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

"All-Stars" Handout

AAPOS Virtual Meeting

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Presented by the

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1. AMBLYOPIA

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

This is a prospective s a randomized clinical trial of 63 amblyopic children (age 4-10 with amblyopic visual acuity 20/40 – 125) randomly assigned to one of four daily contrast increment protocols for 4 weeks, all starting with 20% fellow eye contrast: : 10%, 5%, 0%, or 10% for first 4 weeks then reset to 20% and repeat 10% increment for the final 4 weeks. Children played contrast-rebalanced games for 1 hour/day, 5 days/week. Best-corrected visual acuity, stereoacuity, and suppression were assessed at baseline and every 2 weeks until the 8-week outcome visit. At baseline, mean amblyopic eye best-corrected visual acuity was 0.47 +/- 0.14 logMAR (20/ 60), improving overall to 0.14 +/-0.08 logMAR (1.4 lines; P<0.0001) at 8 weeks. All four protocols resulted in similar improvement in visual acuity (0.13-0.16 logMAR; all Ps < 0.0002). Stereoacuity and suppression also improved (all Ps < 0.05). One limitation of the current study was the absence of long-term follow-up. Although 92% of children had improved visual acuity at 8 weeks, 60% remained amblyopic and returned to patching. Thus, we were unable to determine the lasting effects of binocular treatment. This study suggests that none of the new protocols resulted in less improvement than the original 10% contrast increment protocol. Contrast-rebalanced binocular games yielded significant improvements in visual acuity, stereoacuity, and suppression with or without daily contrast increments.
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2. VISION SCREENING

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

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

3. REFRACTIVE ERROR

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

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

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

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

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

In this double-masked randomized clinical trial conducted in Hong Kong, children meeting the inclusion criteria (>-1.0D of myopia in both eyes, <2.5 D of astigmatism and > 0.5D progression of myopia in

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

1. VISUAL IMPAIRMENT

There are no all-star articles in this section.

5. NEURO-OPHTHALMOLOGY

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

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

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

This retrospective observational case series of 45 children with neurofibromatosis type 1 (NF1) associated optic pathway gliomas (OPGs) with follow up of 10 years or longer was performed at one academic institution. The goal of the study was to better understand the long term follow up in patients with NF1- associated OPGs. The authors reviewed charts of patients over a 22 year period and included only those with at least 10 years of follow up or longer (mean 14 years). They found that a third of patients had moderate to severe visual impairment in one eye and 11% in both eyes. Optic nerve appearance and visual acuity at presentation were the factors that could predict longer term outcomes and that virtually all patients who were asymptomatic at presentation did very well. This paper is unique in that it has very long follow up period. The data in this paper further supports deferring neuroimaging in patients with NF1 who have normal acuity and exam findings. This paper is relevant to the pediatric ophthalmologist because it contributes to a growing but compelling body of literature reminding us that

not all patients with NF1 need neuroimaging, and this point is made stronger by this paper due to it's very long follow up period.

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

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

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

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

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

Horner syndrome in children can present as an isolated benign entity or can be a harbinger of serious pathology. The goal of this retrospective study was to assess the incidence of serious etiology in pediatric

Horner syndrome in a group of 48 patients diagnosed between age 1 month and 17 years. In their cohort, a serious etiology was discovered in 15% of patients including neuroblastoma, nasopharyngeal carcinoma, and desmoid tumor. All of the neuroblastoma patients presented with an isolated Horner syndrome and the tumor was only discovered in the workup of the Horner syndrome. In children without a known cause of Horner syndrome, such as birth trauma, the authors recommend urine catecholamines and imaging of the sympathetic chain to rule out serious etiologies, with an estimate risk (based on this study and their review of prior studies) being around 13%, or 1 in every 8 cases.

6. NYSTAGMUS

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

Summary: Acute nystagmus (AN) is an uncommon neurologic sign in children presenting to pediatric emergency departments. The authors of this retrospective, multicenter, cohort study conducted in Italy describe the epidemiology, clinical features, and underlying causes of AN in a large cohort of children with the goal of identifying features associated with higher risk of severe underlying urgent conditions (UCs). The authors reviewed the clinical records of all patients aged 0 to 18 years presenting for AN to the pediatric emergency departments of 9 Italian hospitals over an 8-year period. Excluded were patients with: (1) abnormal eye movements other than nystagmus (such as ocular flutter, opsoclonus, and/or supranuclear gaze disturbances), (2) patients presenting to the pediatric emergency department because of head injury or (3) epileptic seizures, and (4) patients affected by an already known neurologic condition explaining the nystagmus. Clinical and demographic features and the underlying causes were analyzed. A logistic regression model was applied to detect predictive variables associated with a higherrisk of UCs. Results: A total of 206 patients with AN were included (male-to-female ratio: 1.01; mean age: 8 years 11 months). The most frequently associated symptoms were headache (43.2%) and vertigo (42.2%). Ataxia (17.5%) and strabismus (13.1%) were the most common neurologic signs. Migraine (25.7%) and vestibular disorders (14.1%) were the most common causes of AN. Idiopathic infantile nystagmus was the most common cause in infants < 1 year of age. UCs accounted for 18.9% of all cases, mostly represented by brain tumors (8.3%). The logistic regression analysis showed that cranial nerve deficits, ataxia, or strabismus were strongly associated with an underlying UC. Presence of vertigo or attribution of a nonurgent triage code was associated with a reduced risk of UCs. The authors conclude that AN should be considered an alarming finding in children given the risk of severe UCs. Cranial nerve palsy, ataxia, and strabismus should be considered red flags during the assessment of a child with AN.

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

7. PREMATURITY

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

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

8. RETINOPATHY OF PREMATURITY

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

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

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

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

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

The authors analyzed images previously collected from a large prospective study where non-physician health care workers used narrow field imaging (Pictor) to obtain retinal images of infants being screened for ROP at one institution. Of note, previously, imagers had selected 1-3 images per eye at each imaging session for telemedicine image grading. So, for this study, one imaging session per eye per infant was

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

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

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

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

This study assessed the efficacy and safety of early vitamin A (VA) supplementation to improve outcomes of retinopathy of prematurity in extremely preterm infants. A total of 262 eligible extremely preterm infants underwent randomization; of these, 132 were assigned to the VA group and 130 to the control group. The infants were administered a solution of VA (1,500 IU/day), added to their enteral feeds as soon as minimal feeding was introduced and continued for 28 days or until discharge. With no adverse effects occurring, serum VA of the VA-supplemented infants on Days 14, 28, and postmenstrual 36 weeks was higher than that of the placebo group (P , 0.001). No signs of VA toxicity or increased intracranial pressure were reported. The VA group had lower unadjusted rates of Type 1 retinopathy of

prematurity (1.6 vs. 6.9%, P = 0.030) and bronchopulmonary dysplasia (18.9 vs. 33.8%, P = 0.008) than the control group. Regression analysis revealed an association between serum VA levels and risk of Type 1 retinopathy of prematurity (beta = 22.37). Vitamin A supplementation reduced VA deficiency in extremely preterm infants; it was associated with a decreased incidence of Type 1 retinopathy of prematurity and may also have a positive impact on reducing bronchopulmonary dysplasia. The study introduces a potential method to help decrease risk of ROP progression but needs to be repeated on a larger scale.

9. STRABISMUS

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

The goal of this retrospective population-based cohort study was to report the prevalence of pseudostrabismus in the first year of life and the subsequent diagnosis of true strabismus. The authors looked at all the residence of Olmsted county Minnesota under the age of 1 who were diagnosed with pseduostrabismus over a ten year period using medial record linkage system. They found that 1/113 children had a diagnosis of pseudostrabismus in the first year of life. Most of these patients were diagnosed by a non-ophthalmologist, but confirmed by an ophthalmologist. Approximately half of the infants had at least one follow up and 9 of those (5%) were diagnosed with strabismus at a mean age of 4.5 years. The authors concluded that pseudostrabismus was a common diagnosis but that the prevalence of true strabismus in the cohort of patients diagnosed with pseudostrabismus was lower than in previous reports which range from a rate of 9.6 to 19%. The methods of this paper, while retrospective, are expectedly strong and the authors point out that this population may not be representative of the country as a whole. Based on previous studies, the authors expected rates of true strabismus in the patients initially diagnosed to have pseudostrabismus to be closer to 10%, which they were not. The authors hypothesize that previous studies had selection bias since those patients with follow up tended to be those where the families or pediatricians noted eye deviation. This paper is important to the pediatric ophthalmologist because it suggests that the rate of true strabismus might be lower than we think in patients with pseudoesotropia and perhaps the surveillance that many of us do after diagnosing pseudoesotropia is not necessary.

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

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

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

This retrospective review of 732 patients at one institution over 5 years who had an Ahmed glaucoma valve (AGV) implanted aimed to describe strabismus in patients after this procedure. The authors found that 29 of the patients (4%) developed new-onset strabismus after AGV and of those 21 (72%) had

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

10. STRABISMUS SURGERY

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

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

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

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

Medial Rectus Advancement for Secondary Exotropia

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

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

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

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

12. CATARACT

There are no all-star articles in this section.

13. CATARACT SURGERY

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

Summary: The purpose of this report was to describe outcomes for eyes that received secondary IOL implantation, including a comparison of outcomes with aphakic eyes that did not undergo secondary IOL implantation, and eyes that had primary intraocular lens implantation in early infancy. The stud was a secondary analysis of patients enrolled in the Infant Aphakia Treatment Study (IATS), a randomized clinical trial conducted at multiple clinical centers throughout the United States, that involved review of the details of all secondary intraocular lens surgeries performed. Visual outcomes, refractive outcomes, and adverse events at age 10.5 years were evaluated. Comparisons were made with eyes that remained aphakic and with eyes randomized to primary IOL placement. The IATS included 114 infants with unilateral cataracts, 57 in the aphakic group and 57 in the primary IOL group. Of those randomized to the aphakia with contact lens correction group, 55/57 were evaluated at a 10.5 year study visit and 44% (24/55) of these patients had had a secondary IOL implanted. The median age at the time of surgery was 5.4 years (range 1.7-10.3 years). For secondary IOL surgery, biometry and surgical technique were by surgeon preference. Mean absolute prediction error was 1.00 +/- 0.70 D. At age 10.5 years, the median logarithm of the minimum angle of resolution visual acuity was 0.9 (range 0.2-1.7), similar to Va in the 31 eyes still aphakic (0.8, range 0.1-2.9). The number of eyes with stable or improved Va scores between the 4.5 year and 10.5 year study visits was also similar (78% secondary IOL eyes; 84% aphakic eyes). For eyes undergoing IOL implantation after the 4.5 year study visit (n=22), the mean refraction at age 10.5 years was -3.20 +/- 2.70 D (range -9.90 to 1.10D), compared with -5.50 +/- 6.60 D (n=53, range -26.50 to 3.00 D) in eyes with primary IOL (p=0.03). Importance: While most patients with infantile cataracts are anticipated to receive an IOL at some point, the timing of implantation has been controversial. For one thing, prediction error after pediatric cataract surgery is more variable than after adult cataract surgery. Secondly, significant axial elongation occurs in early childhood, so large degrees of myopic shift can occur in pseudophakic eyes. It has been thought that postoperative myopic shift might be minimized by performing IOL implantation after 5 years of age. This study shows that even with delayed IOL implantation, myopic shift was greater than that anticipated in many eyes. Also, while delayed IOL implantation allows a more predictable refractive outcome range at 10.5 years, the range of refractive error is still large. Finally, the results show that it is important to counsel families that the Va after IOL implantation is not expected to be significantly different than the Va obtained with contact lens or spectacle use. The authors provide a detailed explanation of the limitations of the study, but despite these limitations, the report suggests that there are refractive advantages to delaying secondary IOL surgery until school age. When the elective surgery is performed by an experienced surgeon after age 5 years, the complication rate is low and there are far fewer adverse effects than when IOL implantation is performed in infancy.

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

This study presents the long-term best corrected visual acuity (BCVA) outcome collected from the Infant Aphakia Study (IATS) in 110 of the 114 (96%) children who were initially randomized to aphakic contact lens (CL) versus intraocular lens (IOL) implantation during infancy. These children were enrolled in the multicenter randomized clinical trial with the diagnosis of unilateral congenital cataract and who underwent cataract surgery with or without a primary IOL implantation between 1 and 6 months old and now had mean age of 10.5 years (data collected from July 14, 2015 to July 12, 2019). The authors wanted to compare long-term BCVA from the two main treatment modalities after having unilateral

cataract surgery during infancy. Participants in this study included 58 girls (53%) and 52 boys (47%). BCVA for 27 (25%) children had 20/40 (Snellen equivalent, logMAR 0.30) or better in the treated eye (12 (22%) in the IOL group and 15 (27%) in the aphakic CL group). However, BCVA for 50 (44%) children had 20/200 (Snellen equivalent, logMAR 1.00) or worse in the treated eye (25 (44%) in IOL group and 25 (44%) in the aphakic CL group). Of note, results in the treated eye, after a decade, indicate that the median logMAR acuity was similar in children randomized for the IOL implantation group versus aphakic CL group. The difference in median BCVA between the two groups was small and non-statistically significant; the authors address that the estimate was imprecise: 99% CI for the difference in medians was -0.54 to 0.47. In summary, the results of the BCVA at 10.5 years old in IATS participants were highly variable; only 27 (25%) children achieving excellent BCVA in the treated eye and 50 (44%) children having poor vision in the treated eye. While the two treatment groups had non-statistically significant VA outcomes, the implantation of IOL at the time of unilateral cataract surgery during infancy was neither beneficial nor detrimental to the BCVA with longitudinal evaluation.

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

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

14. GLAUCOMA

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

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

15. REFRACTIVE SURGERY

Therea re no all-star articles in this section.

16. GENETICS

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

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

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

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

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

Genetic variation in PDE6C is associated with achromatopsia and cone dystrophy, with rare reports of cone–rod dystrophy in the literature. PDE6C-related cone–rod dystrophy consists of a severe phenotype characterized by early-onset nystagmus, decreased best-corrected visual acuity, poor color discrimination, progressive constriction of the visual field, and night blindness. This case series describes four patients (two pediatric and two adult) with PDE6C related cone and cone–rod dystrophy, including longitudinal data of a pediatric patient with PDE6C-related cone dystrophy. All patients in this series have decreased best-corrected visual acuity (ranging from 20/125 to 20/250) and poor color discrimination. Three of the four patients had a cone–rod dystrophy, who have ERG showing decreased amplitude on both photopic and scotopic waveforms and a mild to moderately constricted visual field. One of the pediatric patients was diagnosed with cone dystrophy with a preserved peripheral field. The children had no or minor structural retinal changes, whereas the adults had clear macular dystrophy. This study provides important findings on phenotypic variation of novel PDE6C mutations, including evidence of rod involvement. Gene therapy for achromoatopsia is currently in the clinical trial phase; therefore, knowing when clinical findings appear could narrow the therapeutic window and guide treatment.

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

This is a case series of 3 members of an X-linked retinal degeneration family with atypical preservation of visual acuity in the presence of a novel deep intronic splice site RPGR c.779-5T>G variant. Clinical evaluation was performed to evaluate phenotype. The pathogenicity of this variant was assessed by in silico splice prediction tools and purpose- designed in vitro splicing assay, and showed this variant to have reduced efficiency of intron splicing compared with wild type, leading to a population of mutant and normal transcripts. The predicted consequences of the pathogenic variant are potential use of an alternative splice acceptor site, resulting in premature truncation, or complete skipping of exon 8, resulting in a protein with some normal function, which would explain preserved visual acuity. This study demonstrates the important value of a molecular splice assay in confirming new pathogenic variants in noncoding regions.

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

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

Progression of ABCA4-related retinopathy: Prognostic value of demographic, functional, genetic, and imaging parameters.
Müller PL, Pfau M, Treis T, Pascual-Camps I, Birtel J, Lindner M, Herrmann P, Holz FG.

Retina. 2020 Dec 1;40(12):2343-56.

ABCA4-related retinopathy is the most common single-gene retinal dystrophy. Sixty-eight eyes of 37 patients (age range, 14–78 years) with a follow-up time of 10 to 100 months with ABCA4 retinopathy were included. The mean annual progression of retinal pigment epithelium atrophy was 0.89 mm2. The number of atrophic areas, the retina-wide functional impairment, and the age-of-onset category constituted significant predictors for future retinal pigment epithelium atrophy growth, explaining 25.7% of the variability. By extension of a simulated study length and/or specific patient preselection based on these baseline characteristics, the required sample size could significantly be reduced. Trial design based on specific shape-descriptive factors and patients' baseline characteristics and the adaption of the trial duration may provide potential benefits in required cohort size and absolute number of visits.

17. TRAUMA

Utility of Pupillary Light Reflex Metrics as a Physiologic Biomarker for Adolescent Sport-Related Concussion.
Master CL, Podolak OE, Ciuffreda KJ, Metzger KB, Joshi NR, McDonald CC, Margulies SS.
JAMA Ophthalmol. 2020 Sep 24;138(11):1135–41.

This is a prospective cohort study of adolescent athletes between ages 12 and 18 years at a specialty concussion program and private suburban high school recruited between August 2017 to December 2018. The study included healthy control individuals (N=134) and athletes with a diagnosis of sport-related concussion (SRC) (N=98). Results of the pupillary light reflex (PLR) metrics of 134 healthy control individuals and 98 athletes with concussion were recorded a median of 12 days following injury (range of 5 to 18 days). Eight of the 9 PLR metrics were significantly greater among athletes with concussion (maximum and minimum pupillary diameter, peak and average constriction/dilation velocity, percentage constriction, and time to 75% pupillary re-dilation [T75]). The authors noted that teenage girls with concussion exhibiting a longer T75 and this is supported in previous research about the sex-based differences following concussion. This study also found no sex differences in T75 in the control group, similar to previous research. The authors sought to distinguish adolescent SRC from healthy controls using the PLR metrics and advance the utility and importance of an objective physiologic biomarker for concussion. Limitations of the study is that the PLR metrics were measured throughout the day and in turn, the authors were not able to control for diurnal variation. Also, limitations include the setting of private suburban high school and homogenous racial background with 81% control group and 85% athletes with SRC identified as White. In summary, evaluating the PLR metrics in athletes with SRC as compared to healthy teenagers is reminder that objective measurements, such as pupillary light reflex measurements, are an important part of the eye exam. Of note, at this time, the utility of abnormal PLR metrics found in athletes with SRC is not known.

Predictors of visual outcomes in pediatric open globe injuries.
Jacobson A, Liles N, Besirli CG, Bohnsack BL.
J AAPOS. 2020 Dec 1:S1091-8531(20)30298-6. Epub ahead of print.

Ocular trauma continues as a significant cause of morbidity in children. Specific challenges include poor or inaccurate history and poor cooperation for preoperative evaluation. There continues to be study attempting to provide information that can be used to predict final visual outcome. The ocular trauma score (OTS), pediatric ocular trauma score (POTS) and toddler/infant ocular trauma score (TOTS) all try to predict visual prognosis and have demonstrated presenting visual acuity is significantly associated with final visual outcome. Challenges encountered were the difficulty in obtaining acuity in young patients as well as creation of these tools using small studies. The authors sought to identify predictors of visual outcomes using a large cohort in the United States .Authors found that POT and TOTS predict visual outcome moderately well. Amblyopia in younger children remains a challenge especially when the injury results in unilateral aphakia or pseudophakia with subsequent amblyopia. It follow that when presenting visual acuity could not be obtained, age and lens damage were significant predictors for final visual acuity. The authors found that retinal detachment and presenting visual acuity were independently significant predictors of final visual outcome. Authors find that current models have limited predictive value and a large multicenter study population would be useful to create an accurate pediatric ocular trauma predictive model.

Rate of ocular trauma in children operated on for unilateral cataract in infancy—data from the Infant Aphakia Treatment Study.

Traboulsi EI, Drews-Botsch CD, Christiansen SP, Stout AU, Hartmann EE, Lambert SR, Group II.

J AAPOS. 2020 Oct;24(5):301-303.

There is evidence in the adult literature that those with low vision in one eye are more likely to experience injury to their better seeing eye. In that vein, this is a study assessing prospectively collected data as a part of the 10 year data from the Infant Aphakia Treatment Study evaluating children who underwent unilateral cataract extraction in the first year of life with the goal of determining the incidence of injury to the non-operative eye. In the 109 children included in this study, 4 (3.7%) sustained injury to the non-operative eye and 2 (1.8%) to the operative eye during the study period. These injuries ranged from corneal abrasion, traumatic subconjunctival hemorrhage to subluxed intraocular lens. The risk of injury was higher in boys than girls and there was no clear correlation with injury and best corrected visual acuity in the operative eye. This paper is limited by the small number of cases, but the authors conclude that non-operative eyes of children with unilateral cataracts may be more injury prone than the operative eyes.

Intraocular foreign body injury in children: clinical characteristics and factors associated with endophthalmitis
Yang Y, Yang C, Zhao R, Lin L, Duan F, et al
Br J Ophthalmol 2020 Jun;104:780-784.

This was a retrospective analysis of patients <18 years old presenting with an intraocular foreign body (IOFB) between 2003 and 2016. 484 children (484 eyes) were included with mean age of 10.12 years. 84.% were male. Fireworks (28.5%) were the most common cause of injury. Endophthalmitis occurred in 116 patients (24.0%). Lower risk of endophthalmitis was associated with metallic IOFB, intraocular hemorrhage and uveal tissue prolapse. Higher risk was associated with zone II wounds and traumatic lens rupture. Culture was performed in 93 patients of which 26 specimens produced a positive culture. 63.0% were gram-positive bacteria, 29.6 % gram-negative and 7.4% fungal. A correlation between intravitreal antibiotic injection during repair and endophthalmitis could not be analyzed in this study, and visual prognosis was also not analyzed.

18. RETINA

Pediatric diabetic retinopathy telescreening
Strul S, Zheng Y, Gangaputra S, Datye K, Chen Q, Maynard L, Pittel E, Russell W, and Donahue S.
J AAPOS. 2020 Feb; 24:10.e1-5.

This is a retrospective study reviewing medical records of a telemedicine program at tertiary, academic medical center over 17 months. Patients visiting a pediatric endocrinology clinic who met guidelines underwent telescreening for pediatric pediatric diabetic retinopathy (DR) and risk factors for DR were evaluated. Fundus photos of 852 patients age 10-23 were reviewed. 51 (6%) had DR. Older age, longer diabetes duration (*P*=0.003), type 1 diabetes, and higher average glycated hemoglobin (HbA1c) from the year prior to the photography (P=0.02) was associated with increased risk for DR. The duration and higher HbA1C were significant after adjusting for sex, race and age. Limitations of the study are the small sample size and lack of follow-up eye examinations. This study may encourage telescreening for DR in those with risk factors of type 1 diabetes of long duration or high HbA1c.

Clinical implications and cost of electroretinography screening for vigabatrin toxicity
Jastrzembski B, Locke J, Wan M
Can J Ophthalmol. 2020 Jun;55:e98-e100

Although vigabatrin has been reported to cause permanent peripheral visual field loss due to retinal toxicity, monitoring visual function of children on vigabatrin is challenging. Some centers use electroretinography (ERG) to monitor for toxicity, but this is not in widespread use and the utility of this method has not been well studied. The authors of this short report performed a retrospective case series of children with infantile spams screening with ERG. Baseline ERG was performed within a few weeks of starting vigabatrin and then every 4 months on treatment. Dilated exam was also performed. 67 patients were screened over 3 years for a total of 147 ERGS (media 2 per patient). 3 patients had concern for toxicity, 2 based on findings on ERG and 1 due to parental concern. In once case, the concern of decreased flicker response was non consistent on consecutive ERG's. In another the medication was already weaned off by the time of second ERG. The patient with clinical concern did not show abnormalities on ERG. Overall none of the 67 patients had definitive evidence of toxicity on testing, and for the 3 patients who had suspicions of toxicity, the screening did not change clinical management. Average cost for ERG was $599 in outpatient setting and $1466 for inpatient setting, with average of $1716 per patient. The authors conclude that routine ERG screening for vigabatrin toxicity may not be justified given lack of influence on clinical decision making, risks of sedation, and costs.

19. RETINOBLASTOMA / INTRAOCULAR TUMORS

A Multicenter, International Collaborative Study for American Joint Committee on Cancer Staging of Retinoblastoma: Part I: Metastasis-Associated Mortality.
Tomar AS, Finger PT, Gallie B, Mallipatna A, Kivelä TT, Zhang C, Zhao J, Wilson MW, Kim J, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Yousef YA, Nummi K, Ushakova TL, Yugay OV, Polyakov VG, Ramirez-Ortiz MA, Esparza-Aguiar E, Chantada G, Schaiquevich P, Fandino A, Yam JC, Lau WW, Lam CP, Sharwood P, Moorthy S, Long QB, Essuman VA, Renner LA, Català J, Correa-Llano G; American Joint Committee on Cancer Ophthalmic Oncology Task Force.
Ophthalmology. 2020 Dec;127(12):1719-1732.

This study looked at the reliability of the latest edition of the American Joint Committee on Cancer Staging Manual in estimating metastatic and mortality rates in children with retinoblastoma. Retrospective data was accumulated in 2190 children from 18 oncology centers in 13 countries. Clinical and pathologic criteria were evaluated. The overall survival rate was high (>95%) until third level of clinical tumor category was reached, when the survival rate dropped to 89%, and further dropped to 45% with the fourth level of clinical tumor category. Likewise, the risk of metastasis increased with increasing clinical tumor categories. Although the methodology was confirmed to show a stepwise increase in metastasis and mortality with increasing clinical grading, significant compression of the mortality rates in the lower categories of clinical tumor categories limits the effectiveness of those categories in differentiating between survival rates. A simpler classification system might reliably identify good, intermediate, and worse prognoses without all of the various sub-classifications.

A Multicenter, International Collaborative Study for American Joint Committee on Cancer Staging of Retinoblastoma: Part II: Treatment Success and Globe Salvage.
Tomar AS, Finger PT, Gallie B, Mallipatna A, Kivelä TT, Zhang C, Zhao J, Wilson MW, Brenna RC, Burges M, Kim J, Khetan V, Ganesan S, Yarovoy A, Yarovaya V, Kotova E, Yousef YA, Nummi K, Ushakova TL, Yugay OV, Polyakov VG, Ramirez-Ortiz MA, Esparza-Aguiar E, Chantada G, Schaiquevich P, Fandino A, Yam JC, Lau WW, Lam CP, Sharwood P, Moorthy S, Long QB, Essuman VA, Renner LA, Semenova E, Català J, Correa-Llano G, Carreras E; American Joint Committee on Cancer Ophthalmic Oncology Task Force.
Ophthalmology. 2020 Dec;127(12):1733-1746.

This study looked at the reliability of the latest edition of the American Joint Committee on Cancer Staging Manual in estimating treatment success and globe salvage in children with retinoblastoma. Retrospective data was accumulated in 2097 children from 18 oncology centers in 13 countries. Clinical and pathologic criteria were evaluated. As predicted, clinical tumor category level 1 had a high (>88%) rate of globe salvage, with progressively worse outcomes for clinical tumor category level 2 (>57%) and clinical tumor category level 3 (>25%). The risk of treatment, likewise, was significantly greater with increasing clinical tumor category level. Among the oncology centers, however, there was a wide variation in treatment modalities used – enucleation, systemic chemotherapy with focal consolidation, plaque brachytherapy, intra-arterial chemotherapy, and external beam radiation therapy. The existence of so many treatment modalities resulting in similar rates of success suggest that the tumor characteristics, not the treatment modality, might have the most influence on treatment success. Regardless, the data showed that the classification system accurately stratified tumor severity and thus was validated.

Risk Factors for Tumor Recurrence Following Primary Intravenous Chemotherapy (Chemoreduction) for Retinoblastoma in 869 Eyes of 551 Patients
Lauren A. Dalvin, MD; Zeynep Bas, MD; Sameeksha Tadepalli, MD; Raksha Rao, MD; Sarangdev Vaidya, BA; Richard Pacheco, BA; Carol L. Shields, MD
J Pediatr Ophthalmol Strabismus; 2020 Jul;57(4):224-234.

The purpose of the retrospective study was to identify risk factors for retinoblastoma recurrence following chemoreduction (six cycle regimen of vincristine, etoposide and carboplatin). There were 869 eyes of 551 patients with retinoblastoma treated with chemoreduction. The minimum follow up for study inclusion was 3 months and 556 eyes met that minimum follow up. Recurrence was defined as recurrent tumor 3 months or more after initial tumor regression from chemoreduction. Among the 556 eyes, there was main solid tumor recurrence (n = 355, 64%), subretinal seed recurrence (n = 244, 44%), vitreous seed recurrence (n = 162, 29%), and/or new tumor (n = 118, 21%) requiring management with focal therapy (transpupillary thermotherapy, cryotherapy) (n = 294, 53%), intra-arterial chemotherapy (n = 125, 22%), intravitreal chemotherapy (n = 36, 6%), plaque radiotherapy (n = 120, 22%), external beam radiotherapy (n = 57, 10%), and/or enucleation (n = 49, 9%). Of all recurrences, 62% were detected by 1 year, 86% by 2 years, 94% by 3 years, 98% by 5 years, 99% by 10 years, and 100% by 15 years. Risk factors for recurrence on multivariate analysis included younger patient age at presentation (odds ratio [OR] = 1.02 [1.00 to 1.04] per 1 month decrease, P = .02), greater International Classification of Retinoblastoma group (OR = 1.24 [1.05 to 1.47] per 1 more advanced group, P = .01), shorter tumor distance to optic disc (OR = 1.11 [1.01 to 1.21] per 1 mm decrease, P = .03), and presence of subretinal seeds (OR = 1.66 [1.09 to 2.53], P = .02). Retinoblastoma recurrence after chemoreduction is usually detected within the first 3 years following treatment, but there are outliers of recurrence as late as 15 years after diagnosis. Younger patients with more advanced, posteriorly located tumors and subretinal seeds at presentation are at increased recurrence risk.

Screening for Pineal Trilateral Retinoblastoma Revisited: A Meta-analysis
Marcus C de Jong PhD, Wijnanda A Kors MD, Annette C Moll MD PhD, Pim de Graaf MD PhD, Jonas A. Castelijns MD PhD, Robin W. Jansen MD, Brenda Gallie MD, Sameh E. Soliman MD, Furqan Shaikh MD, Helen Dimaras PhD, Tero T. Kivela MD.
Ophthalmology. 2020 May; 127(5):601-607.

This meta-analysis aimed to answer two questions including (1) which age are patients with heritable retinoblastoma at risk of pineal trilateral retinoblastoma (TRb) and (2) does pineal TRb develop earlier if diagnosis of retinoblastoma is made at less than or equal to 6 months of age. PubMed and Embase were used to systematically review the literature. Main analyses of the data only included the studies published in 1995 or later when chemotherapy was introduced as part of the routine management for retinoblastoma. After 185 PubMed search results were reviewed, eighteen articles were deemed to meet inclusion criteria. Review of these manuscripts yielded 15 unique patients with TRb which were then added to the 174 patients that were published in an earlier systematic review. Of these patients, 73% had pineal TRb, 22% had suprasellar, paraseallar or ventricular TRb, 2% had both pineal and nonpineal TRb. 3% of the patients had TRb without specified location. 95% (21/22) of asymptomatic patients were diagnosed before 40 months of age. Whether intraocular retinoblastoma was diagnosed at the age of or less than 6 months versus later did not affect the age at which a pineal TRb was diagnosed. One year was the lead time from asymptomatic to symptomatic pineal TRb. Hence, based on these results, neuroimaging every 6 months was recommended by the authors. Limitations of this study include the heterogeneity of the patients in each separate publication and any case not reported in the literature would not be accounted for by this meta-analysis. The authors also mention that false positive diagnoses of pineal TRb cannot be ruled out based on their review of the published cases.

20. ORBIT

Feasibility of rapid magnetic resonance imaging (rMRI) for the emergency evaluation of suspected pediatric orbital cellulitis.
Jain SF, Ishihara R, Wheelock L, Love T, Wang J, Deegan T, Majerus CR, Oarhe C, Allbery S.
J AAPOS. 2020 Oct;24(5):289.e1-289.e4.

This is a prospective study of 14 patients enrolled over a 22 month period (July1, 2017 to April 30,2019) to evaluate the feasibility of noncontrast rapid magnetic resonance imaging (rMRI), compared with traditional contrast-enhanced computed tomography (CT) in assessing pediatric emergency department patients with suspected orbital cellulitis or orbital abscess. Participants received both contrast orbital CT, with the addition of the noncontrast rMRI. No sedation was used for either examination. All clinical decisions were based on CT findings; rMRI was interpreted within 24 hours of the visit. Three pediatric radiologists, with 8-21 years' experience of pediatric neuroradiology, interpreted the rMRI, masked to the CT and clinical results. Results were analyzed for interobserver bias. Mean age was 5.9 years (range, 0.33-13). Of the 14 patients, 13 (93%) were able to complete the rMRI at 1.5 and 3T; 1 patient (1.67 years of age) was unable to complete the rMRI (no images obtained). Of the 26 unilateral orbital units assessed, 3 were positive for retro septal orbital cellulitis by CT and were diagnosed correctly by rMRI. CT and rMRI findings were concordant in 100% of cases in differentiating preseptal vs orbital cellulitis. The study is limited by the small sample size. This study suggests that an accurate diagnosis of orbital cellulitis can be obtained with an rMRI concordant with contrast-enhanced CT, while sparing the need for intravenous access, no significant difference in time of completion and sparing the child from potential detrimental effects of ionizing radiation.
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21. OCULOPLASTICS

Treatment of Congenital Ptosis in Infants With Associated Amblyopia Using a Frontalis Muscle Flap Eyelid Reanimation Technique
Eton EA, Carniciu AL, Prabhu SS, Wang GM, Kahana A.
Ophthalmic Plast Reconstr Surg. 2021 Jan-Feb 01;37(1):67-71.

The paper aimed to determine the efficacy of a frontalis muscle flap eyelid reanimation technique for correction of severe congenital ptosis and associated amblyopia in infants. The authors performed a retrospective chart review of patients 12 months of age or younger with unilateral or bilateral congenital ptosis and associated amblyopia or deemed at high risk for amblyopia due to visual deprivation. Following ptosis repair via a frontalis muscle flap technique, primary outcomes of postoperative eyelid position and amblyopia reversal were assessed. Seventeen eyes of 12 participants were included for study. Seven of these patients had simple congenital ptosis, and the remainder had ptosis as part of a syndrome. Nine were diagnosed with amblyopia preoperatively, and the remaining 3 were too young for acuity testing but had occlusion of the visual axis by the ptotic eyelid in primary gaze. Postoperatively, the mean margin-to-reflex distance 1 was 2.4 mm (range: 0.0–4.0), and 9 patients (75%) demonstrated no evidence of amblyopia. Only 2 patients had eyelid asymmetry greater than 2 mm, which in both cases was due to lack of frontalis activation by the patient secondary to ongoing visual impairment. The most common complication was lagophthalmos in 6 eyes (35.3%), with no significant associated surface keratopathy. The frontalis muscle flap technique may offer a new and effective approach to treating infants with severe congenital ptosis causing poor eyelid excursion and associated amblyopia while avoiding use of an implant. This technique has not been described in infants in the past although has been used in kids and adults.

Congenital nasolacrimal duct obstruction continues trend for spontaneous resolution beyond first year of life
Nakayama T, Watanabe A, Rajak S, Yamanaka Y, Sotozono C
Br J Ophthalmol 2020 Aug;104:1161-1163.

This study conducted in Japan analyzed the rate of spontaneous resolution of congenital nasolacrimal duct obstruction (CNDLO) in children over age 12 months. They conducted a retrospective, observation case study at a single institution. Patients were included when diagnosed with CNDLO after 12 months of age, and were offered intervention. 133 children (155 cases) were included, and were divided into 62 patients (70 cases) in whom spontaneous resolution occurred and 71 patients (85 cases) who underwent dacryoendoscopic guided probing and stenting. The mean age of resolution was 17.8 months. Probing and stenting was successful in 83/85 cases (97.6%). The results found that resolution of CNDLO after 12 months of age occurred in 45% of infants. Of the patients who accepted intervention, the spontaneous resolution rate could not be estimated, but the authors suggest the true rate of resolution is above 45%. The authors conclude that either approach could be proposed in this patient group.

The Use of Anterograde Percutaneous Transluminal Coronary Angioplasty Balloons in Congenital Nasolacrimal Duct Obstruction: A Cost-Effective Alternative to the Traditional Dacryoplasty Balloons
Bothra N, Gupta N, Nowak R, Ali M
Ophthalmic Plast Reconstr Surg May/June 2020;36:302–304

The paper aimed to assess the efficacy of commonly available coronary angioplasty balloon catheters as a low-cost alternative to the traditional dacryoplasty catheters in select patients of congenital nasolacrimal duct obstruction. This was a prospective, interventional study was performed between July 2018 and December 2018 in children with congenital nasolacrimal duct obstruction, who underwent balloon dacryoplasty using the coronary angioplasty balloon catheters (2.75×10mm, SPALNO, Cardiomac,

Haryana, India). The inclusion criteria were children ≥4 years of age, and/or previously failed probing and/or previous failed intubation. Parameters documented were demographics, techniques, costs, complications, and postoperative outcomes. Twenty-three eyes of 22 children underwent balloon dacryoplasty using coronary angioplasty balloon catheters. The mean age of the patients was 4.33 years (range 1.5–10 years). The procedure was performed in 8 patients (8 eyes, 35%) as the primary procedure. The remaining 14 patients (15 eyes, 65%) had a history of probing, of which 4 eyes had it twice earlier. All eyes underwent balloon dacryoplasty as per standard protocols. The insertion profile and trackability of the coronary catheters were good. At a mean follow up of 6.17 months (range 1.5–9 months), anatomical and functional success was obtained in 87% cases (n = 20/23). No lacrimal passage trauma or injuries were noted during the procedure. The cost of coronary balloon catheter was approximately $60. The present pilot study has shown that outcomes of balloon dacryoplasty in patients with congenital nasolacrimal duct obstruction with coronary balloon catheters is comparable to that of traditional balloons and offers significant economic advantage for developing nations. The study is a good example of the ongoing discussion of proper treatment of CNLDO and provides another method to keep in mind for difficult to treat cases.

Surgical Intervention of Periocular Infantile Hemangiomas in the Era of β-Blockers
Clara J. Men, Lilangi S. Ediriwickrema, Ji Sun Paik, Jennifer Murdock, Michael T. Yen, John D. Ng, Catherine Y. Liu, Bobby S. Korn and Don O. Kikkawa
Ophthalmic Plast Reconstr Surg Nov/Dec 2020;36:70–73

This multicentred retrospective study aimed to examine the role of adjuvant surgical resection of infantile hemangiomas after systemic β-blocker therapy. A standard protocol for oral propranolol was employed by the referring physicians. Ocular indications for surgery included ptosis obstructing the visual axis, high degree of astigmatism causing amblyopia, or disfigurement from residual tumor. Patients underwent complete excision or debulking. Eleven girls and 4 boys were surgically treated with mean operative age of 34.4 months. Patients were followed for a mean of 19.6 months after surgery. Four patients required surgical treatment due to an inability to tolerate medical therapy secondary to drug-related side effects (including bradycardia). The other 11 patients proceeded to surgery due to residual eyelid and orbital lesions despite medical treatment. All 15 patients underwent orbitotomy for residual hemangioma excision. Four patients also underwent simultaneous levator advancement at the time of excision. In all cases, there was resolution of ptosis with clearing of the visual axis. No complications were incurred during the surgical treatment and there were no hemangioma recurrences. This is the first study to report surgical management of periocular infantile hemangiomas recalcitrant to standard therapy in the β-blocker era. In patients with infantile hemangioma who have failed medical therapy, adjuvant surgical treatment still plays an important role. For patients with persistent tumor causing ocular sequelae, surgical intervention aimed at soft tissue debulking and ptosis repair can be successful in achieving excellent functional and aesthetic outcomes with minimal side effects.

22. INFECTIONS

Review of maternal COVID-19 infection: considerations for the pediatric ophthalmologist.
DiSciullo A, Mokhtari N, Fries M.
J AAPOS. 2020 Aug;24(4):209-211.

The purpose of this report is to summarize data regarding pregnancy and the postpartum period for mothers and neonates in the setting of the COVID-19 pandemic. The specific focus of this paper is to elucidate potential transmission risks for pediatric ophthalmologists. The report discusses that pregnant women are at higher risk to contract viral illnesses due to their relative immunosuppressed state and reviews considerations from a labor and delivery, pediatric, and ophthalmic perspective. The authors discuss standard contact precautions and also special considerations for examining infants with unknown COVID status.
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23. PEDIATRICS / SYNDROMES / SYSTEMIC DISEASE

Prevalence of Ophthalmologic Diagnoses in Children With Autism Spectrum Disorder Using the Optum Dataset: A Population-Based Study.
Melinda Y. Chang, Danielle Doppee, Fei Yu, Claudia Perez, Anne L. Coleman and Stacy L. Pineles.
American Journal of Ophthalmology, 2021 Jan; 221:147-153.

This population-based retrospective cohort study of over 10 million claims was designed to understand the relationships between ophthalmic disorders and autism spectrum disorder (ASD). The authors used a de-identified data asset to look at children less than or equal to 19 between 2007 and 2013 who had a diagnosis of ASD or pervasive developmental disorder (PDD) who also had amblyopia, strabismus, optic neuropathy, nystagmus, or retinopathy of prematurity. There was an increased risk of all the ophthalmic disorders in patients who carried a diagnosis of ASD. These results are not surprising because there are increased medical disorders in this population as a whole. The main limitation of the study was the methods since claim reports can limit the information you can obtain. The authors concluded that more work needed to be done to understand this relationship since the mechanisms of why this would occur are not understood. Nonetheless this is an important article because it reminds the pediatric ophthalmologist of the importance of a full eye exam in patients with ASD.

Ocular Complications in School-Age Children and Adolescents after Allogeneic Bone Marrow Transplantation.
Hoehn ME, Vestal R, Calderwood J, et al.
Am J Ophthalmol. May 2020; 213:153-160.

The goal of this retrospective cohort study of 162 patients was to describe the ocular complications in school aged and adolescent patients after allogeneic bone marrow transplantation (BMT). The authors looked at patients aged 7-18 years old who survived at least 1 year after BMT and had a long follow up period ranging from 13 months to 12 years (mean 4 years). The patients were followed at one institution over fifteen years. The authors found that cataract formation was noted in 57 of the 162 patients, (97 eyes – 6 of these eyes needed surgery) and that this was associated with total body irradiation. Fifty-one of the patients developed dry eyes and this was associated with systemic graft vs. host disease. The authors concluded that due to the high incidence of treatable and vision threatening diseases associated with BMT, continued surveillance by a pediatric or general ophthalmologist should occur at least yearly. This study is important because of the increased long-term survival in post BMT pediatric patients. Other studies have looked at these complications in adults and in small children, but this is the only study to look at the outcomes in this age group. The authors point out that the results of this study differ from those in adults in that the pediatric patients had a lower incidence of dry eyes. This paper is important to the pediatric ophthalmologist who is counseling the pre and post BMT pediatric patient and their parents since it has some solid statistics for this age group regarding complications. However, it probably overestimates some of the complications since there have been improvements in the radiation protocols and technology – the authors of the paper do point out these limitations.

Incidence and Prognostic Role of the Ocular Manifestations of Neuroblastoma in Children.
Graef S, Irwin MS and Wan MJ.
Am J Ophthalmol. May 2020; 213:145-152.

The authors of this retrospective cohort study aimed to describe the ocular manifestations of neuroblastoma in a cohort of 523 patients over 28 years at one institution. Median follow up was 4 years. Of the 523 patients, 86 patients (16.4%) had ocular manifestations – 58 at diagnosis and 29 during the disease course. The most common findings were orbital involvement, opsoclonus, and Horner syndrome. Importantly, in 16 patients (3.1%), there were only ocular findings at presentation – 9 with orbital

involvement and 7 with Horner syndrome. Orbital involvement was associated with a worse prognosis. Interestingly Horner syndrome and opsoclonus was associated with a high rate of survival in this cohort. The authors have an interesting discussion about the utility of imaging in isolated anisocoria being likely unjustified and in Horner syndrome being of low utility but possibly associated with neuroblastoma. The limitations of this study were mainly related to its retrospective nature.

24. UVEITIS

Results 5 to 10 years after cataract surgery with primary IOL implantation in juvenile idiopathic arthritis-related uveitis.
Leinonen S, Kotaniemi KM, Kivelä TT, Krootila K.
J Cataract Refract Surg. 2020 Aug;46(8):1114-1118.

Summary: This retrospective case series performed in Helsinki, Finland, looked at results of cataract extraction with primary intraocular lens (IOL) implantation in patients with juvenile idiopathic arthritis (JIA) and uveitis-related cataract. All consecutive patients younger than 20 years with JIA-uveitis–related cataract undergoing cataract extraction with primary IOL implantation in 1 or both eyes from February 2000 to April 2012 were included. Twenty eligible patients with 26 operated eyes were identified; 14 were girls and 6 were boys. All patients had a follow-up of 5 years and 13 patients (16 eyes [65%]) reached 10 years of follow-up. The authors found that preoperative median corrected distance visual acuity (CDVA) was 0.05 in decimal notation. Median CDVA was 1.0 at 5 years and 0.9 at 10 years of follow-up. Two eyes did not reach CDVA 0.5 with the operation, and in 2 eyes, CDVA decreased below 0.5 over the period of 3 to 5 years after the operation. Active uveitis during 3 and 12 months preoperatively was a risk indicator for postoperative CDVA <0.5 at 5 years (P = .005 and P = .00, respectively). The study conclusion was that cataract extraction with primary IOL implantation provides long-standing good visual acuity for young patients with well-controlled JIA-related uveitis.

Importance: Best practices with regards to extraction of JIA-associated uveitic cataracts in pediatric patients have been controversial. Many patients have been left aphakic in this setting due to long-term visual acuities worse in this patient population than in patients with cataracts related to other types of uveitis. This paper indicates that primary IOL implantation using current techniques was well-tolerated in patients with well-controlled JIA-related uveitis. The main limitation of the study is the small number of eyes operated.

Retinal findings in presumed infectious posterior uveitis and correlation with polymerase-chain reaction results
Elyashiv S, Samson M, Jabs D
Retina. 2020 Mar; 40:567–571.

The goal of the study was to correlate demographics, retinal lesion characteristics, and host immune status with the pathogen found on polymerase chain reaction analysis of aqueous fluid in patients with suspected infectious posterior uveitis. Medical records of patients who underwent anterior chamber paracentesis for suspected infectious posterior uveitis and had retinal photographs between 2014 and 2016 at a single institution were reviewed. Data collection included demographics, clinical appearance of the lesions, and polymerase chain reaction results. Fundus photographs were evaluated by two masked observers for the clinical features of the retinitis. Twenty-eight patients were included in the study. There was substantial to almost perfect agreement on retinitis location (k = 0.67) and number (k = 0.76) between the masked photograph graders. Polymerase chain reaction results were positive for herpes simplex virus or varicella zoster virus in 43%, cytomegalovirus in 11%, and toxoplasmosis in 3%; 43% had negative polymerase chain reaction results. Detection of herpes simplex virus or varicella zoster virus on polymerase chain reaction of the aqueous was associated with paucifocal lesions (82%, P = 0.021) and lesions involving the peripheral retina (91%, P = 0.023), consistent with the diagnosis of acute retinal necrosis. These data suggest that the diagnosis of acute retinal necrosis can be reasonably inferred on clinical examination, providing a guide for initial empiric therapy.

25. PRACTICE MANAGEMENT/ HEALTH CARE SYSTEMS / EDUCATION

There are no all-star articles in this section.