for LTFU were using teach-back technique to improve education, providing multiple appointment reminders and offering telemedicine appointments. This study is important in highlighting very practical reasons for LTFU and how practices can make changes to make ensure improvement in follow up care after strabismus surgery.

10. STRABISMUS SURGERY

Dose-Response of Primary Bilateral Medial Rectus Resection in Infantile Exotropia.

Farias LB, Barham R, Costa AL, Wang S, Weakley DR Jr.

J Pediatr Ophthalmol Strabismus. 2022;59(1):24-27.

Prepublication. Posted online: August 26, 2021

For children with basic exotropia, bilateral lateral rectus recession vs unilateral recess and resect both have similar cumulative probabilities of suboptimal outcome at 3 years (46% vs 37%). Bilateral medial rectus resection for large angle exotropia has been reported with mixed success in adults. The purpose of this study was to evaluate the dose-response relationship for primary bilateral medial rectus resection in children with basic exotropia. Two of the lead authors performed the same fornix-based, double-armed technique resection in 49 subjects aged 0.7-18 (mean 6.7 ± 5.3 years) with mean preop deviation 48.3 ± 10.1 at distance and 48.2 ± 8.9 at near, and followed them for 21.9 ± 9.7 (range: 6 to 69 months). 53% maintained surgical success (≤ 10 PD residual XT); 59.1% in the 25-45PD group and 48.1% in the >50 PD groups ($P < .05$). The >50 PD group had a longer mean time to recurrence. Reoperations with bilateral lateral rectus recessions were performed in 26.5% of subjects. There were no overcorrections. The dose-response curve was non-linear; the larger resections yielded more response. The authors concluded that primary bilateral medial rectus resection should be considered as a surgical alternative in childhood exotropia, particularly for moderate and constant deviations. Despite a small sample size, this study was a valuable contribution to the management of basic exotropia in childhood because of strict inclusion criteria and long follow-up period.

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. 2021;1-8.

Pre-publication. Posted online December 20, 2021.

The purpose of this study was to examine the potential impact of socioeconomic disparities on strabismus surgery outcomes. The authors retrospectively reviewed cases of 284 children who underwent strabismus surgery at a tertiary care center and were followed for 11 months or more. They found 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. They concluded that there was no difference in failure rates between patients with Medicaid and patients with private insurance and that Medicaid status was significantly predictive of loss to follow-up. This was a focused, well-designed retrospective that produced an interesting result that counters prejudice - that there was no difference between Medicaid and private insurance in strabismus surgery outcomes.

Integrated Intraoperative Optical Coherence Tomography during Scleral Pass in Strabismus Surgery

J Binocul Vis Ocul Motil. 2021 Dec 7;1-3.

Julia Kuhn, Matthew S Pihlblad

This was a retrospective study conducted at the University of Pittsburgh involving surgical videos using iiOCT (integrated intraoperative optical coherence tomography). The maximal needle depth during scleral passes could be visualized at time of surgery. This study evaluated 47 scleral passes with 45 having sufficient image quality to include in the study. These images were from 15 patients, and most involved horizontal recti muscles. Mean percent scleral thickness and standard deviation was $39 \pm 13.7\%$, range 19-88%. When comparing a second pass to the first pass, there was no statistically significant difference in depth of scleral pass between the two. Limitations of this study is the lack of absolute scleral depth, and there still remains some artifacts limiting accurate interpretation of intraoperative OCT images. Applying this technology to assess consistency in young surgeon trainees would one of many possible future directions for this imaging modality.

11. ANTERIOR SEGMENT

Effect of corneal cross-linking versus standard care on keratoconus progression in young patients: the KERALINK randomized controlled trial.

Larkin DFP, Chowdhury K, Burr JM, Raynor M, Edwards M, Tuft SJ, et al. on behalf of the KERALINK Trial Study Group. *Ophthalmology* 2021;128:1516-1526.

In this randomized, controlled trial, Larkin et al. assessed the safety and efficacy of corneal cross-linking in 10-16 year old participants with progressive keratoconus (KCN). At 18 months, KCN progression occurred in 2 of 30 patients (7%) who received cross-linking plus standard care compared with 12 of 28 patients (43%) who received only standard care, and patients in the cross-linking arm had 90% lower odds of experiencing progression compared with those receiving standard care alone. Patients receiving cross-linking in the study eye achieved significantly better corrected and uncorrected visual acuity and lower steep keratometry than those receiving only standard care, and there were no adverse events associated with the cross-linking. The researchers conclude that participants who received cross-linking were less likely to demonstrate clinically significant progressive KCN and visual loss than those treated with standard care alone and suggest that cross-linking arrests progression of KCN in the majority of young patients and should be considered as first-line treatment in progressive KCN. If the arrest of keratoconus progression induced by CXL is sustained in longer follow-up, particular benefit may be derived from avoiding a later requirement for contact lens wear or corneal transplantation.

New Indicator of Children's Excessive Electronic Screen Use and Factors in Meibomian Gland Atrophy.

Cremers SL, Khan AR, Ahn J, Cremers L, Weber J, Kossler AL, Pigotti C, Martinez A.

American journal of ophthalmology. 2021 Apr 17.

After the onset of the coronavirus disease 2019 pandemic, increased interest has been paid to the effects of electronic use and screen time on the eyes. Given the decreased blink rate associated with electronic screen use, there is an interest in correlations between electronic screen time and ocular surface disease such as meibomian gland dysfunction or atrophy. This was a retrospective study of 41 children aged 6-17 years assessing meibomian gland atrophy (MGA) as measured by meibography and correlating this with questionnaires regarding electronic screen use. Their main finding was that 86% of children with MGA had more than 4 hours of screen time per day and 50% had more than 8 hours per day. A subset of these patients (16) were tested for auto-immune pathology and 62.5% revealed an underlying abnormality. This study is limited due to its small sample size, retrospective nature, and reliance of questionnaire data, but poses an interesting question regarding the physiologic effects of electronic screen use on the eyes.

12. CATARACT

none

13. CATARACT SURGERY

Immediate versus delayed sequential bilateral cataract surgery in children: a cost-effectiveness analysis
Cernat A, Jamieson M, Kavelaars R, Khalili S, Bhambhwani V, Mireskandari K, Moretti ME.
Br J Ophthalmol. 2022 Feb;106(2):211-217.

This is a retrospective cost analysis of children who underwent immediate sequential bilateral cataract surgery (ISBCS) or delayed sequential bilateral cataract surgery (DSBCS) at a tertiary referral paediatric hospital in Ontario, Canada, which has a universal, single-payer system. The cohort included all patients who underwent ISBCS or DSBCS under age 2 years over a 10-year period with or without primary IOL implantation, with the DSBCS group having surgery on the second eye within 8 weeks of the first surgery. Both interventions were modelled over an 8-week time horizon to ensure that all surgery-related costs were captured, but not those related to pre-existing conditions. Surgical effectiveness was measured by clear visual axis bilaterally. Both health system (direct healthcare costs usually incurred by the third-party payer) and societal perspectives (i.e., direct healthcare costs of the surgery, indirect costs like productivity losses for parents due to time off work, etc) were reported. Both ISBCS and DSBCS were found to be equally effective in terms of a clear visual axis bilaterally. Compared with DSBCS, ISBCS resulted in average cost-savings of \$3,775.59 per patient from the societal perspective. From the health system perspective, ISBCS resulted in cost savings of \$2,199.65 compared with DSBCS. The mean overall cost of undergoing ISBCS was \$16,003.66 (95% CI: \$11,096.29 – \$22,720.33) from the societal perspective, while the mean overall cost of undergoing DSBCS was \$19,779.25 (95% CI: \$13,319.61 – \$28,566.18). While multiple factors go into the decision to pursue ISBCS vs DSBCS in children, this study demonstrates the cost-effectiveness and equal efficacy of ISBCS.

A sustained-release intracanalicular dexamethasone insert (Dextenza) for pediatric cataract surgery.
Trivedi RH, Wilson ME.

J AAPOS. 2021 Feb;25(1):43-45.

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

14. GLAUCOMA

none

15. REFRACTIVE SURGERY

none

16. GENETICS

Association of Variants in TMEM45A With Keratoglobus.

Weiner C, Hecht I, Kotlyar A, Shoshany N, Zadok D, Elbaz U, Segev F, Maytal A, Hachmo Y, Michiels C, De Backer O, Shomron N, Einan-Lifshitz A, Pras E. *JAMA Ophthalmol.* 2021 Oct 1;139(10):1089-1095. Keratoglobus is a rare corneal disorder characterized by generalized thinning and globular protrusion of the cornea. Affected individuals typically have significantly decreased vision and are at risk of corneal perforation. This study aims to identify the genetic basis of isolated congenital keratoglobus. Three nonconsanguineous families with keratoglobus were included in this study. Gene sequencing was used to identify truncating and splice site variants in the TMEM45A gene, which fully segregate with the disorder. All affected individuals were homozygous or compound heterozygous for variants in the TMEM45A gene, while unaffected family members were heterozygous carriers. Expression analysis in healthy controls showed that TMEM45A was expressed 23 times higher in the human cornea compared with peripheral blood. Immunohistochemical staining of the TMEM45A protein in normal corneas confirmed its expression in the corneal stroma and epithelium. A TMEM45A knockout mouse model showed structural features consistent with keratoglobus. This study identified a novel genetic variant as a cause of congenital keratoglobus. This is an important finding to help with diagnosis and genetic counseling in patients with keratoglobus, as well as provide a potential future therapeutic target.

CRB1-associated retinal dystrophies: a prospective natural history study in anticipation of future clinical trials.

Talib M, van Schooneveld MJ, Wijnholds J, van Genderen MM, Schalijs-Delfos NE, Klaver CC, Talsma HE, Fiocco M, Florijn RJ, Jacoline B, Cremers FP. *American Journal of Ophthalmology.* 2022 Feb 1;234:37-48.

A wide range of related retinal dystrophies including Leber congenital amaurosis (LCA), retinitis pigmentosa (RP), and cone(-rod) dystrophies (CRDs), can be caused by variants in the crumbs cell polarity complex component 1 (CRB1) gene. The purpose of this single-center, prospective case series is to report on the natural disease course of retinal dystrophies associated with CRB1 and identify clinical end points for future clinical trials. An investigator-initiated nationwide collaborative study that included 22 patients with CRB1-associated retinal dystrophies. Patients underwent ophthalmic assessment at baseline and 2 years after baseline. Clinical examination included best-corrected visual acuity (BCVA) using Early Treatment Diabetic Retinopathy Study charts, Goldmann kinetic perimetry (V4e isopter seeing retinal areas), microperimetry, full-field electroretinography, full-field stimulus threshold (FST), fundus photography, spectral-domain optical coherence tomography, and fundus autofluorescence imaging. Based on genetic, clinical, and electrophysiological data, patients were diagnosed with retinitis pigmentosa (19 [86%]), cone-rod dystrophy (2 [9%]), or isolated macular dystrophy (1 [5%]). Analysis of the entire cohort at 2 years showed no significant changes in BCVA ($P = .069$) or V4e isopter seeing retinal areas ($P = .616$), although signs of clinical progression were present in individual patients. Macular sensitivity measured on microperimetry revealed a significant reduction at the 2-year follow-up ($P < .001$). FST responses were measurable in patients with nonrecordable electroretinograms. On average, FST responses remained stable during follow-up. In CRB1-associated retinal dystrophies, visual acuity and visual field measures remain relatively stable over the course of 2 years. Microperimetry showed a significant decrease in retinal sensitivity during follow-up and may be a more sensitive progression marker. Retinal sensitivity on microperimetry may serve as a functional clinical end point in future human treatment trials for CRB1-associated retinal dystrophies.

Establishing risk of vision loss in Leber hereditary optic neuropathy.

Sanchez MI, Kearns LS, Staffieri SE, Clarke L, McGuinness MB, Meteoukki W, Samuel S, Ruddle JB, Chen C, Fraser CL, Harrison J. *The American Journal of Human Genetics.* 2021 Nov 4;108(11):2159-70. We conducted an updated epidemiological study of Leber hereditary optic neuropathy (LHON) in Australia by using registry data to establish the risk of vision loss among different LHON mutations, sex, age at onset, and mitochondrial haplogroup. We identified 96 genetically unrelated LHON pedigrees, including 56 unpublished pedigrees, and updated 40 previously known pedigrees, comprising 620 affected individuals and 4,948 asymptomatic carriers. The minimum prevalence of vision loss due to LHON in Australia in 2020 was one in 68,403 individuals. Although our data confirm some well-

established features of LHON, the overall risk of vision loss among those with a LHON mutation was lower than reported previously—17.5% for males and 5.4% for females. Our findings confirm that women, older adults, and younger children are also at risk. Furthermore, we observed a higher incidence of vision loss in children of affected mothers as well as in children of unaffected women with at least one affected brother. Finally, we confirmed our previous report showing a generational fall in prevalence of vision loss among Australian men. Higher reported rates of vision loss in males with a LHON mutation are not supported by our work and other epidemiologic studies. Accurate knowledge of risk is essential for genetic counseling of individuals with LHON mutations. This knowledge could also inform the detection and validation of potential biomarkers and has implications for clinical trials of treatments aimed at preventing vision loss in LHON because an overestimated risk may lead to an underpowered study or a false claim of efficacy.

The safety and efficacy of gene therapy treatment for monogenic retinal and optic nerve diseases: A systematic review.

Britten-Jones AC, Jin R, Gocuk SA, Cichello E, O'Hare F, Hickey DG, Edwards TL, Ayton LN. *Genet Med*. 2021 Nov 30:S1098-3600(21)05365-X Epub ahead of print. PMID: 34906485.

The study reviews DNA-based ocular gene therapy treatments for 16 different genetic variants. Study summaries and visual representations of safety and efficacy outcomes are presented for 20 unique full-text publications in RPE65-mediated retinal dystrophies, choroideremia, Leber hereditary optic neuropathy, rod-cone dystrophy, achromatopsia, and X-linked retinoschisis. 2 were randomized control trials and 16 were single group studies using the untreated eye as a control., while 2 had no control. All studies were considered to have a high risk of detection bias due to lack of blinding, selection bias, reporting partial data. Most adverse events were minor. The intravitreal injection delivery had more inflammation and increased IOP. The treatment with most reports was RPE65 gene therapy. 101 individuals aged between 4 and 46 years with variants in RPE65 were treated with subretinal gene therapy since Oc 2007. Two major outcomes where a significant improvement was found were full-field stimulus threshold (FST) test and mobility evaluation assessed using MLMT. Long-term follow-up suggests retinal thinning in treating eyes. The next most common was LHON. 78 individuals with ND4-associated LHON were enrolled and treated with intravitreal gene therapy treatment between 2011 and 2017. 32 males with choroideremia aged 24 and 63 years were treated with subretinal AAV2.REP1 gene therapy (NightStar Therapeutics) from 2012 to 2016. RPGR, achromatopsia, X-linked retinoschisis and rod-cone dystrophy caused by variants in the MERTK gene early phase I/II data were available.

17. TRAUMA

Timing of ocular hypertension after pediatric closed-globe traumatic hyphema: implications for surveillance.

Bowe T, Serina A, Armstrong M, Welcher J, Adebona O, Gore C, Staffa SJ, Zurakowski D, Shah AS. American journal of ophthalmology. 2022 Jan 1;233:135-43.

Traumatic closed globe injuries associated with hyphema are known to cause ocular hypertension, though the exact incidence and timing of this complication are not fully elucidated. This was a study of 305 pediatric patients less than 18 years old who suffered closed globe injury with associated hyphema. Of those patients, 39% developed ocular hypertension. The authors divided the post-injury period into the following categories: presentation, acute (days 1-7), sub-acute (days 8-28), or late (days >28). Ocular hypertension was most common 1-7 days after the injury, but there were a significant number of episodes of ocular hypertension occurring in the late period. Based on their data, the authors propose a risk stratification tool, which is included as a figure in the paper and accounts for multiple factors including degree of hyphema on presentation, presence of ocular hypertension on presentation, pupil damage, steroid use, iridodialysis, angle recess, and traumatic cataract. Overall, this study provides additional information on ocular hypertension after traumatic hyphema and equips the reader with an algorithm through which patient risk can be stratified.

18. RETINA

Patterns of retinal hemorrhage associated with cardiac arrest and cardiopulmonary resuscitation.

Binenbaum G, Forbes BJ, Topjian AA, Twelves C, Christian CW.

J AAPOS. 2021 Dec;25(6): 324.e1-324.e4

Obtaining forensic evidence and testifying in abusive head trauma cases is an important part of the job for many pediatric ophthalmologists. Defense lawyers propose alternative causes for retinal hemorrhages in these cases such as cardiac arrest and cardiopulmonary resuscitation. The authors performed a prospective, single center, consecutive observational study of 18 children who were examined within 48 hours after arrest and CPR in order to determine the prevalence and characteristics of retinal hemorrhages in this clinical scenario. Previous studies had limitations involving examination by nonophthalmologists, inadequate techniques, and inadequate clinical descriptions. The authors found that CPR for cardiac arrest is rarely associated with retinal hemorrhages when there was no other explanation for the retinal hemorrhages. The findings of this study are consistent with previous studies. Pooling of data from previous studies gave a prevalence of retinal hemorrhage following CPR of 3.3% with a pattern of a limited number of posterior pole intraretinal hemorrhages. Strengths were prospective study, dilated exam by ophthalmologist and handling of confounding factors. Although sample size was small, the results were consistent with other studies. This article is important to pediatric ophthalmologists because it provides evidence to support testimony in abusive head trauma cases.

Evaluation of Retinal Structure in Pediatric Subjects with Vitamin D Deficiency.

Aydemir E, Ilhan C, Aydemir GA, Bayat AH, Bolu S, Asik A.

American Journal of Ophthalmology. 2022 Jan 1;233:30-7.

Vitamin D deficiency is common in developing countries, and the American Academy of Pediatrics recommends vitamin D supplementation in the first months of life. The role of vitamin D in eye disease, and specifically, retinal development, is unknown. This is a prospective observational study of 150 children less than 18 years old with and without vitamin D deficiency assessing retinal anatomic structures as measured with OCT. Overall, they found that children with vitamin D deficiency demonstrated choroidal thinning compared to age-matched controls. There were no differences in retinal nerve fiber layer thickness between groups. The authors propose that given the possible neuroprotective effect of vitamin D, its deficiency may lead to problems with retinal development, though acknowledge that the choroidal thinning they identified may not be clinically significant

Clinical Features And Surgical Outcomes Of Encircling Scleral Buckling With Cryotherapy In Familial Exudative Vitreoretinopathy-Associated Rhegmatogenous Retinal Detachment

Huang L, Liang T, Lyu J, Jin H, Zhao P.

Retina. 2022 Jan 1;42(1):55-63.

FEVR is a familial disorder characterized by incomplete retinal vascularization. RD is a serious complication leading too loss of vision in 21-64% of eyes. This is a retrospective study evaluating the clinical features and surgical outcomes of FEVR-RRD patients who underwent ESB surgery. This is a retrospective interventional case series at a single center. All patients were diagnosed with FEVR by FA. Patients were treated with cryo followed by scleral buckling. 24 eyes of 24 patients were included in the study. No patients had their scleral buckle divided later. Stage 3A and 4A FEVR were found in 16 eyes and 8 eyes respectively. Retina reattachment was achieved in 91.67% of eyes after initial surgery. 2 eyes had recurrent RD and required PPV due to PVR. BCVA improved from 0.45 log of minimal angle of resolution to 1.08. A myopic shift of 2.4 diopters was seen postoperatively. Complications such as cataract formation and glaucoma were not seen in this cohort follow up period of 7-104 months. The authors concluded that scleral buckling with cryo as an effective treatment with patients with stage 3A or 4A and grade A or B PVR.

19. RETINOBLASTOMA / INTRAOCULAR TUMORS

Iodine-125 Plaque Radiotherapy for Retinoblastoma Recurrence Following Intra-arterial Chemotherapy
Ruben M, Eiger-Moscovich M, Yaghy A, Tadepalli S, Shields CL.

J Pediatr Ophthalmol Strabismus. 2021;1-8.

Pre-publication. Posted online December 20, 2022

The purpose of this study was to assess the efficacy and toxicity of Iodine-125 (I-125) plaque radiotherapy for retinoblastoma following intra-arterial chemotherapy (IAC). The authors retrospectively reviewed the records of 41 subjects with 41 eyes and retinoblastoma who underwent I-125 plaque therapy for a mean radiation dose to tumor of 3,483 centigray (cGy) delivered at mean rate of 35 cGy/hr. The irradiated site was controlled in 39 eyes (95%) at a median of 20 months after plaque radiotherapy for solid tumor (31 of 33, 94%), subretinal (6 of 6, 100%), and vitreous seeds (2 of 2, 100%). A subgroup of tumors occurring within an ischemic retinal/choroidal field was identified on fluorescein angiography (n = 24) and demonstrated control in 22 of 24 (92%). Using Kaplan-Meier analysis, radiation complications at 2 years included vitreous hemorrhage (37%), retinopathy (28%), papillopathy (18%), and cataract (18%). Five eyes (12%) were enucleated for recurrence outside the irradiated area, chronic vitreous hemorrhage, and/or total retinal detachment. The authors concluded that Iodine-125 plaque radiotherapy provided 95% control for retinoblastoma tumors that failed IAC, including those in ischemic fields untreatable with further chemotherapy. This is a great article that provides insight into the long-term complications of Rb management that are not easily captured or with nearly the magnitude elsewhere.

20. ORBIT

none

21. OCULOPLASTICS

Office- or Facility-Based Probing for Congenital Nasolacrimal Duct Obstruction: A Report by the American Academy of Ophthalmology

David G. Morrison, Gil Binenbaum, Melinda Y. Chang, Gena Heidary, Rupal H. Trivedi, MD, Jennifer A. Galvin, Stacy L. Pineles

Ophthalmology; 2021 June;128(6):920-7

This study was a literature review to compare the safety and efficacy of in-office versus facility-based NLD probing. A total of 21 articles were deemed of sufficient quality for analysis. The most striking finding was level 1 evidence for 2/3s of NLD obstructions spontaneously resolving between 6 months and one year of age. The other strong finding was that bilateral in-office probing was much less effective (67%) than unilateral in-office probing (82%), suggesting that facility-based probing might be indicated for bilateral cases. When analyzing the costs of each approach, despite a higher per procedure cost, facility-based probing at an older age was more cost effective when factoring in the high percentage of spontaneous improvement over time, negating the need for any procedure. Neither approach was associated with any serious adverse effect, either from the procedure or from anesthesia. The evidence provides some support for the authors' conclusion that deferring the procedure until the child is 12 to 18 months of age and performing the procedure in a facility under anesthesia is likely more effective and more cost effective.

Surgical Site Reassessment: An Important Step in Improving Clinical Outcomes Following Pediatric Endoscopic Dacryocystorhinostomy.

Stockhammer Kaner N, Soudry E, Koren I, Gilony D, Avisar I.

J Pediatr Ophthalmol Strabismus. 2021;58(3):168-173.

Published May 1, 2021

Endoscopic dacryocystorhinostomy (DCR) provides solutions to the many drawbacks of the external approach (eg, better nasal visualization, lack of external facial scarring, less surgical trauma to the medial canthal and orbital tissue, less bleeding, a shorter postoperative course, and being less time-consuming than external surgery), but it has many challenges in pediatric patients (eg, poorly-defined/rapidly changing anatomy, small nasal vestibule and cavity, larger inferior turbinates, deviated nasal septum for which septoplasty is contraindicated in kids. This single-center retrospective study of 47 children aged 1.5-17 yrs (mean 6.9yrs) who underwent a total of 68 cases of endoscopic unpowered DCR and 52 surgical site reassessment after tube removal. Of those, 49/52 (94.2%) were deemed to have anatomical success (duct patency on irrigation) and 63 of the original 68 cases were deemed to have clinical success (resolution of symptoms). Only 5 of 68 cases required further treatment (debridement of granulomatous tissue) during re-evaluation. The authors concluded that pediatric endoscopic DCR is an effective surgical procedure for resistant NLDO, and strongly suggest surgical site reassessment to capture and treat incomplete patency. This is an important study reinforcing the role of endoscopic DCR, where available, in the definitive management of NLDO, and it adds key insight into the value of surgical site reassessment at the time of extubation.

22. INFECTIONS

Ophthalmic antibiotic use for acute infectious conjunctivitis in children.

Frost HM, Sebastian T, Durfee J, Jenkins TC.

J AAPOS. 2021 Dec;25(6): 350.e1-350.e7.

Antibiotic treatment is often unnecessary in acute conjunctivitis in children resulting in adverse drug reactions, increased drug costs, drug resistance and disruption of normal flora. The authors used retrospective review to determine factors associated with ophthalmic antibiotic prescribing and changes in prescribing during the COVID-19 pandemic. The authors found a high rate overall (72.7%) for ophthalmic antibiotic use for acute conjunctivitis. Patients diagnosed using nurse-line protocols almost always received (94%) ophthalmic antibiotics as per protocol. Optometrists and ophthalmologists were least likely to prescribe ophthalmic antibiotics. The start of the pandemic saw decreased in person visits and higher telephone visits resulting in marked increase in children who were prescribed ophthalmic antibiotics by nurse-line and other providers. The authors review that the requirement for treatment of conjunctivitis with ophthalmic antibiotics mandated by daycare and schools drives much of the unnecessary prescriptions. These policies also increase health disparities. The authors also list inability to determine etiology of infection as another reason for unnecessary prescribing of ophthalmic antibiotics even though many bacterial infections may also be self-limited and not require the antibiotic therapy. Limitations of the study were inability to determine fill rate for prescriptions, small sample size, possible use of oral antibiotics for treatment which would not have been captured, and single institution study. This study is important because it shows evidence of unnecessary antibiotic use despite CDC prescribing recommendations driven by phone treatment protocols and school/daycare rules for return after illness. The authors opine that this situation begs for an antibiotic stewardship intervention.

23. PEDIATRICS / SYNDROMES / SYSTEMIC DISEASE

Ophthalmologic characteristics and outcomes of children with cortical visual impairment and cerebral palsy

West MR, Borchert MS, Chang M.

JAAPOS 2021; 25: 223.e1-223.e6

This is retrospective medical record chart review of children with cortical visual impairment (CVI) with and without cerebral palsy (CP). A total of 151 children with CVI1CP and 153 children with CVICP were included. Children with CVI1CP were more likely to be diagnosed with significant refractive error (53.6%, optic atrophy (46.4%) and strabismus (82.8%) at presentation. Based on this study cohort, children with CVI1CP had a higher likelihood of ophthalmic comorbidities and may have worse long-term strabismus surgery outcomes than children with CVICP.

24. UVEITIS

Uveitis in Juvenile Idiopathic Arthritis: 18-Year Outcome in the Population-based Nordic Cohort Study
Veronika Rypdal, Mia Glerup, Nils Thomas Songstad, Geir Bertelsen, Terje Christoffersen, Ellen D. Arnstad, Kristiina Aalto, Lillemor Berntson, Anders Fasth, Troels Herlin, Maria Ekelund, Suvi Peltoniemi, Peter Toftedal, Susan Nielsen, Sanna Leinonen, Regitze Bangsgaard, Rasmus Nielsen, Marite Rygg, MD, Ellen Nordal, for the Nordic Study Group of Pediatric Rheumatology
Ophthalmology; 2021 April;128(4):598-608

This study prospectively followed a cohort of 434 patients with JIA to assess the visual and ocular outcomes after 18 years of follow up. Over the study period, 22% developed uveitis, with 90% detected in the first 8 years of exams with a median onset of 1.6 years after diagnosis with JIA. More than half were bilateral and chronic, while more than 1/3 of the remaining patients had recurrent uveitis. More than 30% experienced ocular complications, most commonly cataract formation (31%) and glaucoma (27%). All 8 patients who developed uveitis prior to the diagnosis of JIA developed cataracts. Independent risk factors for visual impairment included shorter duration between onset of JIA and diagnosis of uveitis and positive ANA test. Overall, the reported incidence of uveitis and visual impairment is lower in this study compared with earlier population-based surveys, possibly because of the development of more effective treatments with fewer ocular side effects. Finally, screening more than 8 years after diagnosis of JIA may not be necessary since no patient developed symptomatic uveitis after that duration.

25. PRACTICE MANAGEMENT/ HEALTH CARE SYSTEMS / EDUCATION

The flipped-classroom approach to teaching horizontal strabismus in ophthalmology residency: a multicentered randomized controlled study.

Lu RY, Yanovitch T, Enyedi L, Gandhi N, Gearing M, de Alba Campomanes AG, Cavuoto KM, Gray M, Kemp PS, Silverstein E, Loh AR, Ding L, Cabrera MT.

J AAPOS. 2021 Jun;25(3):137.

The authors used multicentered randomized controlled study to assess resident preference for classroom styles (traditional lecture vs. flipped-classroom) and as a secondary outcome to compare knowledge acquisition of each style when teaching horizontal strabismus in ophthalmology residency. Ophthalmology education typically involves lecture format. Flipped-classroom approach, which involves preclass time reviewing online lectures and classroom time dedicated to discussion based cases, has been shown to provide favorable outcomes in graduate medical education. Most ophthalmology residents (62%) favored the flipped-classroom to traditional method while 85% wanted to see flipped-classroom implemented for at least 25% of their educational sessions. This study correlated with previous studies showing higher learner satisfaction. Flipped-classroom format resulted in similar outcomes to traditional classroom when considering content testing. Increasing seniority correlated with preference for flipped-classroom style. In this study, residents were more likely to complete preparatory work for the flipped-classroom style compared to traditional lecture style. The authors suggest flipped-classroom should be considered for ophthalmology residency education. This study is important because it highlights the need to stay current with new teaching methods in order to improve medical education for ophthalmology residents.

Social media and vision therapy: Perspectives of providers and patients on Instagram.

Johnson A, Khan S, Koo EB.

J AAPOS. 2021 Jun;25(3):166.

The authors analyzed public Instagram posts for content, intent and authorship of the most popular Instagram hashtags involving pediatric ophthalmology. The literature tells us that more than 40% of consumers state that the information they find on social media influences their healthcare decisions. There is increasing use of Instagram posts by the medical community and patients. There has been little analysis of Instagram content concerning pediatric ophthalmology.

Instagram is an unregulated environment where evidence based information as well as controversial topics can be presented. Vision therapy (VT) is a modality used to treat deficits of binocular function, visual processing and perception where exercises are prescribed. There is conflict between ophthalmology and optometry concerning the efficacy of vision therapy. The authors seek to explore the VT presence on Instagram. Analysis of the posts demonstrated statistically significant relationship between the post owner and intent, post owner and diagnosis as well as providing advice. Less than 10% of posts showed evidence based research to support the information in the post. Only 14 of 1,766 posts were created by an ophthalmologist. Instagram provides an unregulated platform for promotion of VT with a lack of scientific evidence. On a positive note, it was also found that social media provides an environment for patients for support, engagement and advocacy. The authors acknowledge limitations of the study that include search issues involving hashtags, inability to access private accounts, using posts in English or English translation and limited scope of Instagram for analysis. This study is important because it highlights an opportunity to reach patients with evidence based information where there is vacuum of credible information.