

What's New and Important in Pediatric Ophthalmology and Strabismus for 2014

**AAPOS, Palm Springs, CA
Workshop, Friday, April 4, 2014
8:30-9:45 AM**

Presented by the
**Professional Education Committee of the
American Association for Pediatric Ophthalmology and
Strabismus**

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1. AMBLYOPIA

The effect of amblyopia treatment on stereoacuity

Stewart CE, Wallace MP, Stephens DA, et al J AAPOS March/April 2013;17:166-173

The Monitored Occlusion Treatment for Amblyopia Study (MOTAS), looked at dose-response function of occlusion with respect to visual acuity and some secondary outcomes. This paper reports the stereoacuity changes during and after amblyopia treatment. Amblyopia caused by anisometropia, strabismus or mixed was treated with a run-in phase of spectacles followed by occlusion therapy in 85 children. Two-thirds of patients had nil stereoacuity at study entry. During the refractive phase, stereoacuity improved from 2400 to 600 log arc sec overall and from 170 to 110 log arc sec in those with some stereoacuity at the outset of the study respectively. During the occlusion phase, stereoacuity improvement was exactly the same overall and similar in those with some stereoacuity at outset (170 to 75 log arc sec). At least one octave of stereoacuity is needed to exceed test-retest variability. This was achieved in 38% of refractive adaptation patients, 28% who received occlusion, and 45% who underwent refractive adaptation and/or occlusion. 44% of patients had nil stereoacuity throughout the study. Poor stereoacuity was associated with poor visual acuity in the amblyopic eye. Poor stereoacuity was also associated with severe strabismus. Anisometropes were more likely than strabismic patients to have better stereopsis at study entry. The authors did not distinguish manifest from latent strabismus. Smaller angle strabismus is generally more likely to be latent or intermittent, skewing stereoacuity to be markedly better as compared to larger angle strabismus, which is more likely to be constant.

Effect of Occlusion Amblyopia after Prescribed Full-Time Occlusion on Long-Term Visual Acuity Outcomes

Susannah Longmuir,; Wanda Pfeifer William Scott, Richard Olson, J Pediatr Ophthalmol Strabismus 2013; 50:94-101 (March/April)

This study was a retrospective study evaluating the incidence of occlusion amblyopia when full time patching was prescribed and determine its effect on long term visual outcomes. Occlusion amblyopia was found to be more common when the child was younger and if occlusion amblyopia did develop, the study found that this actually was beneficial and allows for the development of better vision in the originally amblyopic eye.

Internet-Based Perceptual Learning In Treating Amblyopia

Wenqiu Zhang, Xubo Yang, Meng Liao, Ning Zhang
Eur J Ophthalmol July August 2013; 23(4): 539 – 545

The aim of this study was to address the efficacy of Internet-based perceptual learning in treating amblyopia. A total of 530 eyes of 341 patients with amblyopia were retrospectively reviewed. Internet-based perceptual learning proved better than

conventional treatment in ametropic and strabismic amblyopia older than 7 years. The mean cure time was also shorter for this group (3.06 ± 1.42 months vs 3.52 ± 1.67 months). Internet-based perceptual learning can be considered as an alternative to conventional treatment. It is especially suitable for ametropic and strabismic patients with amblyopia who are older than 7 years and can shorten the cure time of amblyopia.

Efficacy of split hours part-time patching versus continuous hours part-time patching for treatment of anisometropic amblyopia in children: a pilot study

Virender Sachdeva, Vaibhev Mittal, Ramesh Kekunnaya, Amit Gupta, et al. Br J Ophthal July 2013; 97: 874-878.

This prospective, non-randomized, study attempted to evaluate the efficacy of split time patching versus continuous patching in a specific group of 4-11 year old children with anisometropic amblyopia. Inclusion criteria included 2.5 diopters or more of anisometropia, vision between 20/40 to 20/400, and no amblyopia treatment in the previous month. The total hours of patching was determined by severity of amblyopia and varied between children. 44 children were enrolled in the continuous wear and 24 children were enrolled in the split hour wear. After 3 and 6 months of therapy, both groups showed improvements in vision. The difference between the two groups was not statistically significant. Compliance with split patching was only slightly better. Disadvantages to the study include small sample size, non-randomized, non-masked, with parents deciding which group the child would be enrolled in.

The effect of simulated normal and amblyopic higher-order aberrations on visual performance.

Dominguez-Vicent A, Perez-Vives C, Ferrer-Blasco T, et al, may/June J AAPOS 17:3;269-275

The mechanism of idiopathic amblyopia is unclear. Some investigators have hypothesized higher-order aberrations between left and right eyes may be the cause. Lower-order aberrations are corrected with spectacles,, contact lenses or refractive surgery. Higher-order aberrations can only be corrected by adaptive optics. This study simulated amblyopic and normal higher-order aberrations and their effect on visual function. An adaptive optics visual simulator was used to compensate volunteers' ocular aberrations and simulate the wavefront aberration patterns found in healthy and amblyopic eyes in 7 healthy adults. No statistically significant differences in visual acuity and contrast sensitivity were found between both groups for any analyzed contrast level, spatial frequency, and pupil size values. Based on the results it does not appear that higher-order aberrations are a major factor in compromising visual performance of idiopathic amblyopic eyes. Sample size was small in this study. The aberration patterns used were based on pediatric data but this study enrolled adult patients.

Fixation instability in anisometropic children with reduced stereopsis

Birch EE, Subramanian V and Weakley DR
J AAPOS May/June 17:3;287-290

Why is microstrabismus often a result of foveal suppression despite normal peripheral fusion? Why is the microstrabismus usually an esotropic one? The authors tested the hypothesis that bifoveal fusion disruption by anisometropia directly affects ocular motor function. A Nidek MP-1 microperimeter was used with 94 children with anisometropic hyperopia between the ages of 5 and 13. Forty-three healthy controls were also included. This was performed prospectively over a 2.5-year period. Stereoacuity was correlated with fixation instability. All children with normal stereoacuity had stable fixation. Children with nil stereoacuity displayed the most instability. Visual acuity of the poorer seeing eye was correlated to a lesser degree. The eye movement recordings were of sufficient quality in 81/94 children. The flick microesotropic eye movements were actually found to be fusion maldevelopment nystagmus movements (FMNS)(nasalward slowdrift with a temporalward refoveating fast-phase microsaccade). Binocular decorrelation was found to be critical for the development of FMNS; visual acuity impairment is not required. The presented data support the hypothesis that anisometropia disrupts ocular motor development and can cause reduced stereoacuity and abnormal binocular visual experience.

Clinical Translation of Recommendations from Randomized Clinical Trials on Patching Regimen for Amblyopia

Ya-Ping Jin, Amy H.Y. Chow, Linda Colpa, Agnes M.F. Wong *Ophthalmology* April 2013;120:657-662

This is a retrospective cohort study involving children with amblyopia seen from 2007 through 2009 by academic and community ophthalmologists in Toronto, Ontario, Canada. Using PEDIG criteria for defining moderate amblyopia as a visual acuity between 20/40-20/80 and severe amblyopia is defined between 20/100-20/400. The main intervention was patching of the sound eye. The main outcome measures included the number of prescribed patching hours per day and the amblyopic eye visual acuity expressed as logarithm of the minimal angle of resolution (LogMAR). Conclusions: The evidence-based recommendations for amblyopia management have not been widely adopted by practicing academic and community ophthalmologists who practice in large urban center in North America (namely, Toronto, Ontario, Canada).

Comments: This article stresses that although a tremendous amount of medical research has been conducted, one of the greatest current challenges of medicine is that there is a gap in applying research evidence to the process of making informed clinical decisions. This is evident across all groups of decision makers including health care providers, patients, managers and policy makers. In both primary and specialty care across all disciplines.

The article discusses various strategies including the Knowledge-to-Action Cycle framework as a proposed mechanism to translate gains from randomized clinical trials into actual clinical practice.

Quantitative Measurement of Interocular Suppression in Anisometropic Amblyopia A Case-Control Study

Jinrong Li, Robert F. Hess, Lily Y.L. Chan, Daming Deng, *Ophthalmology* August 2013;120:1672-1680

This is a case control study of 45 participants with anisometropic amblyopia and 45 matched controls with a mean age of 8.8 years for each group. The purpose of the study is to assess 1) the relationship between interocular suppression and visual function, 2) whether suppression can be simulated in matched controls by using neutral density filters, and 3) to determine the effects of spectacles or rigid gas-permeable contact lenses on suppression in patients with anisometropic amblyopia. This study was performed in New Zealand.

Conclusions: Interocular suppression plays a key role in the visual deficits associated with anisometropic amblyopia and can be simulated in controls by inducing a luminance difference between the eyes. Accurate quantification of suppression using the dichoptic motion coherence threshold technique may provide useful information for the management and treatment of anisometropic amblyopia.

Interactive binocular treatment (I-BiT) for amblyopia: results of a pilot study of 3D shutter glasses system

N Herbison; S Cobb; R Gregson; I Ash; for the I-BiT study group

Eye; September 2013; 27(9):1077–1083

A computer-based interactive binocular treatment system (I-BiT) for amblyopia has been developed, which utilizes commercially available 3D 'shutter glasses'. The purpose of this pilot study was to report on visual acuity in amblyopic children undergoing iBit. Ten children with anisometropic, strabismic, or strabismic anisometropic amblyopia ages 4-8 years underwent thirty minutes of treatment once weekly for 6 weeks. Treatment sessions consisted of playing a computer game and watching a DVD through the I-BiT system. The system allows both eyes to see certain parts of the image (for example, the player in the computer game) but only presents other parts of the image to the amblyopic eye (for example, the obstacles in the computer game). Six out of nine patients (67%) who completed the treatment showed a clinically significant improvement of greater than 0.1LogMAR (more than one line) of visual acuity. All had previously worn glasses based on cycloplegic refractions for a minimum of eighteen weeks. The study was small and uncontrolled. It is unknown whether visual acuity gains were influenced by bias or learning. The possibility of using video games in the treatment of amblyopia, which is more appealing to children and families than patching or penalization, is intriguing.

The Regional Extent of Suppression: Strabismics Versus Nonstrabismics

Babu JR, Clavagnier SR, Bobier W, Thompson B, Hess RF. Invest Ophthalmol Vis Sci. October 2013;54:6585–6593.

Suppression may be the cause of amblyopia rather than a secondary consequence of mismatched retinal images. Furthermore, the measurement of suppression may have prognostic value for patching therapy. The authors describe a new method for delineating the regional distribution of suppression. This method provides a more global, quantitative rather than binary measure of suppression. The new method is novel in that it does not rely on threshold measures, but on suprathreshold matching. The technique is well suited for use in the clinic as it is relatively fast to administer and provides quantitative information on the distribution of suppression within the central visual field. They used this new method to address two questions. First, is suppression limited to the fovea of strabismic amblyopes or does it involve all of the central 20°? Second, does the strength and regional distribution of suppression differ between strabismic and nonstrabismic forms of amblyopia?

The method involves a dichoptic perceptual matching procedure at multiple visual field locations. They compared a group of normal controls (mean age: 28 + 5 years); a group with strabismic amblyopia (four with microesotropia, five with esotropia, and one with exotropia; mean age: 35 + 10 years); and a group with nonstrabismic anisometropic amblyopia (mean age: 33 + 12 years).

The extent and magnitude of suppression was similar for observers with strabismic and nonstrabismic amblyopia. Suppression was strongest within the central field and extended throughout the 20° field measured, corresponding to the fovea of the fixing eye.

Does amblyopia have a functional impact? Findings from the Dunedin Multidisciplinary Health and Development Study.

Wilson GA, Welch D, Clin Experiment Ophthalmol. 2013 Mar;41(2):127-34

One thousand thirty-seven children born in Dunedin, New Zealand, between April 1972 and March 1973 were assessed from ages 3 to 32 years. Comparison of study members with no amblyopia, recovered amblyopia, possible amblyopia or amblyopia was done. The authors evaluated childhood motor development, teenage self-esteem and adult socioeconomic status (assessed by occupation, education, reading ability and income).

RESULTS: There was no evidence of poorer motor development, lower self-esteem or reduced adult socioeconomic status in study members with amblyopia or recovered amblyopia when compared with those with no amblyopia.

CONCLUSIONS: Amblyopia or having recovered amblyopia does not functionally impact on childhood motor development, teenage self-esteem or adult socioeconomic status within this cohort. The wide range of visual deficits and adaptations that are known to occur in amblyopic vision do not translate into

important 'real life' outcomes for the study members with amblyopia or recovered amblyopia. The age-related cumulative lifetime risk of bilateral visual impairment in amblyopia will be assessed in future studies.

Perceptual learning treatment in patients with anisometropic amblyopia: a neuroimaging study

Jingjing Zhai, Min Chen, Lijuan Liu, Xuna Zhao, Hong Zhang, Xiaojie Luo, Jiahong Gao *British Journal of Ophthalmology* 2013;97:11 1420-1424 November 2013

This study uses functional MRI (fMRI) and diffusion tensor imaging (DTI) techniques to investigate the neuromechanisms of perceptual learning treatment in patients with anisometropic amblyopia. 20 patients with monocular anisometropic amblyopia participated in the study. Participant ages were 11-32 years. Each patient underwent fMRI and DTI before and after 30 days of perceptual learning treatment for the amblyopic eye. For the fMRI imaging, the patients viewed stimuli with either the sound or amblyopic eye and changes in cortical activation after treatment were evaluated. With the DTI exams, the fractional anisotropy (FA) values, apparent diffusion coefficient (ADC) values, the voxel numbers of optic radiations (ORs), and the number of tracks were compared between the ipsilateral and contralateral ORs and also between the previous and posterior scans. The authors reported increased activation via the amblyopic eyes was found in Brodmann Area 17-19, bilateral temporal lobes, and right cingulate gyrus after the perceptual learning treatment. They concluded that perceptual learning treatment for amblyopia had a positive effect on the visual cortex and temporal lobe visual areas in patients with anisometropic amblyopia. The study is limited by the small sample size and limited follow-up, but creates the potential to continue to explore this area in future studies.

Prevalence of Amblyopia or Strabismus in Asian and Non-Hispanic White Preschool Children Multi-Ethnic Pediatric Eye Disease Study

Roberta McKean-Cowdin, PhD, Susan A. Cotter, OD, MS, Kristina Tarczy-Hornock, MD, DPhil, Ge Wen, MSc
Ophthalmology October 2013; 120(10):2117-2124

This is a cross-sectional survey designed to determine the age and race specific prevalence of amblyopia in Asian and non-Hispanic white (NHW) children age 6- to 72-months. This is a population-based multi-ethnic sample of children age 6-

to 72-months located in Los Angeles County and Riverside County in California. The study is designed to evaluate the prevalence of ocular conditions.

Methods: Comprehensive eye examination and in-clinic interviews were conducted with 80% of eligible children age 6- to 72-months as well as determination of optotype visual acuity (VA) in children aged 30- to 72-months. **Results:** Strabismus was found in 3.5% of Asian children and 3.24% of non-Hispanic white children. Amblyopia was detected in 1.81% of Asian children and non-Hispanic white children. The prevalence of amblyopia was higher for each subsequent older age category among non-Hispanic white children. This study showed no significant trend among Asian children.

Conclusions: The prevalence of strabismus was similar in Asian and non-Hispanic white children. It was found to be higher among older children from 6- to 72-months. The prevalence of amblyopia was the same in Asian and non-Hispanic white (NHW) children. The prevalence seemed to be higher among older NHW children but was relatively stable by age in Asian children.

Comment: These findings may help clinicians to better understand the patterns of strabismus and amblyopia and potentially inform planning of preschool vision screening programs. This study supplements previous studies by the same group evaluating strabismus and amblyopia in Hispanic and African-American children. Amblyopia was present in 2.6% of Hispanic children and 1.5% of African-American children age 30- to 72-months. In the Baltimore Pediatric Eye Disease Study (BPEDS), conducted with the same protocol, amblyopia was present in 1.8% of non-Hispanic white children and 0.8% of African-American children. Previous strabismus was found in 2.4% of Hispanic children and 2.5% of African-American children.

A Randomized Trial of Increasing Patching for Amblyopia

Pediatric Eye Disease Investigator Group

Writing Committee: David K. Wallace, MD, MPH, Elizabeth L. Lazar, MSPH, Jonathan M. Holmes, BM, BCh, Michael X. Repka, MD, MBA

Ophthalmology November 2013; 120(11):2270-2277

This is a prospective, randomized, multi-center, clinical trial performed by Pediatric Eye Disease Investigator Group (PEDIG). This includes patients from optometric and pediatric ophthalmology center/practices. A total of 169 children with a mean age of 5.9 years with stable residual amblyopia (20/32-20/160) after 2 hours of daily patching for at least 12 weeks were enrolled in this study.

Intervention: Random assignment to continue 2 hours of daily patching or increase patching time to an average of 6 hours/day.

Main outcome measures: Best corrected visual acuity in the amblyopic eye after 10 weeks.

Results: Ten weeks after randomization, amblyopic eye visual acuity improved an average of 1.2 lines in the 6 hour group and 0.5 lines in the 2 hour group. The improvement of 2 or more lines occurred in 40% of the participants who have patched for 6 hours versus 18% of those patched for 2 hours.

CONCLUSIONS: VISUAL ACUITY IN THE AMBLYOPIC EYE STOPPED IMPROVING AFTER 2 HOURS A DAY WITH PATCHING. THE STUDY SHOWS THAT INCREASING DAILY PATCHING 6 HOURS PER DAY WILL RESULT IN MORE IMPROVEMENT AT THE 10 WEEK OUTCOME VISIT (WHEN COMPARED TO 2 HOURS OF DAILY PATCHING).

Patching compliance with full-time vs part-time occlusion therapy

Jessica Kane, Ron Biernacki , Lisa Fraine , Neva Fukuda , Kelsie Haskins , David G. Morrison
Am Orthopt J 2013; 63:19-23

This retrospective study identified 76 patients with strabismic or refractive amblyopia treated with occlusion therapy during 2011. Full-time patching was prescribed to 22, part-time patching to 45 and 9 patients were switched to full-time patching after failing part-time patching. Visual outcomes for the part-time patching and full-time patching groups were not significantly different. Compliance with patching was assessed using a 5-point scale. Compliance was found to be significantly better in full-time patching group. The duration of treatment required to reach endpoint was significantly different with average duration of full-time patching of 4.7 months vs 11.3 months for part-time patching. The criteria for recommending part-time or full-time to the patients was not documented which may be a source of bias in acuity and compliance analyses. The authors conclude that full-time patching provides the fastest result, yields better compliance and in a small subset of patient improve visual outcomes.

Part-time vs full-time occlusion for amblyopia: evidence for part-time patching

Noelle S. Matta, David I. Silbert, Am Orthopt J 2013; 63:14-18

This article reviews 6 previously published studies pertaining to efficacy of full-time patching and part-time patching of 2, 4, 6 or 8 hours per day. The author highlights two PEDIG studies that 1) showed no difference in outcome for full-time patching vs part-time patching of 6 hours per day and 2) showed no difference in outcome between 6 hours per day and 2 hours per day of part-time patching. The author comments that parents often patch less than the prescribed amount and that if part-time patching is not improving acuity then increasing the prescribed number of hours per day may provide benefit. The authors conclude that there are several options for patching protocols and the patient and family

dynamics should be considered in selecting a patching protocol in addition to response to previous patching treatment.

Factors predicting recurrence in successfully treated cases of anisometropic amblyopia

Rohit Saxena, Shraddha Puranik, Digvijay Singh, Vimla Menon, Pradeep Sharma, Swati Phuljhele *Indian J Ophthalmol* 2013;61:630-1.

Successfully treated anisometropic amblyopes aged 4–12 years were followed up for 1 year after stopping therapy. Best corrected visual acuity (BCVA), refractive error, stereoacuity and contrast sensitivity were evaluated at baseline and follow-up.

Conclusions: Significant numbers of children suffer recurrence of amblyopia after stopping therapy. Older age, better BCVA after stopping therapy and greater magnitude of improvement in BCVA are important risk factors for recurrence. Careful follow-up is essential for early detection and management of recurrence.

Visual Functions in Amblyopia as Determinants of Response to Treatment

Singh V, Agrawal S J *Pediatr Ophthalmol Strabismus* 2013;50(6):348-354

The aim of the study was to evaluate the role of visual acuity, accommodation, contrast sensitivity, fixation, mesopic visual acuity and stereopsis as determinants of visual improvement in amblyopia treatment. This was a prospective, interventional study including 114 eyes of 69 patients. Patients with refractive error were included after wearing appropriate refractive correction for 4 weeks. Amblyopia treatment consisted of suitable refractive correction and conventional occlusion therapy 6 hours per day for mild to moderate amblyopia (visual acuity 0.70 or better) and full time for one month followed by 6 hours per day for severe amblyopia (visual acuity 0.80 or worse). Actual occlusion was usually less than prescribed amounts based on records kept by parents. Analysis of visual acuity and other visual functions revealed a significant association of eccentric fixation and poor contrast sensitivity with severe amblyopia. Improvement from baseline in various grades of amblyopia was observed at both 3 and 6 months. The percentage improvement was maximum in mild amblyopia and minimum in severe amblyopia.

The authors found that the initial visual acuity and accommodation are strong determinants of response to amblyopia therapy. Stereopsis and mesopic visual acuity have some value as determinants. Further studies on these determinants may guide future amblyopia treatment.

Anterior Visual Pathways in Amblyopia: Quantitative Assessment with Diffusion Tensor Imaging

Gumustas S, Altintas O, Anik Y, et al

J Pediatr Ophthalmol Strabismus 2013;50(6):369-374

The purpose of this study was utilize diffusion tensor imaging (DTI) to detect abnormalities in the anterior visual pathways in children with unilateral and bilateral amblyopia. DTI is an MRI technique used to evaluate white matter integrity and neuronal connectivity. This was a cross-sectional, observational study of 10 patients with unilateral amblyopia, 5 with bilateral amblyopia and 10 control children. The study results demonstrated statistically significant changes in the prechiasmatic pathways in both the affected and sound fellow eye of patients with unilateral amblyopia. This was not noted in the bilateral amblyopia group. This may indicate a functional underdevelopment of the anterior visual pathway affecting both eyes in patients with unilateral amblyopia.

2. VISION SCREENING

The challenges to ophthalmic follow-up care in at-risk pediatric populations

Williams S, Wajda BN, Alvi R, et al J AAPOS march/April 2013;17:140-143

Give Kids Sight Day and the Eagles Eye Mobile are two non-governmental programs providing comprehensive vision care accessible to low-income, underinsured and uninsured children. The authors attempted to identify the barriers impeding follow-up in these children. With both programs only 30% of children's families were successfully contacted. Telephone numbers were out-of-service, invalid, or unavailable in 42%. Extenuating circumstances or voice-mail only, limited communication in 22%. Some families had more than one barrier. All families who could not be reached by telephone were sent a letter and a questionnaire. The response rate from this was 0%. Overall 71% of children did not receive a scheduled follow-up appointment. This study focuses on an inner-city population with low socioeconomic status. Cell phones have increased call screening. Clearly better communication protocols need to be established. Increasing contact information and education at the time of the initial contact may help.

Plusoptix photoscreening may replace cycloplegic examination in select pediatric ophthalmology patients

Silbert DI, Matta NS and Andersen K J AAPOS March/April 2013; 17:163-165

The standard of care for a pediatric ophthalmic examination has included a cycloplegic refraction and a dilated fundoscopic examination. The authors sought to

determine whether or not a normal acuity, normal alignment/motility check combined with a normal autorefractor/photoscreener would suffice. A retrospective evaluation of children who had an undilated plusoptix S04 or plusoptix A09 photoscreening was performed, including half for review. Children who were referred for a medical or ophthalmic condition requiring dilation were excluded. Children with acuity <20/30 or alignment/motility problems were excluded as well. Two hundred and twenty-two children out of 451 (49%) who were photoscreened/autorefracted had normal results. Of the 222, 32 were excluded for not meeting inclusion criteria. Of the remaining 190 patients, 186 had no abnormal findings on dilated examination and cycloplegic refraction. Optic nerve cupping with normal intraocular pressures, moderate hyperopia, a non-visually significant cataract, and refractive amblyopia from moderate astigmatism were the causes of the 4 abnormal examinations. One must remember when reviewing this study, that children with strabismus, amblyopia, or medical pathology would most likely be excluded based on inclusion criteria so the applicability of the information is confined to children with normal acuity and alignment with no serious medical or ophthalmic conditions. This group would be expected to have very rare instances of pathology, but if autorefractor/photoscreener alone eliminates dilated exam and cycloplegic retinoscopy, those children would be missed. Most children referred to a pediatric ophthalmologist do not have both normal motility and acuities so evaluation of this group of patients is not modified by the results of this paper. Rather the children who often do not see an eye care provider (routine, normal screenings), probably do not need a cycloplegic evaluation or dilated fundus exam.

Calibration and Validation of Nine Objective Vision Screeners With Contact Lens-Induced Anisometropia

Robert W. Arnold, Bethanne Davis; Laura E. Arnold; Kayla S. Rowe; Jodi M. Davis J Pediatr Ophthalmol Strabismus 2013; 50:184-190 (March/April)

Nine objective vision screeners were used on 2 patients who were emetropic. The patients were placed in various power contact lenses and the screeners were put to the test to validate them in terms of being able to diagnose amblyopia. Screeners were found to be valid including the iphone (although the article did say the iphone was found to be too sensitive)

Reliability and Validity of an Automated Computerized Visual Acuity and Stereoacuity Test in Children Using an Interactive Video Game

Dae Joong, Hee Kyung Yang, Jeong-Min Hwang. Am J Ophthalmol June 2013; 156 (1): 195-201.

This retrospective study evaluated 102 children between the ages of 3-7 years reliability on automated interactive video game as compared to Snellen acuity results. Results showed the average Snellen acuity was 0.22+/- 0.19 log MAR, while the computerized results were 0.18+/- 0.14 logMAR on the initial test, and 0.22+/- 0.17 logMAR on the second test. The results seem to reliability and validity compared to the Snellen visual acuity chart and distance Randot Stereotest.

Test-retest reproducibility of accommodation measurements gathered in an unselected sample of UK primary school children

Paul Adler, Andrew Scally, Brendan Barrett. Br J Ophthal May 2013; 97:592-597.

This study determined the reproducibility of accommodation measurements gathered in primary school children as well as determining intra observer variability. The near point of accommodation was measured on 137 children with average age of 8.1 years. Testing was performed on 3 different occasions. Binocular amplitudes and monocular amplitudes were determined. Results showed that children aged 4-12 years exhibit monocular accommodation of 19 diopters. Larger accommodative amplitude was measured with binocular testing. Seventy-four percent of children who showed an amplitude less than 12 diopters will exhibit a normal measurement on retesting. In addition, great intra-observer variability was noted.

Li-Hong Li, Na Li, Jun-Yang Zhao, Guo-ming Zhang, et al. Br J Ophth

Findings of perinatal ocular examination performed on 3573, healthy full-term newborns

Li LH, Li N, Zhai JY, Fei P, et al, B J Ophthal 2013 May:97(5):588-91

This study prospectively looked at 3573 babies born and examined their eyes within the first week of life to determine what ocular pathology may be detected early after birth. Only healthy babies born after 37 weeks gestation with apgars of 7 or greater were evaluated. During these examinations, 871 (24.4%) of abnormal cases were detected. The majority were retinal hemorrhages, 769 cases (21.52%). Of these cases, 215 were significant retinal hemorrhages, representing 6.02%. One case of retinoblastoma was detected. The long term impact of these abnormalities at birth and significant retinal hemorrhages is unknown; the authors raised concern that these events may lead to the development of amblyopia and/or anisometropia.

Unmet Visual Needs of Children with Down Syndrome in an African Population: Implications for Visual and Cognitive Development

Ada E. Aghaji, Linda Lawrence, Ifeoma Ezegwui, Ernest Onwasigwe
Eur J Ophthalmol May – June 2013; 23(3): 394 – 398

A group of 30 Nigerian students with Down syndrome aged 5-15 were evaluated in a school for the mentally challenged. Uncorrected refractive errors were identified in 76% of these children. Also, one-third had ptosis, one-third strabismus, 13% nystagmus and 3% cataracts. The authors stressed the unmet visual needs of such patients and recommended early screening and treatment.

Fetal ocular measurements by three-dimensional ultrasound

Bojikian KD, de Moura CR, Tavares IM, et al
J AAPOS June 2013 17:3;276-281

The goal of this study was to obtain normative data for fetal eye volume and evaluate reproducibility. This was a prospective, longitudinal observational study,

involving 71 eyes of 37 fetuses between 17 and 40 weeks gestational age. The normative data can be helpful when assessing fetal eyes with risk of genetic diseases that affect ocular growth. Three-dimensional ultrasound was performed. A strong correlation between orbital measurements and gestational age was found. Both manual and sphere mode methods were performed. The two measurements were highly correlated. However, the sphere measurement was consistently greater than the manual measurement. The authors comment that as gestational age advanced, it became difficult to measure both eyeballs, because the fetal head is frequently engaged in the pelvis. Also this data only comments on normal gestational growth; and does not help if abnormal growth occurs after gestation. Finally, any abnormalities found in-utero are not treatable at this time.

The accuracy of the plusoptiX Ao8 photoscreener in detecting risk factors for amblyopia in central Iowa

Bloomberg JD and Suh DW J AAPOS June 2013 17:3;301-304

This was a retrospective review of consecutive patients aged 5 month-5 years seen in one practice over a two-month period. All patients were screened with the plusoptiX Ao8 photoscreener (POAP) and received a complete pediatric ophthalmology examination. Of the 290 children examined, 190 (66%) were found to have amblyopia or amblyogenic risk factors during the examination, based on AAPOS referral criteria guidelines. POAP offered a testability rate of 98%, sensitivity of 87%, specificity of 88%, positive predictive value of 93%, and negative predictive value of 78%. The sensitivity of detecting smaller angle strabismus (≤ 20 prism diopters) was 52%. POAP showed high sensitivity for detecting amblyopia and amblyogenic risk factors. Also, it does not require expert interpretation of the results, which allows more widespread use. The low rate of detecting smaller angle strabismus caused the authors to recommend adding a cover-test or stereotesting. In this study, photoscreening and the examination could have been performed as far apart as 6 months, which could induce different results and alter the data. Also the POAP detects risk factors for amblyopia but does not detect the condition directly. The patients screened are not representative of the pediatric population at-large, as the prevalence of amblyopia or risk factors was much higher than the general population. This may inflate the positive predictive value reported.

Prevalence and Causes of Visual Impairment in Asian and Non-Hispanic White Preschool Children Multi-Ethnic Pediatric Eye Disease Study

Kristina Tarczy-Hornoch, Susan A. Cotter, Mark Borchert, Rohit Varma,
Ophthalmology June 2013; 1220-1226

This is a population-based cross-sectional study designed to determine the prevalence and cause of decreased visual acuity in a multi-ethnic sample of children 30 to 72 months of age currently living in Los Angeles. All eligible children underwent comprehensive ophthalmic evaluation including monocular visual acuity testing,

cover testing, cycloplegic autorefraction, fundus evaluation, and visual acuity retesting with refractive correction.

Conclusions: Seventy percent of all decreased visual acuity, in both Asian and non-Hispanic White populations, occurred as a result of uncorrected refractive error or amblyopia resulting from uncorrected refractive error.

A Comparison of Referral Criteria used by the PlusoptiX Photoscreener

Eric Singman, Noelle Matta, Jing Tian, David Silbert
Strabismus. September 2013;21(3):190-194

There are multiple referral criteria available for the plusoptiX photoscreener. The authors evaluated the sensitivity, specificity, and predictive value of 7 different referral criteria used for the plusoptiX photoscreener on the same cohort of children. 109 children were examined with a thorough pediatric ophthalmic exam and with the plusoptiX photoscreener. Of these, 58 (53%) were confirmed to demonstrate amblyopia risk factors, according to 2003 AAPOS criteria. The plusoptiX referral criteria were adjusted to match 7 published referral paradigms. When comparing the 7 differing referral paradigms to the newly approved (2013) AAPOS criteria, the sensitivity/specificity were respectively: Matta/Silbert 98%/68%, Arthur (2) 73%/92%, Arnold 92%/90%, Arthur 86%/85%, PediaVision 90%/92%, plusoptiX 98%/35%, AAPOS 87%/87%.

The authors conclude that the "Arnold" criteria is the best at maximizing sensitivity and specificity utilizing the 2003 "AAPOS" criteria and the "Arnold" and "PediaVision" were best at maximizing sensitivity and specificity for the newly accepted AAPOS referral criteria. Screening programs will need to decide the level of sensitivity and specificity that they wish to obtain, but for most screening programs the "Arnold" criteria may be preferred.

Flip Chart Visual Acuity Screening for Amblyopia Risk Factors Compared to the PlusoptiX A09 Photoscreener, Tests Performed by a Lay Screener

David I. Silbert, M.D., Noelle S. Matta, CO, CRC, COT, Abby Brubaker *Binocular Vision and Strabology Quarterly, Simms-Romano's* 2013; 28(4):222-8.

This study compared visual acuity screening performed by a lay screener to plusoptiX A09 photoscreener for the detection of amblyopia risk factors. One lay screener was trained to test monocular visual acuity using the 10 foot Patti Pics single crowded chart and the plusoptiX photoscreener. All patients underwent a complete examination with cycloplegic refraction after screening and this was the standard against which the screening methods were compared. Children failed the Patti Pics screening if they failed to reach 20/40 vision in either eye. The plusoptiX determined pass or fail based on pre-set referral criteria. 71 children

were screened ages 3-10 years. Flip chart-screening was found to have a sensitivity of 83%, specificity of 44%, and false positive rate of 56% and false negative rate of 17%. For the plusoptiX system the sensitivity was 94%, specificity 89%, false positive 11%, and false negative 6%. The authors concluded that the plusoptiX photoscreener was more sensitive and specific than flip-chart screening in making appropriate referrals. They feel the plusoptiX photoscreener operated by a lay screener is a reliable method to screen for amblyopia risk factors.

Measuring Contrast Sensitivity Using the M&S Smart System II versus the Pelli-Robson Chart

Manokaraanathan Chandrakumar, Linda Colpa, Y. Arun Reginald, Herbert C. Goltz, *Ophthalmology* October 2013; 120(10):2160-2161

This is a study from the Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, Ontario, Canada.

This study compared contrast sensitivity using the M&S Smart System II versus the Pelli-Robson chart. Contrast sensitivity refers to the inability of the visual system to detect differences in luminance between an object and its background. Assessment of contrast sensitivity provides valuable information in the early detection and monitoring of ocular diseases, as well as evaluating the impact of therapy. The most widely used clinical spatial contrast sensitivity test is the Pelli-Robson chart (Clement Clarke International, Essex, UK).

The M&S Smart System II (MSSS-II; M&S Technologies Inc, Niles, IL) includes a computer-generated, letter-based contrast sensitivity test. Luminance of the liquid crystal display (LCD) screen can be adjusted to recommended levels of 85 candelas/m². The results of the bland-Altman analysis demonstrated that the M&S Smart System II test and Pelli-Robson chart show comparable contrast sensitivity values for both visually normal participants and patients.

Conclusion: the close agreement of the contrast sensitivity threshold suggests that the updated version of M&S Smart System II, when carefully calibrated, can be used as an alternative method to the Pelli-Robson chart in the measurement of contrast sensitivity in a wide variety of ophthalmic conditions in both children and adults.

Development of the Functional Vision Questionnaire for Children and Young People with Visual Impairment The FVQ_CYP

Valerija Tadic, Andrew Cooper, Phillippa Cumberland, Gillian Lewando-Hundt, *Ophthalmology* December 2013; 120(12):2725-2732

This study was performed at multiple institutions in the United Kingdom. Questionnaire development with the objective to develop a novel age-appropriate

measure of functional vision (FV) for self-reporting by visually impaired children and young adults.

Participants: A representative patient sample of visually impaired children and young people aged 10 to 15 years of age, visual acuity of the logarithm of the minimal angle of resolution (logMAR) worse than 0.48, and a school-based (nonrandom) expert group sample of visually impaired students aged 12 to 17 years.

Methods: A total of 32 qualitative semistructured interviews supplemented by narrative feedback from 15 visually impaired children and young people were used to generate draft instruments.

Results: A total of 712 qualitative statements were evaluated.

Conclusions: We have developed a novel, psychometrically robust self-report questionnaire for children and young people (FVQ_CYP) that captures the functional impact of visual disability from their perspective. The authors feel that their questionnaire has potential as a complimentary adjunct to objective clinical assessments in routine pediatric ophthalmology practices and research.

The use of the PlusoptiX photoscreener for vision screening

Laurence P. Tidbury, Anna R. O'Connor, *Br Ir Orthopt J* 2013; 10: 11–16

The aim of this review article is to evaluate data published in the past 5 years to determine whether the PlusoptiX photoscreener is an appropriate alternative to conventional screening. Seven published studies were identified ranging in sample size from 109 to 286 subjects. Each study included comparison of the PlusoptiX screening to a “standard” method of vision screening. However the “standard” used in each study is not described in this review article. The authors conclude that the referral criteria published by Matta et al. and republished in this paper, yielded the most favorable balance between sensitivity (99%) and positive predictive value (95%). The Matta referral criteria differ from the manufacturer’s referral criteria by small increases in referral thresholds for hyperopia, astigmatism and anisometropia. The authors note that the PlusoptiX device demonstrated a better balance of sensitivity and positive predictive value than crowded logMAR acuity alone.

Uptake, referral and attendance: results from an inner city school based vision screening programme

Alison Bruce , Louise Outhwaite , *Br Ir Orthopt J* 2013; 10: 41–45

The aim of this retrospective study is to evaluate the rate of follow-up with an eyecare provider after referral is made by a school screening program in Bradford, England. Of the 5409 children screened, 866 were referred for complete eye examination. Almost 45% of those referred failed to attend an initial appointment eyecare provider. Approximately 1/3 of the patients who failed to attend the initial appointment did attend a subsequent appointment after

receiving recall letter. The authors conclude that improvement in the uptake of screened children into the British eyecare system is needed.

Preschool vision screening: update on guidelines and techniques.

Alley CL. *Curr Opin Ophthalmol*. 2013 Sep; 24(5):415-20.

Preschool vision screening (PVS) is recommended by the AAO, AAPOS and the AAP to detect preventable and treatable vision loss secondary to amblyopia. The goal of PVS is to identify children with amblyopia or amblyopia risk factors such as high refractive errors, anisometropia, media opacities and strabismus. Children identified with amblyopia or amblyogenic risk factors are then referred to an eye care specialist for further evaluation. Vision screening rates remain low due to multiple barriers although some large-scale screening programs and new instruments (photoscreeners/handheld autorefractors) have been developed in recent years to address these barriers. Referral guidelines for instrument based PVS were updated in 2013 in order to increase the likelihood of identifying children at risk for developing amblyopia and reduce unnecessary referral rates. Guidelines are based on age and allow for higher refractive errors in younger children. Children ages 12-30 months with astigmatism greater than 2.0 D, hyperopia greater than 4.5 D and anisometropia greater than 2.5 D should have a formal ophthalmic evaluation. Individuals between 31-48 months with astigmatism greater than 2 D, hyperopia greater than 4.0 D and anisometropia greater than 2.0 D should be examined by an eye care specialist as well. The guidelines for older children were not changed.

Utility of an open field Shack-Hartmann aberrometer for measurement of refractive error in infants and young children

Harvey EM, Miller JM and Schwiegerling J, *J AAPOS* October 2013; 17:494-500

Measurements of refractive error with autorefractors in children who are not cycloplegic often show "instrument myopia". A number of methods have been attempted to address this with varying success. The pediatric wavefront evaluator (PeWE) is a handheld open-field Shack-Hartmann aberrometer designed to measure refractive error in infants and children without cycloplegia. The open-field design attempts to limit instrument myopia, and the continuous video capture increases the quality of the images for analysis. The current study evaluates the feasibility of PeWE use in children ages 6 months to <8 years, its effectiveness for relaxing accommodation, and its accuracy compared to cycloplegic autorefraction. This was a longitudinal study over 3 years and the majority of subjects were American-Indian (high rates of astigmatism). 1425 subjects had 2841 encounters. Technical problems occurred with 143 encounters and these were excluded. Success in obtaining a measurement was greater at near than distance and increased significantly with age. Children <2 years old showed less change in measurements at near versus distance than older

children, and also trended towards greater variability of measurements. PeWE noncycloplegic measurements correlated significantly with cycloplegic Retinomax K-plus2 measurements but tended to produce a myopic shift of 1 diopter at distance and 2 diopters at near. Overall the rates of obtaining a measurement with this technique are less than ideal for a screening test. Also the <2 year old age group showed more variability in measurements, but this is a key age group that we would want to obtain accurate results in. The test was also limited in providing good data on the magnitude of spherical refractive error. This machine studied a group of patients with a high-degree of astigmatism and the results may not be applicable to all patient populations. The instrument is not commercially available and requires significant data processing. Also results were compared to cycloplegic autorefraction, rather than the gold standard of cycloplegic retinoscopy.

Results of a community vision-screening program using the Spot photoscreener

Ransbarger KM, Dunbar JA, Choi SE, et al
J AAPOS October 2013;17:516-520

This study describes and validates results with the Spot photoscreener. The photoscreener uses infrared technology to determine ocular alignment and refractive error and was used by lay operators in a community-based vision-screening program. Children were age 6-72 months. Referral criteria resembled guidelines published by the Vision Screening Committee of AAPOS, or if strabismus was present. 503/8317 children that were screened were excluded (out of age range, or incomplete records). More than ¾ of children screened were reported to be Hispanic. The Spot photoscreener 'failed' 30.6% (23.8% astigmatism, 11.3% ocular misalignment, <2% anisometropia, myopia, hyperopia, anisocoria). Of those referred only 16.4% had a documented eye examination. Only ¾ received an examination which included cycloplegia. In 55.7% there was confirmation of the reason for referral. Positive predictive value was better for astigmatism (73.5%), than ocular misalignment (52.0%). False-positive rate was 34.0%. This study shows a very poor rate of confirmatory examinations which is a cause for concern. Based on the poor degree of follow-up and the poor validity of the screening test, a different vision-screening program plan would probably be appropriate.

Stereoacuity norms for school-age children using the Frisby stereotest

Anketell PM, Saunders KJ and Little J-AJ AAPOS December 2013; 17:582-587

The Frisby stereotest does not require spectacles and is a real-depth free space stereotest. This study provides normative crossed and uncrossed data for this

test for school-aged children and evaluates the relationship of this test with TNO stereoacuity scores. 205 participants completed testing with both stereotests, but 19 were excluded due to an interocular acuity difference and/or anisometropia. Of the remaining 186 patients, 7 failed the TNO stereotest. Frisby stereoacuity scores were statistically significantly different across age groups. Older groups scored better than younger groups. This was not the case for TNO stereoacuity testing. Frisby crossed stereoacuity scores were statistically significantly higher than uncrossed scores, in the younger aged groups. Frisby and TNO stereoacuity scores were statistically significantly different. Frisby scores were better than TNO scores and the two tests showed a positive but weak correlation. Frisby testing has monocular cues. It may be that the two tests are measuring different aspects of stereoacuity. The tests are not interchangeable.

Pupil size and anisocoria in children measured by the plusoptiX photoscreener

Silbert J, Matta N, Tian J, et al J AAPOS December 2013; 17:609-611

PlusoptiX photoscreeners (POX), use infrared light so pupil size does not change while measurements are made. This study evaluated records from 2007 to 2010 and identified 1306 children ranging in age from <1 to 17 years. The mean pupil size was 5.7 mm. Anisocoria of >0.4mm was found in 19.1% of patients. Anisocoria of 1mm or more was found in 2.3% of patients. Average pupil size increased rapidly during the first ten years of life and then slowly thereafter. This study only had a small number of patients in the category >12 years of age.

Accuracy of Noncycloplegic Retinoscopy, Retinomax Autorefractor, and SureSight Vision Screener for Detecting Significant Refractive Errors. Marjean Taylor Kulp, Gui-shuang Ying, Jiayan Huang, Maureen Maguire, Graham Quinn, et al. *IOVS March 2014* 55:1378-1385.

Purpose. To evaluate, by receiver operating characteristic (ROC) analysis, the ability of noncycloplegic retinoscopy (NCR), Retinomax Autorefractor (Retinomax), and SureSight Vision Screener (SureSight) to detect significant refractive errors (RE) among preschoolers.

Methods. Refraction results of eye care professionals using NCR, Retinomax, and SureSight ($n = 2588$) and of nurse and lay screeners using Retinomax and SureSight ($n = 1452$) were compared with masked cycloplegic retinoscopy results. Significant RE was defined as hyperopia greater than +3.25 diopters (D), myopia greater than 2.00 D, astigmatism greater than 1.50 D, and anisometropia greater than 1.00 D interocular difference in hyperopia, greater than 3.00 D interocular difference in myopia, or greater than 1.50 D interocular difference in

astigmatism. The ability of each screening test to identify presence, type, and/or severity of significant RE was summarized by the area under the ROC curve (AUC) and calculated from weighted logistic regression models.

Results. For detection of each type of significant RE, AUC of each test was high; AUC was better for detecting the most severe levels of RE than for all REs considered important to detect (AUC 0.97–1.00 vs. 0.92–0.93). The area under the curve of each screening test was high for myopia (AUC 0.97–0.99). Noncycloplegic retinoscopy and Retinomax performed better than SureSight for hyperopia (AUC 0.92–0.99 and 0.90–0.98 vs. 0.85–0.94, $P \leq 0.02$), Retinomax performed better than NCR for astigmatism greater than 1.50 D (AUC 0.95 vs. 0.90, $P = 0.01$), and SureSight performed better than Retinomax for anisometropia (AUC 0.85–1.00 vs. 0.76–0.96, $P \leq 0.07$). Performance was similar for nurse and lay screeners in detecting any significant RE (AUC 0.92–1.00 vs. 0.92–0.99).

Conclusions. Each test had a very high discriminatory power for detecting children with any significant RE.

Synopsis: This study showed that noncycloplegic retinoscopy, Retinomax Autorefractor, and SureSight Vision Screener each had a very high power for detecting preschool children with significant refractive errors.

A Prospective Comparison Between Cyclopentolate Spray and Drops in Pediatric Outpatients

Syrimi M, Jones SM, Thompson GM. J Pediatr Ophthalmol Strabismus 2013; 50(5):290-295

This prospective study aimed to determine if cyclopentolate spray is better tolerated than cyclopentolate drops and if adequate cycloplegia was achieved by the spray for refraction. Likert questionnaires were given to guardians to grade distress levels. Adequacy of cycloplegia was assessed by a questionnaire given to the examining physician. The study found that children 7 years or younger were significantly less distressed with cyclopentolate spray as opposed to drops. Children over 7 disliked the drops and spray equally. A considerable percentage of children (16.9%) did not have adequate cycloplegia for dynamic retinoscopy, mainly in those with dark irides. The authors conclude cyclopentolate spray may be less distressing for younger children in comparison to drops, but may not provide adequate cycloplegia.

3. REFRACTIVE ERROR

Effect of Day Length on Eye Growth, Myopia Progression, and Change of Corneal Power in Myopic Children

Dongmei Cui, Klaus Trier, Soren Munk Ribel-Madsen, *Ophthalmology* May 2013; 120:1074-1079

This is a cross-sectional study of 235 children ages 8 to 14 years of age found to have myopia during screening for a government sponsored clinical trial in Denmark. The purpose of this study was to investigate whether axial eye growth, nearsighted progression, or corneal power change in Danish myopic children varies with the length of day (between 7 and 17.5 hours of daylight during the calendar year).

Two hundred and thirty-five children ages 8 to 14 years of age were screened. Cycloplegic refraction was measured using an autorefractor, axial eye length, and corneal power using an automatic combined noncontact partial coherence interferometer and keratometer. An astronomical table was used to calculate the number of daylight hours during the measurement period.

Conclusions: Eye elongation and myopic progression seem to decrease in periods with longer days and to increase in periods with shorter days. Children should be encouraged to spend more time outside during daytime to prevent nearsightedness.

Comments: The first article from European investigators supports numerous articles from Asian investigators who reported a decrease in myopic progression when children spend more time outdoors. This is the first study that I have reviewed that correlates daylight hours with myopic progression.

Outdoor Activity during Class Recess Reduces Myopia Onset and Progression in School Children

Pei-Chang Wu, Chia-Ling Tsai, Hsiang-Lin Wu, Yi-Hsin Yang, *Ophthalmology* May 2013; 120:1080-1085

This is a prospective, comparative, consecutive, interventional study of 571 students recruited from 2 nearby schools located in the suburban area of Southern Taiwan. School students were 7 to 11 years of age. The aim of the study was to investigate the effect of outdoor activity during class recess on the nearsighted changes among elementary school students in the suburban area of Taiwan.

Outcome measures: Data were obtained by means of parental questionnaires, ocular evaluations including axial length, and cycloplegic autorefraction at the beginning and at the end of 1 year.

Conclusions: Outdoor activities during class recess and school have a significant effect on nearsighted onset and nearsighted/myopic shift. Such activities have a prominent effect on the control of nearsighted shift especially in nonmyopic children.

Prevalence and 5- to 6-Year Incidence and Progression of Myopia and Hyperopia in Australian Schoolchildren

Amanda N. French, Ian G. Morgan, Paul Mitchell, Kathryn A. Rose, *Ophthalmology* July 2013; 120:1482-1491

This study was performed in South Wales, Australia. The purpose of the study was to determine the prevalence, incidence, and change in refractive errors for Australian schoolchildren and examine the impact of ethnicity and sex. This is a population-based cohort study.

Conclusions: In Sydney, myopia prevalence (14.4%) and incidence (2.2%) and was thought to be lower than other locations. However, in European Caucasian children at age 12 there was a significantly higher prevalence of nearsightedness in a younger sample suggest a rise in prevalence consistent with international trends. Progression of myopia was similar for children of East Asian and European Caucasian ethnicity, but lower than reported in children of East Asian ethnicity. This suggested that environmental differences may have some impact on progression. Another paper correlated myopia progression with environment, daylight hours, and activity out-of-doors.

Prescription of atropine eye drops among children diagnosed with myopia in Taiwan from 2000 to 2007: a nationwide study

Y-T Fang; Y-J Chou; C Pu; P-J Lin, et al. *Eye*. March 2013;27(3):418-24

This population-based cross-sectional study from Taiwan was conducted to examine the atropine eye drop prescription trend for children diagnosed with myopia, and to determine the factors associated with the prescription of atropine eye drops. The study was conducted using a national representative sample from the National Health Insurance claims data. All school children between 4 and 18 years of age who had visited an ophthalmologist and were diagnosed with myopia between 2000 and 2007 were included. The main outcome measure was the proportion of subjects who were prescribed atropine eye drops in each year. Logistic regression was used to identify the factors associated with atropine eye drops being prescribed.

Atropine eye drop prescriptions for children diagnosed with myopia increased significantly from the school years 2000 (36.9%) to 2007 (49.5%). There was also a shift from prescribing high concentrations (0.5 and 1%) of atropine eye drops to lower concentration ones (0.3, 0.25, and 0.1%) within this period. Atropine eye drops were more frequently prescribed to 9–12-year-old children (OR=1.26–1.42), compared with those 7–8 years old, and to children from families with a high socioeconomic status (OR=1.19–1.25). They were prescribed less often to those living in mid to low urbanized areas (OR=0.65–0.84) compared to highly urbanized areas.

In Taiwan, which has a high rate of myopia, 49.5% of school-aged children are being prescribed atropine eye drops, primarily at low concentrations. Lower concentrations of atropine may decrease myopia progression without causing as much pupillary dilation and photophobia. However, this study was not designed to assess efficacy or side effects of atropine use in myopia.

Prescription of atropine eye drops among children diagnosed with myopia in Taiwan from 2000 to 2007: a nationwide study.

Y.T. Fang, Y.J. Chou, C. Pu, P.J. Lin, et al.
Eye (Lond). 2013 Marh; 27(3):418-24

In this study, the investigators sought to determine how frequently atropine eye drops are prescribed to children diagnosed with myopia. This study conducted in Taiwan utilized the national health insurance research database which is a compulsory database meant for all citizens in Taiwan, thus yielding a 99% coverage rate. In this population of all children between the ages of 4 to 18 years who visited ophthalmology, 68% were diagnosed with myopia. For those children diagnosed with myopia, the use of atropine increased between the years of 2000 and 2007, so that in 2009 49.5% of the children diagnosed with myopia were treated with atropine. It is more likely that the children between the ages of 9 to 12 were given atropine than those aged 7-8. In addition, the strength of atropine used decreased between the years of 2000 to 2007 with concentrations as low as 0.3, 0.25, and 0.1%, the others found that patients from a higher socioeconomic status tend to use atropine more often. In Taiwan, the atropine is used as a modality to slow the progression of myopia.

Risk Factors for Incident Myopia in Australian Schoolchildren The Sydney Adolescent Vascular and Eye Study

Amanda N. French, Hons, Ian G. Morgan, Paul Mitchell, Kathryn A. Rose,
Ophthalmology October 2013; 120(10):2100-2108

The Sydney Adolescent Vascular and Eye Study (SAVES) is a 5- to 6- year longitudinal follow-up to the Sydney Myopia Study cohort. In this report the authors investigated whether risk factors previously associated with prevalent myopia (including parental myopia, near work, time spent outdoors) were also associated with incident myopia in a large population-based sample of Australian school children.

Methods: Cycloplegic autorefraction was measured at baseline and follow-up. Myopia was defined as a spherical equivalent refraction of -0.50 diopters. Children were classified as having incident myopia if they were nonmyopic at baseline and then later developed myopia in either eye or both eyes at follow-up. A comprehensive questionnaire determined the amount of time children spent outdoors doing near work for a week at baseline as well as ethnicity, parental myopia and socioeconomic status.

Main outcome measures: Incident myopia

Results: Children who became myopic spent less time outdoors than children who did not become myopic. Children who became myopic performed significantly more near work (19.4 hours vs. 17.6 hours), particularly in the younger cohort but not in the older cohort. Children with one or two parents who were myopic also had greater odds of developing incident myopia. Children of

East Asian ethnicity had a higher incidence of nearsightedness/myopia compared with children of European ethnicity.

A LESS HYPEROPIC REFRACTION AT BASELINE WAS THE MOST SIGNIFICANT PREDICTOR OF INCIDENT MYOPIA. THE ADDITION OF TIME OUTDOORS, NEAR WORK, PARENTAL MYOPIA AND ETHNICITY SIGNIFICANTLY IMPROVED THE PREDICTIVE POWER. THIS WAS MORE PRESENT IN THE YOUNGER COHORT THAN IN THE OLDER COHORT.

Conclusions: Time spent outdoors was inversely proportional (negatively associated) with the incidence of myopia in both the young and older age cohorts in Australian school children. Furthermore, near work and parental myopia were additional significant risk factors for development of myopia primarily in the younger cohort.

Reviewers Comment: This study reports similar findings of the “Collaborative and Longitudinal Evaluation of Ethnicity and Refractive Error Study” performed in the United States (CLEERE Study Group) in 2011. The study was by Jacobson (2008), Parssinen (1993) and Rose (*Ophthalmology* 2008). The association between outdoor activity and myopia seen in teenage children was reported in the *British Journal of Ophthalmology* 2009. There was also a study based in Taiwan (2010) and Europe (2012).

The current working theory is that there may be a protective effect preceded by release of retinal dopamine in response to typically higher intensity lighting that occurs outdoors. This has been shown in chicks and primates to block the development of deprivation myopia.

Prevalence of Myopia, Hyperopia and Astigmatism in Non-Hispanic White and Asian Children Multi-Ethnic Pediatric Eye Disease Study

Ge Wen, MSc, Kristina Tarczy-Hornoch, Roberta McKean-Cowdin, Susan A. Cotter, *Ophthalmology* October 2013; 120(10):2109-2116

This is a population-based sample of 1,501 non-Hispanic white children and 1,507 Asian children age 6 to 72 months from Los Angeles County and Riverside County, California. The purpose of the study was to determine the age, gender and ethnicity-specific prevalence of nearsightedness/myopia, farsightedness/hyperopia and astigmatism in non-Hispanic white (NHW) and Asian preschool children.

Methods: Eligible children underwent in-home and in-clinic interview and a comprehensive eye examination including cycloplegic autorefraction from 100 census tracts.

Conclusion: Hyperopia was the most common refractive error in both Asian and non-Hispanic white children. Myopia was relatively more prevalent among Asian children compared to non-Hispanic white children. The prevalence of astigmatism was greatest in infants. Myopia showed relatively stable prevalence across age groups, whereas farsightedness prevalence decreased after infancy and then increased again in older age groups.

Reviewer comments: These findings support earlier non-population based studies. The classic study of Cook and Glasscock of newborn infants found a lower incidence of nearsightedness in white children compared with African-American children using Atropine cycloplegia. The non-population based Collaborative and Longitudinal Evaluation of Ethnicity Refractive Error Study (CLEERE) of older school age children reported similar patterns for the prevalence of nearsightedness and farsightedness in non-Hispanic whites and Asians compared with African-Americans and Hispanics.

Myopic Control in Children through Refractive Therapy Gas Permeable Contact Lenses: Is it for Real?

B. Koffler, J. Sears. Am J Ophthal December 2013;vol. 156:(6); 1076-1081.

This review article analyzes the safety and efficacy of orthokeratology as a treatment for myopia in children through multiple studies. They review the history of orthokeratology going back to the 1950s up to the most current studies. Orthokeratology has been suggested to affect axial length development by treating peripheral hyperopia. The Stabilizing Myopia by Accelerated Reshaping Technique (SMART) study was the first large scale study looking at reverse geometry overnight orthokeratology. 162 children were examined and the orthokeratology lenses were compared to regular soft lenses which were changed every month. This study occurred in 10 clinics throughout the US. After 3 years, 85% of the orthokeratology patients had 20/20 vision and 99% achieved 20/40 or better. Another study reviewed was "Influence of Overnight Orthokeratology on Axial Length in Childhood Myopia" in Japan. The mean axial length change was 0.39+/- .27 mm. The spectacle group had an axial length change of 0.61+/- .24 mm. The difference was statistically significant. The last study reviewed was a randomized study by Cho and Cheung. This study concluded that children 7-8 years of age had a faster rate of axial length elongation than older children. The authors suggest that with new lens design, orthokeratology is a viable option.

The Effects of Glasses for Anisometropia on Stereopsis

JY Lee, JIY Seo, SU Baek. Am J Ophthalmology December 2013; vol 156: 6; pages 1261-1267.

This retrospective study was concerned with the effect anisometropic glasses had on stereopsis. Eight years of records were retrospectively reviewed and

compared to a similarly matched control group. 106 patients were in the anisometropic group and 56 in the control group. 31 cases of the anisometropia were spherical myopia, 51 spherical hyperopia and 16 were astigmatic, 8 were mixed. Stereopsis did not vary significantly between the 4 groups. However, the spherical hyperopic group did seem to have the more reduced stereopsis. Review of all these cases showed that even cases of severe anisometropia maintained normal to equivocal stereopsis with their glasses on. Of course, anisometropic children showed worse stereopsis than isoametropic children. This study found that a high degree of anisometropic is clinically tolerable with corrective lenses.

The possible association of attention deficit hyperactivity disorder with undiagnosed refractive errors

Fabian ID, Kinori M, Ancrì O, et al J AAPOS October 2013; 17:507-511

The authors attempted to determine if there is an association between ADD/ADHD and refractive errors (specifically hyperopia and astigmatism) or impaired binocular function. Patients were recruited from an ADD/ADHD clinic over a 10-month period and their records were reviewed retrospectively. Healthy control subjects were also recruited. 56 ADD/ADHD children and 66 controls were included. Mean age was 9.5 years and 9.0 years respectively. The ADD/ADHD group consisted of 80% boys while the control group was 50% boys. Over ¼ of the patients in the ADD/ADHD group were taking ADD medications. There was no difference in main outcome measures between the two groups. There was a statistically greater degree of astigmatism in the ADD/ADHD group but absolute astigmatism measures were mild (none > 0.75 D). There was a slight statistical difference in the mean NPC (4.1 +/- 1.8 cm for the control group and 5.3 +/- 2.3 cm for the ADD/ADHD group). Two patients in the ADD/ADHD group had borderline convergence insufficiency but no patients in the control group displayed this. ADD medication use did not alter clinical parameters. The authors' hypothesis was not supported. The authors assumed the control group was ADD free and examiners were only partially masked to subject groups. Finally the ADD/ADHD group had a preponderance of boys, unlike the control group.

Defocus incorporated soft contact lens slows myopia progression in Hong Kong Chinese school children: a 2-year randomised clinical trial.

C. Lam, W. Tang, D. Tse, Y. Tang, C. To. Br J Ophthal 2014; 98: 40-45.

This study looked at DISC lens wear to slow childhood myopia. This was a 2 year randomized trial on 221 children between 8-13 years of age. Patients were randomly assigned between single vision contacts or DISC lens. 128 children

completed the study. Myopia progressed more slowly in 25% of the DSC group. There was also less axial elongation. The myopia progressed 46% less in the DISC group than the standard group.

Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%

Chia, W. Chua, L. Wen, A. Fong, Y. Goon, D. Tan. *Am J Ophthal* Feb 2014; 157(2): 451-457.

This prospective randomized double masked study looked at 400 myopic children between the ages of 6-12 years of age received atropine in one of the three doses for 24 months. After that time, the children were evaluated at 26, 32, and 36 months and spherical equivalent, axial length, visual acuity, pupil size, and accommodation were assessed. 356 children completed the study. Myopic progression was greatest in the 0.5% group. Axial length was also greater in the 0.5% group. Accommodation was less in the 0.5%, but pupil size and near visual acuity had no change from preop. This study concluded that there was a myopic rebound after atropine was stopped. The 0.1% atropine effect was more sustained. A problem with the study is that there was no real control group but the information is still interesting and a low risk option.

Seasonal Variations in the Progression of Myopia in Children Enrolled in the Correction of Myopia Evaluation Trial. Jane Gwiazda, Li Deng, Ruth Manny, Thomas T. Norton, and for the COMET Study Group. *IOVS February 2014 55:752-758.*

Purpose. To investigate monthly and seasonal variations in the progression of myopia in children enrolled in the Correction of Myopia Evaluation Trial (COMET).

Methods. An ethnically diverse cohort of 469 myopic 6- to <12 year-old children was randomized to single vision or progressive addition lenses and followed for 3 years with 98.5% retention. Progression of myopia was measured semiannually by noncycloplegic autorefractometry (Nidek ARK 700A) and annually by cycloplegic autorefractometry, with the former measurements used in these analyses. The semiannual progression rate was calculated as (change in spherical equivalent refraction between two consecutive semiannual visits/number of days between the two visits) times 182.5. Months were categorized as the midpoint between two visit dates. Seasons were classified as winter (October through March) or summer (April through September). The seasonal difference was tested using a linear mixed model adjusting for demographic variables (age, sex, ethnicity), baseline refraction, and treatment group.

Results. Data from 358 children (mean [±SD] age = 9.84 ± 1.27 years; mean myopia = -2.54 ± 0.84 diopters [D]) met the criteria for these analyses. Myopia progression varied systematically by month; it was slower in April through

September than in the other months. Mean progression in winter was -0.35 ± 0.34 D and in summer was -0.14 ± 0.32 D, a statistically significant difference (0.21 D, $P < 0.0001$). The same seasonal pattern was found by age, sex, ethnicity (except in the small sample of Asians), lens type, and clinical center.

Conclusions. The slower progression of myopia found in summer is likely related to children's spending more time outdoors and fewer hours in school. The data have clinical implications regarding the time of year and the frequency with which myopic children have eye examinations and the need for precise timing of visits in clinical trials testing new myopia treatments. (ClinicalTrials.gov number, NCT00000113.)

Synopsis: Myopia progression in children was found to vary systematically by month; it was slower in April through September than in the other months. These data have implications for both mechanisms of eye growth and clinical management of myopia.

The Influence Of Compliance With The Use Of Refractive Correction In Hyperopic Children On Accommodation

Stamatis D. Gatzonis, Vasiliki P. Follidi, Eur J Ophthalmol November-December 2013; 23(6): 876 - 880

This article offers a testing technique to evaluate compliance with full-time hyperopic eyeglasses use. The authors evaluated 52 children age 2.5 to 9 with cycloplegic refraction of hyperopia > 3 D. These children were fully corrected (if ET was present) or partially corrected. A dry autorefraction measurement was made at 3 and 6 months interval. Thirty-seven children were full-time wearers. Their autorefraction on both visits was equal to their cycloplegic refraction. The non-compliant 15 children had an autorefraction reading of significantly less hyperopia (even myopia), consistent with prolonged and strong accommodative tone. The authors concluded that full-time use of hyperopic spectacles leads to relaxation of accommodation in children and is an accurate indicator of compliance.

4. VISION IMPAIRMENT

The Short- and Long-term Effects on the Visual System of Children Following Exposure to Maternal Substance Misuse in Pregnancy.

Kurt Spiteri Cornish, Monica Hrabovsky, Neil W. Scott, Elizabeth Myerscough, et al. Am J Ophthal July 2013; 156(1): pg. 190-194.

This retrospective study evaluated 301 children born to mothers misusing substances during pregnancy. The incidence of substance abuse in pregnancy is on the rise and this study attempted to evaluate the prevalence of ophthalmic morbidities over a 5 year period. Out of the 301 children, 96 (31.9%) were referred

for ophthalmic evaluation. Forty-six (15.3%) were diagnosed with strabismus, and eleven (3.7%) were diagnosed with nystagmus. The control group of 1035 children demonstrated 218 (2.8%) with strabismus and 3 (0.004%) with nystagmus. This study suggests that this subgroup of children should be monitored more carefully for ophthalmic problems.

Visual Outcome in infants born to drug-misusing mothers prescribed methadone in pregnancy

L. McGlone, R. Hamilton, D. McCulloch, J. MacKinnon, M. Bradnam, H. Mactier. *BR J Ophthal* 2014; 98: 238-245.

This prospective study looked at clinical visual and electrophysiological outcomes at 6 months. Past studies demonstrated abnormal VEPs in neonates exposed to maintenance methadone. This study was performed in Glasgow. 107 Infants were recruited within 3 day of life during 2008-2010. Premature children were excluded prior to 36 weeks gestation. Normative data was also collected from babies not exposed to drugs in utero. (81 drug exposed and 26 normal) All infants were evaluated at 6 months by a pediatrician and optometrist. 40% of the drug exposed babies failed visual assessment. 11% had nystagmus. 25% had strabismus. 22% had reduced visual acuity. 27% of the VEPs were non detectable. This study shows that methadone exposure has effects upto 6 months of age shown clinically and through electrophysiology.

How to help children with neurodevelopmental and visual problems: a scoping review.

C. Williams, K. Northstone, C. Borwick, M. Gainsborough, J. Roe, S. Howard, S. Rogers, J. Amos, JM Woodhouse. *Br J Ophthal* 2014; 98: 6-12.

This study defined a PICO format of population, intervention, comparator, outcome. This was performed through abstracted data: 4450 abstracts with 107 papers for inclusion. The strongest data was provision of spectacles and the use of ultraviolet light as environmental modification of training. Some help occurred with training for oculomotor ability. It is important that all children with neurodevelopmental problems have a visual evaluation by a specialist.

Preventable Visual Impairment in Children With Nonprofound Intellectual Disability

Lokman Aslan, Murat Aslankurt, Adnan Aksoy, Hatice Altun *Eur J Ophthalmol*, November-December 2013; 23(6): 870 – 875

The authors evaluated and compared 215 children with non-profound intellectual disability (DI) (90 of which had Downs syndrome(DS)) with 116 healthy subjects. Full ophthalmologic examinations in each subject were recorded and analyzed

for statistical analysis. The pediatric population with intellectual disability has a high prevalence of preventable visual impairments, refractive errors, strabismus, and cataracts. The prevalence of strabismus and refractive errors was more frequent in children with Down's syndrome. The prevalence of preventable visual impairment in cases of Down's syndrome and intellectual disability as compared to controls is as follows: refractive errors 61.1/ 45.6% (DS/DI) vs 11.2% in controls; strabismus 33.2/15.2% (DS/DI) vs. 3.5% in controls, cataract (7.8/ 6.4%(DS/DI), and nystagmus 7.8%/4% (DS/DI) and glaucoma 0.8% (only ID) Cataracts, glaucoma, and nystagmus were not observed in the control group.

5. NEURO-OPHTHALMOLOGY

Retinal Nerve Fiber Layer Thickness Using Spectral-Domain Optical Coherence Tomography in Patients with No Light Perception Secondary to Optic Atrophy

Syliva L Goth, Andrew Harrison, Alana L Grajewski, and Michael S Lee . *J Neuro-Ophthalmol* March 2013; 33:37-39.

Spectral domain OCT is used to evaluate eyes with longstanding no light perception (NLP) visual acuity secondary to optic atrophy in order to ascertain the lower limit of measured mean retinal nerve fiber layer (RNFL). A retrospective cross-sectional chart review identified 10 patients with NLP acuity for a mean of 3.72 (+/- 1.2) years secondary to optic atrophy. Etiologies of optic atrophy included optic nerve sheath meningioma, autoimmune optic neuropathy, other meningioma, neuro-myelitis optica, trauma and glaucoma. The Spectralis Spectral Domain OCT (Heidelberg Engineering, Heidelberg Germany) was used to quantify mean RNFL thickness. The range was 28-40 um with a mean of 34.18. This is thinner than the lower limit previously reported with the Stratus Time Domain OCT (45.42 um) however the latter is an older technology capable of less resolution. The study validates the clinically important fact that "complete" optic atrophy leaves an anatomically measurable RNFL of about 34 um. This layer is thought to be comprised of retinal blood vessels, glial cells and dead or non-functioning ganglion cell axons.

Idiopathic Intracranial Hypertension: Relation between Obesity and Visual Outcomes

Aimee J Szewka, Beau B Bruce, Nancy J Newman, and Valerie Biousse, *J Neuro-Ophthalmol* March 2013 213; 33:4-8.

The retrospective chart review was designed to determine whether patients with idiopathic intracranial hypertension (IIH) and severely elevated body mass index (BMI \geq 40) (n=158) had worse visual outcomes than those with IIH and BMI 30-39.9 (n=172). Patients with BMI \geq 40 were more likely to present initially with severe papilledema (p=0.02) and there was a trend to more severe vision loss in one or both eyes of these patients, after controlling for sex, race, hypertension and sleep apnea.

The 10 unit increase in BMI increased the odds ratio of severe vision loss by 1.4 (95% confidence interval 1.03-1.91 P=0.03)

The Clinical Validity of the Spontaneous Retinal Venous Pulsation

Sui H Wong; Richard P White, *J Neuro-Ophthalmol March 2013; 33:17-20.*

The investigators determine the specificity and positive predictive value of the presence of spontaneous venous pulsations (SVP) in indicating normal intracranial pressure. Opening pressure with lumbar puncture was assessed to determine the possibility of elevated intracranial pressure in 106 patients with relevant clinical indications. Fundus examinations by two distinct observers were carried out prior to the spinal tap. Thirteen of these patients had a documented opening pressure ≥ 30 cmwater; SVP were present in 11 of these 13. Of the remaining 93 patients with ICP ≤ 30 cm water, 83 had SVP and 10 did not. The sensitivity and positive predictive value of the presence of SVP indicating the presence of normal ICP were 0.89 and 0.88 respectively. However, noting that 11 of 13 patients with elevated ICP had document SVP; the presence of this clinical sign clearly does not rule out the possibility of elevated ICP

Mechanical Oscillopsia after Lower Eyelid Blepharoplasty with Fat Repositioning

Sumeer Thinda, Michael S Vaphiades and Louise Mawn, *J Neuro-Ophthalmol March 2013; 33:71-73.*

A patient who underwent transcutaneous lower eyelid blepharoplasty with fat repositioning developed oscillopsia with any mechanical movement of the face. The movement was most notable with chewing, infraducting, moving the mouth or pressing in the cheek or lower eyelid. Exploration of the surgical site revealed cicatricial tissue between the inferior oblique muscle and the anterior superficial musculo-aponeurotic complex; severing of these adhesions relieved the oscillopsia.

Visual Field Improvement after Pituitary Surgery in Patients with McCune-Albright Syndrome

Jin Ma, Chan Zhao, Renzhi Wang, Feng Feng, et al *J Neuro-Ophthalmol March 2013; 33 26-29.*

McCune Albright Syndrome is a sporadic congenital disorder associated with café-au-lait spots, polyostotic fibrous dysplasia and endocrinopathies. Pituitary tumor is present in 66% of cases that have documented growth hormone excess. Optic canal narrowing associated with the fibrous dysplasia has been assumed to be the major source of vision loss, yet other investigations have found that the presence of growth hormone excess is the factor statistically associated with vision decline. In this report, three patients with McCune Albright Syndrome were found to have growth hormone secreting pituitary tumors with chiasmal compression in addition to marked optic canal narrowing with thickening and deformity of craniofacial bones. Notable improvement in acuity and reduction in visual field loss resulted from simple transsphenoidal pituitary resection without surgery to the optic canals. In a prior study by Lee, JS, et al NEJM 2002; 347:1670-76, a large cross sectional analysis of

a case controlled cohort failed to demonstrate that narrowing of the optic canals was associated with visual loss; at this time optic canal decompression is only indicated in patients with fibrous dysplasia and acute or progressive visual impairment clearly from this source. The purpose of this report is to point out the importance of remembering the potential contribution of the highly treatable optic chiasmal compression that may be found in patients with McCune Albright Syndrome.

Grey and white matter changes in children with monocular amblyopia: voxel-based morphometry and diffusion tensor

imaging study. Qian Li, Qinying Jiang, Mingxia Guo, Chunquan Cai, Xiaohui Yin. Br J Ophthal April 2013; 97: 524-529.

VBM provides whole brain analysis of group differences in the grey and white matter volume. The DTI provides structural and functional information about white matter. The authors looked at these techniques to see if global brain change is peculiar to amblyopia. 40 children were evaluated, 20 normal and 20 with amblyopia. Compared with the normal children, grey matter volume was reduced in the left inferior occipital gyrus, bilateral parahippocampal gyrus, and left supramarginal/postcentral gyrus in the monocular amblyopes. The white matter was decreased in the left calcarine and the bilateral inferior frontal and right precuneus areas. This study supports previous suggestions that amblyopia affects higher levels of the visual pathway as well as the primary visual cortex.

Cyclic (alternate day) vertical deviation- possible forme fruste of ocular neuromyotonia

Roper-Hall G, Cruz OA, Espinoza GM, and Chung SM
J AAPOS June 2013 17; 3:248-252

The authors report 3 consecutive adult patients with 48-hour cyclic hypotropia. Sustained contraction of a vertically acting extraocular muscle lasted 24 hours and then was absent for 24 hours. Two patients had thyroid eye disease and the third had a cavernous sinus schwannoma. Two patients improved with medications (carbamazepine and gabapentin), while the other improved spontaneously. Based on the behavior of the strabismus and the response to membrane-stabilizing medications, the authors posit a relationship of the cyclic vertical strabismus to ocular neuromyotonia. The authors state the importance of early recognition, especially when patients report 'good' and 'bad' days. Acquired incomitant cyclic deviations require neuroimaging to rule out a neurologic cause.

Dominant Optic Atrophy: Novel OPA1 Mutations and Revised Prevalence Estimates

Patrick Yu-Wai-Man, Patrick F. Chinnery, *Ophthalmology* August 2013; 120:1712

Autosomal-dominant optic atrophy (DOA) is classified as a mitochondrial disorder and is the most common inherited optic nerve disorder seen in clinical practice. Two

causative genes have been identified in patients with dominant optic atrophy; OPA1, which accounts for 50%-60% of cases, and OPA3, which is relatively rare having been identified in only isolated families in association with premature cataracts. OPA1 mutations have a high penetrance rate, but the disease phenotype is characterized by marked intra- and interfamilial variability.

The purpose of this paper is to report the identification of additional 8 families of confirmed pathogenic OPA1 mutations.

Conclusions: The authors reported that their updated epidemiologic data has firmly established dominant optic atrophy as an important cause of inherited visual failure and the urgent need for effective treatments to help patients with this disabling form of mitochondrial blindness.

Dural Puncture Induced Intracranial Hypotension Causing Diplopia

Padmaja Sudhakar, Jonathan D. Trobe, and Jeffrey Wesolowski, *J Neuro-ophthalmol* June 2013 213; 33:106-112

The authors present six cases where diplopia from 6th nerve palsy resulted from intracranial hypotension; the hypotension occurred after typically after removal of an epidural catheter that had been placed, initially, for medication delivery. Dural puncture upon removal of the catheters resulted in unintended CSF leak, postural headache and in these rare cases, 6th nerve palsy. The 6th nerve palsy is thought to result from traction on the brainstem as it sinks downward because of lowered intracranial pressure. Resolution of the leak results in recovery of 6th nerve function. The paper is important as new onset 6th nerve palsy is typically seen as an ominous sign requiring a significant evaluation to detect the cause. Awareness of this rare but relatively benign etiology fact can avert unnecessary workup and concern.

Visual and Neurological Outcomes following Endovascular Stenting for Pseudotumor Cerebri Associated with Transverse Sinus Stenosis

Martin G Radvany, David Solomon, Satnam Nijjar, Prem S. Subramanian, Neil R Miller, et al. *J Neuro-Ophthalmol* June 2013 33:117-122.

A subgroup of patients with presumed idiopathic intracranial hypertension (IIH) have been noted to have cerebral dural sinus stenosis, particularly involving the transverse sinuses. It remains unclear whether these stenoses are caused by, or are responsible for, the associated elevation in intracranial pressure. The authors present a series of 12 patients with transverse sinus stenosis and IIH who had failed medical therapy and were subsequently treated with endovascular venous stenting. This procedure proved to be effective in reducing intracranial pressure and treating the associated visual symptoms as well as reducing headache and pulsatile tinnitus in nearly all cases.

Drug Related Mitochondrial Optic Neuropathies

Michelle Y Yang; Alfredo A. Sadun, *J Neuro-Ophthalmol* June 2013 33:172-178

Mitochondrial optic neuropathies typically affect the papillo-macular bundle as the associated fibers are small, unmyelinated, and exercise high energy demand. A

variety of medications cause “mitochondrial optic neuropathy” as they interfere with mitochondrial function. These medications include chloramphenicol, ethambutol, linezolid, erythromycin, streptomycin and anti-retroviral drugs. Awareness of the possible undesirable side effect resulting from using these medications can help reduce morbidity if the association is recognized and the patient treated by discontinuing the medication; early recognition can permit recovery and may help prevent permanent loss.

Cranial autonomic symptoms in pediatric migraine are the rule, not the exception Gelfand AA, Reider AC, Goadsby PJ. *Neurology* July 30, 2013; 81(5):431-6.

The presence of cranial autonomic symptoms often leads to a misdiagnosis of “sinus headache” in adult migraineurs, leading to unnecessary treatments and delaying appropriate migraine therapy. This cross-sectional study examined the frequency of cranial autonomic symptoms in pediatric/adolescent patients with migraine at 4 different sites over the course of the study period. Of 125 pediatric migraineurs, 62% had at least one cranial autonomic symptom based on current International Classification of Headache Disorders, second edition (ICHD-II) criteria, and 70% based on proposed ICHD-III criteria. The majority had more than one cranial autonomic symptom and the symptoms tended to be bilateral. Age, sex, laterality of headache, presence of aura, and whether migraine was episodic vs chronic did not influence the likelihood of having cranial autonomic symptoms. The authors concluded that in pediatric/adolescent migraine, the presence of cranial autonomic symptoms appears to be the rule rather than the exception. They recommended that clinicians should be careful to consider migraine when evaluating a child with headache and associated ocular or nasal symptoms so as to avoid giving a misdiagnosis of sinus headache.

Ophthalmic Artery Ischemic Syndrome Associated With Neurofibromatosis and Moyamoya Syndrome

Matthew T. Witmer, Richard Levy, Kaleb Yohay, Szilard Kiss, *JAMA Ophthalmol.* April 2013;131(4):538-539.

The authors present the first description of a patient with evidence of retinal and choroidal infarction, and consequent necrosis, from ophthalmic artery ischemia associated with moyamoya syndrome and neurofibromatosis type 1. Moyamoya syndrome predisposes patients to cerebrovascular ischemia as the result of stenosis of the intracranial portion of the internal carotid arteries and their proximal branches. Stenoses of intracranial blood vessels lead to collateral circulation which on cerebral angiography produces an appearance of puff of smoke or MoyaMoya in Japanese. This finding is seen in patients with NF-1, Down syndrome and sickle cell disease. Their patient underwent a neurosurgical procedure, pial synangiosis, a cerebral revascularization procedure in which a donor scalp artery is sutured to the surface of the brain. The authors recommend close ophthalmic and neurological follow-up for these patients.

Optic Pathway Gliomas: Neoplasms, Not Hamartomas

Grant T. Liu, James A. Katowitz, Lucy B. Rorke-Adams, Michael J. Fisher, JAMA Ophthalmol. May 2013; 131(5):646-650.

Optic pathway gliomas (OPG) are a significant neuroophthalmic cause of visual loss in children. Whether OPG are hamartomas or neoplasms is an important distinction with regard to visual prognosis and treatment. The objective of this article was to provide evidence, from review of the literature, that OPG are neoplasms. Histopathology and growth patterns suggest they are slow growing neoplasms. Chemotherapy should be administered if progression can be documented in order to prevent visual loss.

Incidence and Associated Endocrine and Neurologic Abnormalities of Optic Nerve Hypoplasia

Brian G. Mohney, Ryan C. Young, Nancy Diehl, JAMA Ophthalmol. July 2013;131(7):898-902.

This paper determined the incidence of optic nerve hypoplasia in a population-based cohort in Olmstead County, Minnesota, as well as the rate of neurologic, endocrine and developmental abnormalities. In this 25 year retrospective review, the incidence was calculated as 2.4/100,000 patients age less than 19 years old or 1/ 2287 live births. Mean age at diagnosis was 2.1 years and 53% were male. Eighty four percent had bilateral optic nerve hypoplasia. Associated conditions included primiparity in 42%, prematurity in 32% and maternal diabetes in 16%. Ocular findings included reduced visual acuity in 47%, strabismus in 42% and nystagmus in 26%. Associated systemic findings included developmental delay in 63%, neurologic deficits in 53% and endocrine dysfunction in 26%.

Marked Recovery of Vision in Children with Optic Pathway Gliomas Treated With Bevacizumab

Robert A. Avery, DO, MSCE; Eugene I. Hwang, MD; Regina I. Jakacki, MD; Roger J. Packer, MD JAMA Ophthalmol. 2014; 132 (1) Jan 2014:111-114.

Optic pathway gliomas may be associated with vision loss, either central or visual field defects. Standard treatment with carboplatin and vincristine provides mild improvement (0.2 logmar) in visual acuity in one third of patients. The authors present 4 patients with optic pathway gliomas, 2 associated with neurofibromatosis type 1 and 2 sporadic, 3 of whom initially were treated with chemotherapy and/or proton beam therapy but experienced progressive visual loss. These children were then treated with bevacizumab (Avastin), a monoclonal antibody with activity against vascular endothelial growth factor (VEGF). Bevacizumab was administered intravenously at a dose of 10mg/kg per dose every 2-3 weeks. Bevacizumab works through inhibition of angiogenesis which was associated with improved visual acuity and visual field deficits in these children.

Optic Neuropathy Due to Biotinidase Deficiency in a 19-Year-Old Man

Scott R. Haines, MD; Reid A. Longmuir, MD JAMA Ophthalmol. 2014; 132(2) Feb 2014:228-230.

Biotinidase deficiency is an autosomal recessive condition in which the normal recycling of biotin is deficient. If untreated, infants with biotinidase deficiency will develop neurologic problems including optic atrophy. The authors present a 19 year old patient, diagnosed as an infant with biotinidase deficiency who took supplements until age 10. During college the patient engaged in occasional binge drinking of alcohol and presented at age 19 with decreased central acuity (20/70 OD, 20/25 OS), dyschromatopsia, optic atrophy and cecocentral scotomas on visual field testing. Biotin supplements were prescribed (20mg/day), with subsequent improvement of visual acuity (20/20 each eye) and minor visual field deficits. The most common nutritional deficiencies causing optic neuropathy involve vitamin B12, vitamin B1, and folic acid. The authors emphasize that biotin deficiency should also be included as a possible cause of optic neuropathy.

Isolated Third, Fourth, and Sixth Cranial Nerve Palsies from Presumed Microvascular versus Other Causes A Prospective Study

Madhura A Tamhankar, MD, Valerie Biousse, MD, Gui-Shuang Ying, MD, PhD, Sashank Prasad, MD, PhD
Ophthalmology November 2013; 120(11):2264-2269

This is a multi-center study done at multiple centers in North America. This is a prospective, multi-center, observational case series designed to estimate the proportion of patients presenting with isolated third, fourth or sixth cranial nerve palsy of presumed microvascular origin versus other causes. A total of 109 patients aged 50 years or older with acute isolated ocular motor nerve palsy were evaluated. Magnetic resonance imaging was done on each patient.

Main outcome measures: Causes of acute isolated ocular motor nerve palsy (presumed microvascular or other) as determined with early MRI and clinical assessment.

Results: Twenty-two of the 109 enrolled patients had cranial nerve III palsy. Twenty-five of the 109 patients had cranial nerve IV palsy and 62 of the 109 patients had cranial nerve VI palsy. A cause other than presumed microvascular ischemia was identified in 18 patients (16.5%). The presence of one or more vasculopathic risk factors was significantly associated with presumed microvascular cause. Vasculopathic risk factors were present in 61% of the patients with other causes.

Conclusions: In patients with acute, isolated ocular motor nerve palsies a substantial portion of patients had other causes including neoplasm, giant cell arteritis and brainstem infarction. Brain MRI and laboratory work-up have a role

in the initial evaluation of older patients with isolated, acute ocular motor nerve palsies regardless of whether vascular risk factors are present.

Reviewers comment: The take home story for this multi-center study is that all patients who presented with acute ocular nerve palsies regardless of whether they have underlying microvascular disease should have completed neuro-radiologic imaging.

Reliability of Magnetic Resonance Imaging for the Detection of Hypopituitarism in Children with Optic Nerve Hypoplasia

Raghu H. Ramakrishnaiah, Julie B. Shelton, Charles M. Glasier, Paul H. Phillips, *Ophthalmology* January 2014; 121(1):387-391

This is a study from the Department of Radiology, Arkansas Children's Hospital, and Department of Neuro-Ophthalmology, John A Moran Eye Center, University of Utah.

This is a cross-sectional study of 101 children with clinical optic nerve hypoplasia who underwent magnetic resonance imaging of the brain and orbits and a detailed pediatric endocrinology evaluation.

The purpose of this study is to identify hypopituitarism in children with optic nerve hypoplasia because they are at risk for developmental delays, seizures or death.

The purpose of this study is to determine the reliability of neurohypophyseal abnormalities on magnetic resonance imaging (MRI) for the detection of poor function of the pituitary gland in children with optic nerve hypoplasia.

Main outcome measures: Sensitivity and specificity of MRI findings for the detection of hypopituitarism.

Conclusions: Neurohypophyseal abnormalities on MRI are sensitive and specific indicators of hypopituitarism in children with optic nerve hypoplasia.

Neurohypophyseal abnormalities including absent pituitary infundibulum and ectopic posterior pituitary bright spot occurred in 33 of the 101 children evaluated. Magnetic resonance imaging disclosed neurohypophyseal abnormalities in 27 of the 28 children with hypopituitarism. A normal neurohypophysis occurred in 67 of 73 children with normal endocrinologic function (specificity 92%).

Update in pediatric optic neuritis.

Collinge JE, Sprunger DT. *Curr Opin Ophthalmol.* 2013 Sep;24(5):448-52.

Optic neuritis in children tends to be bilateral (50-75%) and is most commonly caused by inflammation after infection or vaccination. Recent publications suggest that optical coherence tomography (OCT) in children with optic neuritis can be a useful tool to monitor recovery and assess prognosis. MRI of the brain and orbits with fat suppression and lumbar puncture with evaluation of the cerebral spinal fluid (CSF) are standard diagnostic tests performed in children with suspected optic neuritis. Additional studies are recommended by some specialists and include: aquaporin-4 antibodies (neuromyelitis optica or NMO

IgG), antimyelin oligodendrocyte glycoprotein (MOG) and a mri of the spine. There are no trials or guidelines for the treatment of pediatric optic neuritis in contrast to the Optic Neuritis Treatment Trial (ONTT) for adults. Intravenous corticosteroids remain the mainstay of treatment for pediatric optic neuritis. Recent studies report successful treatment of refractory or atypical cases with additional rounds of intravenous corticosteroids, intravenous immunoglobulin (IVIG) and plasmapheresis. Disease-modifying antirheumatic drugs (DMARDs) have been used in adults at risk for developing multiple sclerosis, but no studies have been done in children.

Structural Brain MRI Abnormalities in Pediatric Patients with Migraine. Rocca MA, Messina R, Colombo B, *et al. J Neurology* 2014; 216:350-7.

Morphometric MRI studies in adult patients with migraine have consistently demonstrated atrophy of several gray matter (GM) regions involved in pain processing in adults. The authors explored the regional distribution of GM and white matter (WM) abnormalities in pediatric patients with episodic migraine and their correlations with disease clinical manifestations. MRIs were acquired from 12 pediatric migraine patients and 15 age-matched healthy controls. GM and WM volumetric abnormalities were estimated using voxel-based morphometry ($p < 0.05$, family-wise error corrected). Compared to controls, pediatric migraine patients experienced a significant GM atrophy of several regions of the frontal and temporal lobes which are part of the pain-processing network. They also had an increased volume of the right putamen. The left fusiform gyrus had an increased volume in patients with aura compared to patients without aura and controls, whereas it was significantly atrophied in patients without aura when compared to the other two groups. No abnormalities of WM volume were detected. In migraine patients, regional GM atrophy was not correlated with disease duration and attack frequency, whereas a negative correlation was found between increased volume of the putamen and disease duration ($r = -0.95$, $p < 0.05$). These results show that GM morphometric abnormalities do occur in pediatric patients with migraine. The presence of such abnormalities early in the disease course, and the absence of correlation with patient clinical characteristics suggest that they may represent a phenotypic biomarker of this condition.

Cranial autonomic symptoms in pediatric migraine are the rule, not the exception Gelfand AA, Reider AC, Goadsby PJ. *Neurology* July 30, 2013; 81(5):431-6.

The presence of cranial autonomic symptoms often leads to a misdiagnosis of “sinus headache” in adult migraineurs, leading to unnecessary treatments and delaying appropriate migraine therapy. This cross-sectional study examined the

frequency of cranial autonomic symptoms in pediatric/adolescent patients with migraine at 4 different sites over the course of the study period. Of 125 pediatric migraineurs, 62% had at least one cranial autonomic symptom based on current International Classification of Headache Disorders, second edition (ICHD-II) criteria, and 70% based on proposed ICHD-III criteria. The majority had more than one cranial autonomic symptom and the symptoms tended to be bilateral. Age, sex, laterality of headache, presence of aura, and whether migraine was episodic vs chronic did not influence the likelihood of having cranial autonomic symptoms. The authors concluded that in pediatric/adolescent migraine, the presence of cranial autonomic symptoms appears to be the rule rather than the exception. They recommended that clinicians should be careful to consider migraine when evaluating a child with headache and associated ocular or nasal symptoms so as to avoid giving a misdiagnosis of sinus headache.

Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Friedman DI, Liu GT, and Digre KB. *Neurology* 2013:81.

The pseudotumor cerebri syndrome (PTCS) may be primary (idiopathic intracranial hypertension) or arise from an identifiable secondary cause. Characterization of typical neuroimaging abnormalities, clarification of normal opening pressure in children, and features distinguishing the syndrome of intracranial hypertension without papilledema from intracranial hypertension with papilledema have furthered our understanding of this disorder. The authors propose updated diagnostic criteria for PTCS to incorporate advances and insights into the disorder realized over the past 10 years. In particular, with regard to pediatric patients, the authors suggest the following criteria for diagnosing pseudotumor cerebri syndrome: 1. Papilledema, 2. Normal neurologic examination except for cranial nerve abnormalities, 3. Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion and no abnormal meningeal enhancement on MRI with and without gadolinium and normal MR venogram, 4. Normal CSF composition, 5. Elevated lumbar puncture opening pressure (≥ 280 mm CSF in children). A diagnosis can also be made without papilledema if 2-5 are present with at least three of the following signs: empty sella, flattening of the posterior aspect of the globe, distension of the perioptic subarachnoid space, and transverse venous sinus stenosis.

Failure of stem cell therapy to improve visual acuity in children with optic nerve hypoplasia

Fink C, Garcia-Filion P, and Borchert M J AAPOS October 2013;17:490-493

Anecdotal reports of improvement in visual acuity in patients with optic nerve hypoplasia (ONH) exist, after injection stem cells into the CSF. However, spontaneous visual acuity improvement in patients with ONH has also been

reported. This study evaluated the effectiveness of stem cell therapy improving acuity in children with ONH. It was agreed that 10 subjects, between the ages of 7 and 17 years with ONH, would be identified by a company in China which offers this therapy. A three-year window was decided upon. There would also be a pool of control subjects. Treated subjects would receive stem cells (IV, LP, and retrobulbar), as well as growth factors. The company also added alternative therapies, such as acupuncture, exercise therapy, and functional electrical stimulation, which were not part of the protocol. Only two patients were enrolled during the enrollment period. Slight visual improvements were noted in the two subjects, but the control subjects also had slight visual acuity improvements at the 9-month exam. The company stated they only enrolled two patients because no other patients met the age eligibility criteria. However, this is questionable since the authors of this paper believe there were other patients who received therapy during this time period who did meet inclusion criteria. Since all 4 patients (treated or not) had a slight acuity improvement a learning curve of the ATS protocol may have occurred. Obviously with only 2 subject patients and 2 control patients, not much can be said about treatment effect, but the limited enrollment of study patients during the 3-year period, as well as the addition of other therapies outside the protocol, make treatment claims spurious.

Racial variation in optic nerve head parameters quantified in healthy newborns by handheld spectral domain optical coherence tomography

Allingham MJ, Cabrera MT, O'Connell RV, et al J AAPOS October 2013; 17:501-506

There are no reports of OCT characterized optic nerve head (ONH) parameters in healthy neonates. This was a prospective, observational study using handheld SD-OCT imaging. 58 infants were included of which 24 were male, and about 1/3 were white, Hispanic or African-American. Five neonates had elevation of the ONH that was not noted on dilated fundus exam. Two subjects showed macular abnormalities (1 cystoid macular edema and 1 subfoveal fluid). Of these 7 patients with abnormalities 3 were lost to followup. Of the remaining cases of ONH elevation or CME all had resolved by 3 months of age., except for the one infant with bilateral ONH elevation. 95% of infants had evidence of a persistent Cloquet's canal. For white, black and Hispanic newborns, the mean vertical disk diameter was 1.29 +/- 0.15, 1.38 +/- 0.14, and 1.38 +/- 0.14 mm respectively. Mean vertical cup diameter was 0.44 +/- 0.15mm, 0.56 +/- 0.23mm, and 0.46 +/- 0.30mm respectively. Mean vertical cup/disk ratio was 0.34 +/- 0.10, 0.40 +/- 0.17 and 0.33 +/- 0.20mm respectively. There was no correlation between C/D ratio and birth weight. Racial differences showed trends but were not statistically significantly different. The infants in this study were evaluated with a handheld device with no sedation, which could affect results. Eye to eye comparisons in the same subject could not be analyzed because data could only be obtained in one eye in 36% of infants.

Using autofluorescence to detect optic nerve head drusen in children

Gili P, Flores-Rodriguez P, Yanguela J, et al
J AAPOS December 2013; 17:568-571

Optic nerve head drusen (ONHD) in children are often hidden. Ocular ultrasonography is considered the most reliable way to diagnose (ONHD). This study evaluated the usefulness of fundus autofluorescence imaging in diagnosis of ONHD. Consecutive patients over a 7-year period with possible pseudopapilledema were included. A blue exciter filter and greenish-yellow barrier filter were used to capture successive images with increasing glash power until retinal vessels appeared black. By this point, whitish spots indicating ONHD indicated a positive test. Twenty-four patients with pseudopapilledema were included. B-scan U/S confirmed ONHD in 32 eyes of 18 patients (14 were OU). 26/32 of the positive B-scans were associated with buried drusen. Autofluorescence was positive in 30/32 eyes (94%. 24/26 buried drusen and 6/6 visible ONHD). Interobserver agreement was excellent. This modality appears to have a role in diagnosis.

Eye Movement Alterations During Reading in Patients With Early Alzheimer Disease. Gerardo Fernández, Pablo Mandolesi, Nora P. Rotstein, Oscar Colombo, Osvaldo Agamennoni, and Luis E. Politi. *IOVS December 2013 54:8345-8352.*

Purpose. Eye movements follow a reproducible pattern during normal reading. Each eye movement ends up in a fixation point, which allows the brain to process the incoming information and to program the following saccade. Alzheimer disease (AD) produces eye movement abnormalities and disturbances in reading. In this work, we investigated whether eye movement alterations during reading might be already present at very early stages of the disease.

Methods. Twenty female and male adult patients with the diagnosis of probable AD and 20 age-matched individuals with no evidence of cognitive decline participated in the study. Participants were seated in front of a 20-inch LCD monitor and single sentences were presented on it. Eye movements were recorded with an eye tracker, with a sampling rate of 1000 Hz and an eye position resolution of 20 arc seconds.

Results. Analysis of eye movements during reading revealed that patients with early AD decreased the amount of words with only one fixation, increased their total number of first- and second-pass fixations, the amount of saccade regressions and the number of words skipped, compared with healthy individuals (controls). They also reduced the size of outgoing saccades, simultaneously increasing fixation duration.

Conclusions. The present study shows that patients with mild AD evidenced marked alterations in eye movement behavior during reading, even at early

stages of the disease. Hence, evaluation of eye movement behavior during reading might provide a useful tool for a more precise early diagnosis of AD and for dynamical monitoring of the pathology.

Synopsis: Eye movements during reading follow a reproducible pattern in healthy subjects. We show here that patients at early stages of Alzheimer disease display gross alterations in this pattern. These findings might contribute to early diagnosis of this disease.

6. NYSTAGMUS

Reading Performance in Infantile Nystagmus

Niraj Barot, Rebecca J. McLean, Irene Gottlob, Frank A. Proudlock,
Ophthalmology June 2013;120:1232-1238

This is a prospective cross-sectional study involving 71 participants with infantile nystagmus (37 idiopathic, 34 with albinism). These 71 participants were compared with 20 age-matched controls. The purpose of the study was to characterize reading deficits in infantile nystagmus to determine optimal font size for reading in infantile nystagmus and investigate whether visual acuity and severity of nystagmus are good indicators of reading performance in infantile nystagmus.

Methods: Reading performance was assessed using Radner reading charts and was compared with near logarithm of minimal angle resolution (logMAR) visual acuity (VA), nystagmus intensity, and foveation characteristics quantified by using eye movement recordings. The eXpanded Nystagmus Acuity Function (XNAF) was used to evaluate foveation.

Conclusions: Maximum reading speeds can be near normal in infantile nystagmus when optimal font sizes are provided even in individuals with poor visual acuity or intense nystagmus. However, reading performance in infantile nystagmus is acuity sensitive to font size limitations. Font sizes for optimal reading speeds in infantile nystagmus may be as much as 6 logMAR lines worse than the near visual acuity.

Comments: This article emphasized the importance of teacher consultants for visually impaired (TCVI) and evaluation of all children with nystagmus regardless of etiology. Furthermore, ophthalmologists should test reading in their office to see what font size is the most affective in optimizing reading proficiency. These findings should be communicated with the teacher consultant who will make the ultimate decision as the most appropriate font size.

Anatomic Features and Function of the Macula and Outcome of Surgical Tenotomy and Reattachment in Achiasma

Avery H. Weiss, James O. Phillips, John P. Kelly, *Ophthalmology* July 2013;120:1469-1475

Achiasma is a rare condition characterized by failure of the nasal retinofugal fibers to decussate at the optic chiasm. As a result, nasal and temporal retinofugal fibers of each eye are routed to the ipsilateral visual cortex. Monocular visual fields are normal in spatial extent, suggesting that each brain hemisphere maps the entire visual field.

This is a case series performed in Seattle, Washington. It consists of 2 children with isolated achiasma. Ophthalmologic examinations, brain magnetic resonance imaging, full field and multi-focal electroretinography (MERG), visual evoked potentials, spectral-domain optical coherence tomography (OCT), and eye-movement recordings were performed. Bilateral tenotomy and resection was performed in 1 patient.

Visual acuity before and after surgery, macular anatomic features and function, and eye velocity before and after tenotomy and replacement (T&R) surgery were considered in the main outcome measures.

Conclusions: The findings that the macula is normal and achiasma suggest that reduced central acuity is the result of retinal image motion from nystagmus. Two-muscle tenotomy and replacement (T&R) procedures reduce horizontal retinal image motion and can improve visual acuity in achiasma or patients with infantile nystagmus.

Comments: This is an article supportive of tenotomy and replacement surgery not only achiasma but for patients with infantile nystagmus. The eye movement recordings can be seen on page 1471. It should be mentioned that the conclusion and study are based on the evaluation of 2 patients, but surgery was only performed on 1 of the patients.

Investigating the Relationship Between Foveal Morphology and Refractive Error in a Population With Infantile Nystagmus Syndrome

Healey N, McLoone E, Mahon G, Jackson AJ, Saunders KJ, McClelland JF.. *Invest Ophthalmol Vis Sci*. April 2013;54:2934–2939.

The authors explored associations between refractive error and foveal hypoplasia in infantile nystagmus syndrome (INS). 50 participants with INS (albinism n = 33, nonalbinism infantile nystagmus [NAIN] n=17) aged 4 to 48 years were recruited for study. Cycloplegic refractive error and logMAR acuity were obtained. Spherical equivalent (SER), most ametropic meridian (MAM) refractive error, and better eye acuity (VA) were used for analyses. SD-OCT was used to obtain foveal scans, which were graded using the Foveal Hypoplasia Grading Scale.

Participants with more severe foveal hypoplasia had significantly higher MAMs and SERs ($P = 0.005$ and $P = 0.008$, respectively). There were no statistically significant associations between foveal hypoplasia and cylindrical refractive error ($P = 0.144$). Analyses demonstrated significant differences between participants with albinism or

NAIN in terms of SER and MAM ($P = 0.001$). There were no statistically significant differences between astigmatic errors between participants with albinism and NAIN. Controlling for the effects of albinism, results demonstrated no significant associations between SER, and MAM and foveal hypoplasia (partial correlation $P > 0.05$). Poorer visual acuity was associated statistically significantly with more severe foveal hypoplasia ($P = 0.001$) and with a diagnosis of albinism ($P = 0.001$). Increasing severity of foveal hypoplasia is associated with poorer VA, reflecting reduced cone density in INS. Individuals with INS also demonstrate a significant association between more severe foveal hypoplasia and increasing hyperopia. However, in the absence of albinism, there is no significant relation between refractive outcome and degree of foveal hypoplasia, suggesting that foveal mal-development in isolation does not impair the emmetropization process.

Visual Deprivation and Foveation Characteristics Both Underlie Visual Acuity Deficits in Idiopathic Infantile Nystagmus

Felius J, Muhanna ZA. Invest Ophthalmol Vis Sci. May 2013; 54:3520–3525.

Previously, the attained level of visual acuity (VA) was modeled in terms of foveation characteristics of the nystagmus waveform, that is, the patient's fixation stability at the time of testing. The authors present evidence for an additional component of VA loss associated with the (partial) binocular visual deprivation experienced during the sensitive period of visual development. The premise of their approach is that pendular nystagmus waveforms are typically associated with poor foveation characteristics and thus may lead to binocular visual deprivation, whereas jerk-like waveforms with extended foveation periods usually have much better foveation. Binocular grating VA and eye movement recordings were obtained from 56 children with IIN and documented waveform history from longitudinal visits. VA was modeled in terms of foveation characteristics (Nystagmus Optimal Fixation Function, NOFF) and of each child's time course of pendular nystagmus during the sensitive period. Mean VA was $0.25 + 0.19 \log\text{MAR}$ below age norms, and the mean foveation fraction was 0.28 ($\text{NOFF} - 0.9 + 2.3 \log\text{its}$). Nystagmus had a median onset at age 3 months and transitioned to waveforms with extended foveation at age 35 months. The best fit of the model showed the following: Poor foveation (0.01 foveation fraction) was associated with $0.60 \log\text{MAR}$ acuity deficit; this deficit gradually reduced to zero for increasingly better foveation; pendular nystagmus during each decile of the sensitive period was associated with an additional $0.022 \log\text{MAR}$ deficit. The model accounted for 57% of the variance in VA and provided a better fit than either component alone.

VA in IIN is explained better if, besides the child's foveation characteristics, an additional component is taken into account representing the nystagmus induced visual deprivation during the sensitive period. These findings may have implications for the timing of treatment decisions in children with IIN.

Dalfampridine in patients with downbeat nystagmus—an

observational study Classen J, Feil K, Bardins S, et al. Journal of Neurology August 2013; 260(8):1992-6.

The authors investigated the effects of dalfampridine, the sustained-release form of 4-aminopyridine, on slow phase velocity (SPV) and visual acuity (VA) in patients with downbeat nystagmus (DBN) and the side effects of the drug. In this proof-of-principle observational study, ten patients received dalfampridine 10 mg bid for 2 weeks. Recordings were conducted at baseline, 180 min after first administration, after 2 weeks of treatment and after 4 weeks of wash-out. Mean SPV decreased from a baseline of $2.12 \text{ deg/s} \pm 1.72$ (mean \pm SD) to $0.51 \text{ deg/s} \pm 1.00$ 180 min after first administration of dalfampridine 10 mg and to $0.89 \text{ deg/s} \pm 0.75$ after 2 weeks of treatment with dalfampridine ($p < 0.05$; post hoc both: $p < 0.05$). After a wash-out period of 1 week, mean SPV increased to $2.30 \text{ deg/s} \pm 1.6$ ($p < 0.05$; post hoc both: $p < 0.05$). The VA significantly improved during treatment with dalfampridine. Also, 50 % of patients did not report any side effects. The most common reported side effects were abdominal discomfort and dizziness. The authors concluded that Dalfampridine is an effective treatment for DBN in terms of SPV and that it was well-tolerated in all patients.

Effect of Four Horizontal Rectus Muscle Tenotomy and Replacement (TAR) Alone and in Combination with Recessions for Strabismus, on Visual Function and Eye Movements in Patients with Infantile Nystagmus Syndrome (INS) Without Abnormal Head Posture (AHP).

Mohammad Reza Akbari, Marjan Akbari-Kamrani, Arman Mohseni, Alireza Keshtkar Jafari, et al *Binocular Vision and Strabology Quarterly, Simms-Romano's*. 2013;28(4):211-21.

This study compares the effect of four horizontal rectus muscle tenotomy and replacement (TAR) alone or 2 muscle TAR in combination with bilateral horizontal muscle recession for strabismus in patients with infantile nystagmus syndrome (INS) without abnormal head posture (AHP). This was a prospective interventional case series of 14 patients. Subjects were older than 18 years of age with INS and best corrected visual acuity of 20/400-20/30. Outcomes were evaluated with best corrected visual acuity and nystagmus intensity as evaluated by eye movement recordings pre and post operatively. Nystagmus amplitude and velocity decreased 28.7% with 4 muscle TAR and 21.9% with 2 muscle TAR paired with strabismus recessions. Visual outcome of 2 muscle TAR with recessions was less when compared with 4 muscle TAR. The authors conclude that 4 muscle TAR and 2 muscle TAR with strabismus recessions improve both visual function and eye movement recordings in INS. The authors found better results in more visually impaired patients.

Potential of Handheld Optical Coherence Tomography to Determine Cause of Infantile Nystagmus in Children by Using Foveal Morphology

Helena Lee, Viral Sheth, Mashal Bibi, Gail Maconachie, *Ophthalmology* December 2013; 120(12):2714-2724

This is a prospective, case-control study designed to investigate the feasibility of handheld ultra-high-resolution spectral-domain optical coherence tomography

(SD-OCT) in young children with nystagmus, to determine its sensitivity and specificity in classifying foveal abnormalities. There were a total of 50 patients with nystagmus and 50 healthy control subjects with a mean age of 3.2 years were studied.

Conclusions: This study demonstrates excellent feasibility of HH SC-OCT in the diagnosis of conditions associated with infantile nystagmus. The HH SC-OCT also provided a good classification of foveal abnormalities. The HH SC-OCT in early childhood could facilitate focused investigators and earlier diagnosis. This may have some value in time sensitive treatment such as gene therapy.

This study was performed by the Ophthalmology Group, University of Leicester, Leicester Royal Infirmary, Leicester, United Kingdom

Visual Acuity Deficits in Children with Nystagmus and Down Syndrome

J. Felius, C. Beauchamp, D. Stager, Sr. Am J of Ophthal Feb 2014; 157(2): 458-462.

This was a prospective cross sectional study with 16 children with Down's Syndrome and nystagmus. 93 age matched children with infantile nystagmus were the control group. Binocular teller acuity cards and eye movement recordings were used to measure the patients. This study found a 4 line difference between the two groups of patients. It appears nystagmus accounts for some of the visual decrease in Down's patients, but can not account for all of the visual decrease.

7. PREMATURITY

Congenital Nasolacrimal Duct Obstruction in Premature Children

Silvia Helena Tavares Lorena, João Amaro Ferrari Silva, Marinho Jorge Scarpi, J Pediatr Ophthalmol Strabismus 2013; 50:239-244 (July/August)

The purpose of this study was to compare premature babies to full term babies and to determine the incidence of congenital nasolacrimal duct obstruction (CNLDO). A retrospective chart review was performed that evaluated 400 infants – 200 premature and 200 full term infants. Of the 400 infants, 53 NLD in 32 premature children and 9 NLD in 7 full term infants were diagnosed with CNLDO. The study concluded that there was a higher incidence of CNLDO in premature infants than in full term infants.

RetCam image analysis of the optic disc in premature infants.

J.W. Park, S.W. Park, H. Heo. Eye (Lond). 2013 Oct;27(10):1137-41

Doctors analyzed images from ninety-seven premature infants to those in correlation with parents with optic nerve with gestational age or birth weight. They found that over 70% of premature infants had a cup to disc ratio 0.15 or less. They found that there was no correlation between birth weight and gestational age with appearance with the optic disc. The disc appearance were not followed longitudinally. The appearance of the optic disc could not predict gestational age in this group of patients.

Preterm Birth and Later Retinal Detachment A Population-Based Cohort Study of More than 3 Million Children and Young Adults

Anna-Karin E Bonamy, Gerd Holmstrom, Olof Stephansson, Jonas F. Ludvigsson, *Ophthalmology* November 2013; 120(11):2278-2285

This is a nationwide Swedish cohort study based on population registries in at least 4 different cities and Sweden. The objective of this study is ophthalmologic complications after preterm birth.

Participants: Of 3,423,697 subjects born in Sweden between 1987 and 2008. Of this number, 1,271,725 were born between 1973 and 1986 before the national screening program for retinopathy of prematurity started and 2,151,972 were born between 1987 and 2008. The participants were followed from 1 year of age until 2009.

Methods: Unadjusted and adjusted hazard ratios (HRs) for retinal detachment were calculated using Cox proportional hazards regression.

Main outcome measures: Incident retinal detachment, as defined by a diagnosis in the Swedish Patient Register. This involved (both inpatient and hospital-based outpatient data).

Results: During median follow-up 17.4 years, 1,749 subjects were diagnosed with retinal detachment. Among the 188,852 subjects born prematurely (that is less than 37 week gestation) there were 124 cases of retinal detachment. The adjusted hazard ratio for retinal detachment after an extremely premature birth (less than 28 weeks gestation) was 19.2. The corresponding hazard ratio in subjects born between 28 and 31 weeks was only 4.32. Moderate preterm birth (32-36 weeks) was not associated with any increased risk for retinal detachment.

Conclusions: Birth before 32 weeks of gestation is associated with a substantially increased relative risk of retinal detachment, particularly for those infants born at less than 28 week gestation. These findings may have implications for ophthalmologic follow-up in children and adults born very prematurely.

8..ROP

Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: Findings at 4 to 6 years of age Quinn GE, Dobson V, Davitt BV, et al J AAPOS April 2013;17:124-128

Children who participated in the ETROP study had their refractive errors recorded between ages 4 and 6. There were 401 enrolled infants, all of whom developed prethreshold ROP in one or both eyes. Infants were either treated at an earlier stage of ROP (ET) or conventionally managed (CM) with treatment or not if regression occurred. Myopia and high myopia were defined as spherical equivalent of ≥ -0.25 D of myopia and ≥ -5.00 D of myopia respectively. Both ET and CM patients had $>60\%$ myopia and more than a third of eyes displayed high myopia. In the CM group, $>75\%$ of infants who required treatment developed myopia, but $<50\%$ of infants whose ROP regressed and did not require treatment developed myopia. Rates of myopia increased early in life, but stabilized at the 4-, 5-, and 6-year examinations. There was no difference in median monthly rate of change between ET and CM eyes. More than 20% of infants had myopia > -8.00 D by age 4 years. Based on this study, patients who required treatment for their ROP had higher rates of myopia, but there was no difference between the ET and CM groups. Most of the myopic progression occurred by age 3 years. Plus disease and the zone of the ROP also affected prevalence of myopia and high myopia. This information is helpful when counseling patients on risks of myopia and the course of progression.

Clinical characteristics of children with severe visual impairment but favorable retinal structural outcomes from the Early Treatment for Retinopathy of Prematurity (ETROP) study

Siatkowski RM, Good WV, Summers CG, et al J AAPOS April 2013;17:129-134

This study describes visual function abnormalities in children who were enrolled in ETROP, with visual impairment despite relatively normal ocular structure. This cohort was selected from children who had completed the 6-year examination. Evaluations occurred for 342 of the 370 surviving children. Thirty-nine (11%) met inclusion criteria. Normal bilateral fundus exams were present in 25/39 (64%). Macular ectopia or straightening of temporal vessels was seen in one or both eyes of 11 patients. One patient had a stage 4B detachment in one eye. Eighteen children had optic atrophy in one or both eyes. Three patients had isolated increased cupping of the optic disk, and another nine had cupping associated with optic atrophy. Thirty children had nystagmus. About half of those with nystagmus had optic atrophy and half did not. Of the 39 included patients, 25 had definite CVI, 12 had combined anterior and posterior pathway disease, and 2 had indeterminate cause of visual loss. Optic atrophy is not specific for subcortical/cortical visual loss and is often present in ROP and other retinal disease. Hypoxic prenatal brain damage or damage to the lateral geniculate nucleus can cause optic atrophy. PVL can cause nonglaucomatous cupping of the optic disk. Many PVL patients often have nystagmus as well, which may indicate combined or isolated posterior visual

pathway disease. The authors found that postgeniculate disease as the only or main factor to cause visual impairment was uncommon (25/342). Despite occurring infrequently, it is still a higher rate than that seen in the CRYO-ROP study, which may be due to increased survival of younger infants in the current study. Manifest nystagmus can be seen in the setting of anterior visual pathway disease or with posterior visual pathway disease. Therefore manifest nystagmus in isolation, cannot help localize the etiology of visual loss. Also, the absence of cupping or optic atrophy does not rule out posterior pathway involvement as the cause of decreased visual acuity. Combining an evaluation of neurologic status, developmental status and visual function can help determine possible posterior pathway involvement in vision loss.

Comparison of fentanyl and morphine in laser surgery for retinopathy of prematurity

Orge FH, Lee TJ, Walsh M, and Gordon K J Aapos April 2013;17:135-139

There is no consensus as to the best choice of anesthesia for laser photocoagulation in the treatment of ROP. Fentanyl's action is more rapid and briefer with better CNS penetration. It is more potent and can cause adverse respiratory effects. This study provides pilot data on intravenous sedation during ROP laser ablation. The medical records of consecutive preterm neonates undergoing laser treatment of ROP over a 3-year period were reviewed retrospectively. Morphine was used for the first two years and then fentanyl was substituted. The primary outcome was rate of change in ventilation status after anesthesia administration during ROP surgery. A total of 40 neonates (53 treatments) were reviewed and 35 treatments were analyzed (no more than one per infant). Seventeen subjects were in the morphine group and 18 were in the fentanyl group. The rate of any change in ventilation status, as well as the rate of change in ventilation status greater than one level, was greater in the morphine group. More patients (5/17) in the Morphine group experienced any worsening of ventilation status than in the Fentanyl group (1/18). Ventilation status declined two or more levels in 3/17 in the Morphine group and 0/18 in the Fentanyl group. None of these differences were statistically significant because of the small group sizes. The Morphine group also had 1 episode of temperature instability, 6 apneic events, and 7 bradycardic events, versus 0, 2, and 5 respectively. Fentanyl caused slightly more desaturation events (12 versus 9). True change in ventilation status of one level or greater, was 5.30 times more common in the Morphine group. Overall there was a trend towards fewer adverse events with Fentanyl, but the sample sizes are small. Also the two agents were used sequentially and there may have been other factors in the NICU that changed as well. A larger prospective study would be needed to truly determine whether the use of one of these agents is less likely to cause side effects.

Patent Ductus Arteriosus and Indomethacin Treatment as Independent Risk Factors for Plus Disease in Retinopathy of Prematurity

Irena Tsui, Edward Ebani, Jamie B. Rosenberg, Juan Lin, Robert M. Angert, Umar Mian, J Pediatr Ophthalmol Strabismus 2013; 50:88-92 (March/April)

The authors discuss factors that may be related to causing plus disease or retinopathy of prematurity requiring disease. A retrospective, cross-sectional study evaluated patients who were on indomethacin and had patent ductus arteriosus. The main outcome measure was increased rate of plus disease or ROP requiring treatment. The study concluded that PDA and indomethacin were associated with plus disease and ROP requiring treatment but this was not significant after adjusting for other risk factors. PDA was strongly related to bronchopulmonary dysplasia and blood transfusions which may explain the results.

Intravitreal Bevacizumab for Retinopathy of Prematurity: Refractive Error Results

Bjorn C. Harder, Frank C. Schlichtenbrede, Stefan Von Baltz, Waldemar Jendritza et al. Am J Ophthalmol June 2013; 155 (6): pg. 1119- 1124.

This retrospective study compared babies with ROP treated with laser to those babies treated with intravitreal Bevacizumab. The outcomes of treatment were reported as well as refractive outcomes after the ROP regressed. The study group consisted of 23 eyes of 12 children with acute posterior stage of ROP or stage 3+ with neovascularization in 5 adjacent sectors. These children received an injection of either 0.375 mg or 0.625 mg (depending on treating physician). The control group consisted of 26 eyes of 13 children with similar treatment criteria. These children were monitored for one year. No children in the study group required a second injection. One child in the control group received intravitreal Bevacizumab and another child developed a partial retinal detachment. At the end of the follow up period, refractive error was evaluated. The study group showed a mean refractive error of -1.04 ± 4.24 diopters versus the control group with a mean refractive error of -4.41 ± 5.50 diopters. Refractive astigmatism was monitored as well with the study group showing a mean of -1.0 ± 1.04 diopters and the control showing 1.82 ± 1.41 diopters.

Retinopathy of Prematurity in Extremely Low Birth Weight Infants in Turkey

Selim Demir, Osman Sayin, Canan Aygün, Hüseyin Ortak, et al J Pediatr Ophthalmol Strabismus 2013; 50:229-233 (July/August)

The purpose of the study was to determine the incidence of retinopathy of prematurity in extremely low birth weight infants (less than 1000g) in Turkey. 225 infants were found to have ELBW from January 2003 to September 2011. Low birth weight infants have a higher incidence of retinopathy of prematurity (ROP). With advances in neonatology, ELBW infants are surviving and as such, screening, diagnosis and treatment of ROP is even more important now.

The effectiveness of policy changes designed to increase the attendance rate for outpatient retinopathy of prematurity (ROP) screening examinations

Barry GP, Tauber K, Emmanuel G, et al *J AAPOS* June 2013 17:3;296-300

The authors reviewed records of consecutive neonatal intensive care unit patients at one hospital, before and after the implementation of policy changes, to determine attendance rates for the first outpatient appointment after discharge. The policy changes included education forms, streamlined scheduling, and a patient log. Attendance on the recommended date was increased from 22/52 (42%) prior to policy change, to 46/57 (81%) after policy implementation. The number of patients who met the criteria for conclusion of the acute retinal screening examination also improved significantly, from 90% pre- to 100% post-implementation. Exclusion criteria included fetal demise, hospital transfer, NICU discharge before first ROP screening, and completion of ROP screening as an in-patient. The groups had similar rates of mean round-trip travel for the appointments, and percentage of infants whose surname changed after discharge. Because multiple intensive policies were instituted simultaneously, it cannot be determined which of these policies were most effective. This was a retrospective study and the patients in the post-implementation arm of the study were all enrolled during the first year of the new policy changes. It is possible that over time the implementation of the policy and enthusiasm for its enforcement will wane, and results might worsen. However, ROP examination follow-up compliance is critical, and the authors are to be commended for attempts to increase parental compliance.

Letter to the editor: mechanism and management of retinopathy of prematurity.

Rajesh Rao; Brian Diouhy *N Engl J Med*; March 2013; 368(12):1161

The authors urge additional study of the VEGF-fibronectin pathway as a potential target for medical and surgical therapy for patients with ROP. Cleavage of fibronectin induces posterior vitreous detachment, which decreases vitreoretinal traction and reduces the need for vitreoretinal surgery. Use of autologous plasmin enzyme, which cleaves fibronectin, during vitreoretinal surgery was associated with improved outcomes in stage 4 and 5 ROP. Ocriplasmin was recently approved by the FDA as an agent to cleave fibronectin and modulate the vitreoretinal interface. We may hear about ocriplasmin in the treatment of stage 4 and 5 ROP in the near future.

Letter to the editor: mechanism and management of retinopathy of prematurity.

Bonnie Jasany; Ruchi Nanavati; Nandkishor Kabra *N Engl J Med*; March 2013; 368(12):1161-2

The authors discuss the growing interest in propranolol as a treatment for stage 2 retinopathy of prematurity. The interest in this drug arose from observations that it may reduce VEGF levels in infantile hemangiomas. Mouse models have not shown

promise for propranolol as an ROP drug, but there is a human trial currently ongoing (Propranolol in Newborns with Retinopathy of Prematurity: PROP-ROP).

Alternative methods for the screening of retinopathy of prematurity: binocular indirect ophthalmoscopy vs wide-field digital retinal imaging

M A Sekeroglu; E Hekimoglu; H T Sekeroglu; U Arslan *Eye*; September 2013; 27(9):1053–1057

The study compared wide-field digital retinal imaging using the Retcam shuttle with binocular indirect ophthalmoscopy for retinopathy of prematurity (ROP) screening. 58 infants of gestational age 24 to 32 weeks (median 30 weeks) and birth weight 760 to 2000 g (median 1335 g) in a Turkish hospital were enrolled in the study. They had a total of 124 bilateral eye examinations performed. Two ophthalmologists experienced in ROP exams performed the exams: one did the indirect ophthalmoscopy with scleral depression, whereas the other (masked to the results of indirect ophthalmoscopy) performed the imaging. The authors calculated the sensitivity and specificity of wide-field digital imaging, compared to the “gold standard” indirect ophthalmoscopy in the detection of any stage ROP and treatment requiring ROP. The sensitivity for any stage ROP was 58.6 and for treatment requiring ROP was 100%. The specificity was 100% for any stage ROP and for treatment requiring ROP, meaning that the wide-field digital retinal imaging did not “overcall” ROP. This study showed that wide field retinal imaging was excellent for the diagnosis of severe and treatment-requiring ROP. However, it was suboptimal for detecting any ROP because of difficulty imaging the periphery, which becomes problematic in terms of deciding when to terminate ROP screening. A potential statistical critique of the study is using the individual eye, rather than the patient, as a unit of analysis. Another limitation is that an experienced ophthalmologist acquired the images, and perhaps acquired better images than would be acquired by a technician. One of the purported benefits of wide field digital retinal imaging is having non-ophthalmologists screen babies in settings with insufficient ophthalmologist screeners.

Posterior to the ridge laser treatment for severe stage 3 retinopathy of prematurity

A L Ells; G A Gole; P Lloyd Hildebrand; A Ingram; et al. *Eye*. April 2013; 27(4):525-30

The authors report a case series from Alberta Children’s Hospital in which additional laser treatment, called ‘posterior laser’, was delivered posterior to the neovascular ridge, for eyes with severe stage 3 ROP in zone II. Eighteen eyes of 11 infants were treated with posterior laser. These were babies with mean birth weight of 688 grams (552-930 g) and mean gestational age of 24 weeks (23-28). Fourteen of these eighteen laser treatments were performed after standard anterior laser had failed, and four were performed as a primary treatment. The authors did not specify why this was performed as primary treatment in four eyes. Sixteen of the eighteen treated eyes had regression of the neovascular ridge, and two eyes went on to stage 4A detachments requiring vitrectomy. The authors presented morphological criteria for

posterior laser treatment, including thick stage 3 in four confluent temporal clock hours, but acknowledge that the morphological criteria have not been validated. Studies are necessary in which a control arm receives standard anterior laser treatment.

Astigmatism and biometric optic components of diode laser-treated threshold retinopathy of prematurity at 9 years of age

C-S Yang; A-G Wang; Y-F Shih; W-M Hsu *Eye*. March 2013;27(3):374-81.

The study assessed the prevalence of astigmatism and described ocular biometry among nine year-old children who had received diode laser treatment for threshold ROP as neonates. 24 children (46 eyes) were included in the study. They underwent cycloplegic refraction using an autorefractor, keratometry, and A scan ultrasound biometry. Their refractive errors and biometric data were compared with data obtained from a national survey of full-term age-matched controls.

The laser-treated eyes had a mean astigmatism of 3.47 D, whereas control eyes had 0.08 ± 0.90 D ($P < 0.001$). Laser-treated eyes had a mean spherical equivalent of -4.49 D, whereas control eyes had -0.44 ± 1.48 D ($P < 0.001$). 50% of the laser-treated eyes had high astigmatism (>3.0 D). Most laser-treated astigmatic eyes (97.7%) showed with-the-rule astigmatism, with the mean plus cylinder axis at 89 degrees. The astigmatism in the refraction was highly correlated with the corneal astigmatism. The corneas were significantly steeper vertically ($P = 0.003$) and flatter horizontally ($P = 0.031$) in eyes with laser-treated ROP when compared with age-matched full-term controls. The eyes with laser-treated ROP also show significantly thicker lens (3.93 mm) and shallower anterior chamber depth (ACD; 2.92 mm) than full-term controls ($P < 0.001$).

The authors conclude that there is a higher prevalence and greater magnitude of astigmatism in eyes with laser-treated threshold ROP compared with full-term controls, due to vertical corneal steepening. They recommend continued follow up of ROP treated children to detect amblyogenic refractive errors.

Need for Revised Screening Protocol for Early Detection of Retinopathy of Prematurity in Infants Born Before 25 Weeks

In Reply. Michael P. Blair, Michael J. Shapiro, *JAMA Ophthalmol*. April 2013;131(4):546-547.

The authors reiterate that the aim of their study was to describe reactivation patterns and progression to RD after the 54 week BEAT-ROP endpoint. Treatment is suggested when plus disease returns or extraretinal fibrovascular tissue growth is seen, either posteriorly or anteriorly. Additionally, to reduce the follow-up burden and prevent late reactivation, the authors recommend laser treatment of persistent avascular retina past 60 weeks' postmenstrual age since one cannot predict which eyes may reactivate months or years later.

Recurrence of Retinopathy of Prematurity Following Bevacizumab Monotherapy: Is It Only the Tip of the Iceberg?

Kamiar Mireskandari, Gillian G. W. Adams, Nasrin N. Tehrani JAMA Ophthalmol. April 2013;131(4):544-545.

Comment on Berrocal and Moshfeghi's paper on late recurrence of ROP after Avastin injection. Their average time to recurrence after injection was up to 35 weeks). In BEAT_ROP, the endpoint was 55 weeks PMA. This endpoint needs to be extended. However in Berrocal study, questions about the study patients, a 32 week larger infant who developed APROP and did poorly. The definition of recurrence as not just ROP.

Only complete vascularization to the ora and no active disease can be considered successful.

Plus Disease in Retinopathy of Prematurity Qualitative Analysis of Diagnostic Process by Experts

Nina J. Hewing, David R. Kaufman, R. V. Paul Chan, Michael F. Chiang, JAMA Ophthalmol. August 2013;131(8):1026-1032.

Plus disease, the most significant diagnostic finding in defining severe treatment - requiring ROP, has definable clinical features, but diagnostic consistency among practitioners is a problem. This study examines the cognitive process 6 experts used in their analysis of infants with Plus, pre-Plus or no Plus disease. The experts were asked to use a "think out loud" model and were videotaped describing their reasoning. They also were asked the type and location of anatomical details, such as arterial and venous dilation and tortuosity, which contributed to their decision making. The study found that experts differed in their reasoning process, retinal features which were focused on, and interpretation of the same features.

Bilateral Effect of Unilateral Bevacizumab Injection In Retinopathy of Prematurity

Cagatay Karaca, Ayse Ozturk Oner, Ertugrul Mirza, Osman Ahmet Polat, et.al. JAMA Ophthalmol. August 2013;131(8):1099-1101.

The authors describe 4 infants with aggressive posterior ROP who were administered intravitreal bevacizumab 0.625mg in one eye and whose Plus disease and extraretinal neovascularization regressed significantly in the contralateral uninjected eye. All uninjected eyes eventually received laser ablation to the avascular retina since the response to bevacizumab was insufficient to halt disease activity sufficiently. The authors highlight that this anti-VEGF agent must cross the blood retinal barrier since there were visible effects in the contralateral uninjected eye. Other studies demonstrate detectable serum levels of bevacizumab after unilateral or bilateral intravitreal injection, as well as depressed serum levels of VEGF. Systemic effects on the developing vasculature of other organs can only be speculated, but serve as a cautionary tale in the use of this powerful agent, which suppresses vascular activity in the retina and probably beyond.

High-flow nasal cannulae in very preterm infants after extubation.

BJ Manle, LS Owens, LW Doyle, et al.

N Engl J Med. October 2013; 369(15):1425-33.

Pediatric ophthalmologists performing retinopathy of prematurity exams may struggle with the logistics of performing an examination on a baby receiving continuous positive airway pressure (CPAP). This study was a multicenter, randomized, noninferiority trial that assigned 303 very preterm infants to receive treatment with either high-flow nasal cannulae or nasal CPAP after extubation. The primary outcome was treatment failure within 7 days. The use of high-flow nasal cannulae was noninferior to the use of nasal CPAP, but the result was close to the preset 20% margin of noninferiority.

CPAP can cause nasal trauma, and it adds some challenges to performing ROP screening. Noninferiority, however, may be too low of a bar to change neonatal practice from CPAP to high flow nasal cannulae.

Choroidal Thickness in Patients With a History

of Retinopathy of Prematurity Wei-ChiWu; Chia-Pang Shih, Nan-KaiWang, Reyin Lien, et.al. *JAMA Ophthalmol.* 2013;131(11):1451-1458. November 2013

The authors postulate that the cause of visual deficits in children with retinopathy of prematurity (ROP) is not fully understood. The role of the choroid in ROP is not understood and this study sought to correlate choroidal thickness with visual function. The study design involved a cross sectional study of patients age 6 to 14 years old with a normal posterior pole who either had threshold ROP and received treatment and those with regressed ROP who never received treatment. Outcome measures included visual acuity and optical components and measurement of choroidal thickness by optical coherence tomography (OCT). Forty nine patients were studied. Choroidal thickness is thinner in patients with threshold ROP compared with the patients with spontaneously regressed ROP. A thinner choroid is associated with worse vision in these patients. This study might imply the association of choroid circulation with ROP.

Noncontact High-Resolution Ultra-Wide-Field Oral Fluorescein Angiography in Premature Infants With Retinopathy of Prematurity

Timothy H.M. Fung, Mahiul M. K. Muqit, David J. Mordant, Lewis M. Smith, et.al. *JAMA Ophthalmol.* 2014;132(1):108-110. January 2014

Fluorescein angiography in premature infants is typically performed with Retcam (Clarity Medical Systems), a contact lens-based system, following the intravenous injection of fluorescein. This imaging system is capable of providing up to a 130° field of view of the retinal vasculature in any single image. The authors present the technique and images from noncontact high-resolution ultra-wide field oral fluorescein angiography using the Optos Panoramic 200MA imaging system (Optos PLC). In the three patients described, the authors promote this technique as

a safe and effective alternative to examining the retinal vasculature in premature infants with ROP. The authors suggest that the main advantage of using the Optos Panoramic 200MA imaging system for acquiring fluorescein angiograms is that it can provide up to a 200° field of view of the retinal vasculature without sedation and without inserting an intravenous line or contact lens.

Ophthalmologic Outcome at 30 Months' Corrected Age of a Prospective Swedish Cohort of Children Born Before 27 Weeks of Gestation

The Extremely Preterm Infants in Sweden Study

Gerd E. Holmstrom, Karin K.Ilen, Ann Hellstrom, Peter G. Jakobsson, et.al. JAMA Ophthalmol. 2014;132(2):182-189. February 2014

The authors present the results of an eye exam performed at corrected age of 30 months in a cohort of children (n=411) born before 27 weeks of gestation who were enrolled in EXPRESS (Extremely Preterm Infants in Sweden Study). Visual acuity deficits or eye problems were found in one third of this cohort of patients. Outcome measures included visual acuity, refractive error and strabismus. Visual impairment was identified in 3.1% of the children, and 1.0% were blind. Refractive errors, defined as myopia greater than 3 diopters (D), hypermetropia greater than 3D, astigmatism 2D or more, and/or anisometropia 2 D or more, were found in 25.6% of the children, and 14.1% had manifest strabismus. There were significant associations between visual impairment and treated ROP (P = .02), cognitive disability (P < .001), and birth weight (P = .02). Multiple regression analyses revealed significant associations between strabismus and treated ROP (P < .001), cognitive disability (P < .01), and cerebral palsy (P = .02) Refractive errors were significantly correlated with severity of ROP (right eye, P < .001; left eye, P < .01). Children who had been treated for ROP had the highest frequency (69.0%) of eye and visual abnormalities.

Visual Outcomes After Early Vitreous Surgery for Aggressive Posterior Retinopathy of Prematurity

Noriyuki Azuma, Makiko Ito, Tadashi Yokoi, Yuri Nakayama, et.al. JAMA Ophthalmol. 2013;131(10):1309-1313. October 2013

This is a retrospective non-randomized study of patients with aggressive posterior retinopathy of prematurity (AP-ROP) who underwent early vitreous surgery with lensectomy when retinal detachment developed despite laser treatment. Best corrected visual acuity (PLT or Landolt rings) in patients who had total retinal reattachment with age range of 8 months to 4 years. The vitreoretinal surgeon intervened with vitreous surgery when fibrovascular tissue (FT) proliferated and progressed circumferentially for 6 or more continuous clock hours with a tractional retinal detachment (Stage 4). Of the 103 eyes (57 patients) that underwent early vitreous surgery for AP-ROP, vision was measured in 58 (32 patients). Of the eyes with a total retinal reattachment, postoperative vision ranged from 20/250 to 20/40 in 68.9%.

Reduction in screening for retinopathy of prematurity through risk factor adjusted inclusion criteria

A J van Sorge, N E Schalijs-Delfos, F T Kerckhoff, L J van Rijn, et al, *British Journal of Ophthalmology*. 2013;97:9 September 1143-1147

This paper attempts to propose new national screening guidelines for retinopathy of prematurity in the Netherlands. In Central Netherlands a decrease in the incidence of overall and severe retinopathy of prematurity (ROP) has been seen in infants with birth weight (BW) < 1000 g. The study group consisted of patients included in the NEDROP study, a prospective inventory of ROP in preterm infants born in the Netherlands in 2009. The database contains data for greater than 95% of all infants with gestational age (GA) <32 weeks and or BW <1500 g. Five models were examined, which looked at GA and BW in combination with no, one, or a set of 5 risk factors. A precondition was that no infants with severe ROP would be missed. Risk factors were determined by logistic regression. The model that included all infants with severe ROP screened infants with GA <30 weeks and/or BW <1250 g and a selection of infants with GA 30-32 weeks and/or BW 1250-1500 g with at least one of the following risk factors: artificial ventilation, sepsis, necrotizing enterocolitis, postnatal glucocorticoids, or cardiotonica. This model would not pick up 4.8% of infants with mild ROP and would reduce infants eligible for screening by 29%. It appears that in the Netherlands screening may be reduced safely using the new guidelines. However, use of these new criteria will require pediatricians or neonatologists to evaluate the risk factors in the GA 30-32 weeks and/or BW 1250-1500 g group to make sure that no infants are missed.

Length of Day during Early Gestation as a Predictor of Risk for Severe Retinopathy of Prematurity

Michael B. Yang, Sujata Rao, David R. Copenhagen, Richard A. Lang, *Ophthalmology* December 2013; 120(12):2706-2713

This is a retrospective cohort study from Cincinnati Children's Hospital. There were 343 premature infants born between 1998 and 2002. The range of weight was 401 grams to 1,250 grams at birth. The purpose of the study was to determine whether day length during early gestation was associated with severe retinopathy of prematurity.

Methods: For each infant, average day length (80 hours) was calculated during different cumulative time periods and time windows after the estimated date of conception (EDC).

Main outcome measures: Association of average day length during early gestation with severe ROP.

Conclusions: Higher average day length during early gestation was associated with a lower risk for severe ROP and may imply a role for prophylactic light treatment during early gestation to decrease the risk of severe ROP.

Reviewers Comment: The 2 graphs and figure 4 demonstrate the seasonal distribution based on the month of conception of all 343 premature infants and the cohort. Babies born between June and August have lower percentage of severe ROP; whereas, as babies born December through February had a much higher incidence of severe ROP.

Socioeconomics of retinopathy of prematurity case in the United States

Rebecca S. Braverman, Robert W. Enzenauer *Am Orthopt J* 2013;63:92-96

A survey regarding care for patients with ROP was sent to 710 US members of AAPOS. Completed questionnaires were returned by 283 (40%). Seventy-three percent of respondents reported screening at 1 or 2 NICUs. Sixty-seven percent indicated travel time of 30 minutes or less to perform inpatient ROP care. Forty-eight percent responded that they have contracts to perform ROP care. Forty-five percent felt that they are compensated adequately for ROP screening however 47% felt that they would generate more income if they stopped performing ROP screening services. Mean monthly contracts ranged from \$4,190/month in the South to \$6,477/month in the Midwest but this was not a statistically significant difference. Forty-three percent had some or all of their malpractice insurance covered by the hospital. Seventy percent were responsible for inpatient consultations in addition to ROP service. The authors conclude that financial liabilities pose a threat to the future of ROP care.

The KIDROP model of combining strategies for providing retinopathy of prematurity screening in underserved areas in India using wide-field imaging, tele-medicine, non-physician graders and smart phone reporting

Anand Vinekar, Clare Gilbert, Mangat Dogra, Mathew Kurian, et al *Indian J Ophthalmol* 2014;62:41-9.

(KIDROP) program for retinopathy of prematurity (ROP) screening in underserved rural areas using an indigenously developed tele-ROP model. KIDROP currently provides ROP screening and treatment services in three zones and 81 neonatal units in Karnataka, India. Technicians were trained to use a portable Retcam Shuttle (Clarity, USA) and validated against ROP experts performing indirect ophthalmoscopy.

6339 imaging sessions of 1601 infants were analyzed. A level III technician agreed with 94.3% of all expert decisions. The sensitivity, specificity, positive predictive value and negative predictive value for treatment grade disease were

95.7, 93.2, 81.5 and 98.6 respectively. The kappa for technicians to decide discharge of babies was 0.94 ($P < 0.001$). Only 0.4% of infants needing treatment were missed.

Conclusions: This is the first and largest real-world program to employ accredited non-physicians to grade and report ROP. The KIDROP tele-ROP model demonstrates that ROP services can be delivered to the outreach despite lack of specialists and may be useful in other middle-income countries with similar demographics.

Screening for Retinopathy of Prematurity in China: A Neonatal Units–Based Prospective Study. Yu Xu, Xiaohong Zhou, Qi Zhang, Xunda Ji, Qin Zhang, Jianxing Zhu, Chao Chen and Peiquan Zhao. *IOVS* December 2013 54:8229-8236.

Purpose. To analyze the incidence and severity of retinopathy of prematurity (ROP) in China, and to explore the workload implications of applying different criteria.

Methods. A prospective, neonatal units–based study undertaken in two tertiary level hospitals in Shanghai, China, from January 1, 2010 to December 31, 2012. All infants with birth weight (BW) of 2000 g or less and/or gestational age (GA) of 34 weeks or less were screened for ROP. Retinopathy of prematurity was classified using the international classification, and was treated in accordance with the recommendations of the Early Treatment for Retinopathy of Prematurity Cooperative Group.

Results. A total of 2825 (93.7%) of 3014 eligible infants were screened, and ROP was diagnosed in 503 infants (17.8%). One hundred ninety-one infants (6.8%) had type 1 or worse ROP and were treated with laser or vitrectomy. The mean GA of ROP patients was 29.9 ± 2.1 weeks and their mean BW was 1425 ± 266 g. Infants who needed treatment for ROP had a mean GA of 29.3 ± 2.1 weeks and mean BW of 1331 ± 330 g. Among these treated infants, 18 infants (9.4%) exceeded the United Kingdom's (UK) screening criteria, and 28 (14.7%) exceeded the criteria used in the United States (US). If narrower criteria, as in GA less than or equal to 33 weeks and/or BW less than or equal to 1750 g were adopted, almost 16.9% fewer infants would not have been examined, with no infant missing treatment.

Conclusions. Larger, older infants are at risk in China and screening criteria used in the US and UK may not be suitable for China. Further population-based studies are recommended to determine the necessity of modifying the current ROP screening protocol. **Synopsis:** Retinopathy of prematurity (ROP) is emerging as a major cause of treatable childhood blindness in middle income countries. There are scarce data regarding the incidence of ROP in China. United Kingdom and United States screening criteria might not be appropriate for detecting all infants at risk in China.

Fluorescein Angiography–Based Diagnosis For Retinopathy Of Prematurity: Expert-Non Expert Comparison

Rosanna Guagliano, Donatella Barillà, Chiara Bertone, Anna Maffia,
Eur J Ophthalmol November-December 2013; 23(6): 881 - 886

This is a multicenter retrospective observational study of diagnostic data from 48 eyes of 24 premature infants with classical ROP, stage II, as evaluated by RetCam 3 and fluorescein angiography (FA). Average gestational age was 25.4 weeks, average weight 804.7 g. In order to evaluate accuracy and inter-rater reliability, trainee ophthalmologists (non-expert) were compared to expert ophthalmologists. Results: The FA images appear to be easier to interpret (84.8% agreement) than RetCam images (78.9% agreement), both by expert and non expert ophthalmologists. The results confirm that FA is a good examination technique with a high degree of reliability, even where trainee practitioners are involved. This suggests that retinopathy management can be improved by entrusting diagnostic responsibilities to trainee ophthalmologists, in order to extend access to correct diagnosis, recognition of threshold lesions, and prompt treatment.

COMBINED INTRAVITREAL BEVACIZUMAB INJECTION AND ZONE I SPARING LASER PHOTOCOAGULATION IN PATIENTS WITH ZONE I RETINOPATHY OF PREMATURITY

Kim, Jaeryung;
Jan:34(1)77-82
Kim, Sang Jin , Chang, Yun Sil; Park, Won Soon, Retina 2014

This is a retrospective chart review of 10 premature infants (18 eyes) who received intravitreal bevacizumab (0.25mg) combined with Zone 1 sparing laser photocoagulation for Type 1 ROP in Zone 1. All 18 eyes showed prompt regression of neovascular pathology and plus disease without recurrence at mean follow-up of 83.6 weeks. The rationale for combined treatment is possible synergy of both treatment modalities. This would allow a lower dose of bevacizumab and thereby fewer systemic effects, and less posterior laser application to preserve the central retina. Laser was applied confluent anterior to the margin of Zone 1. Past studies have reported poor outcomes for Zone 1 ROP. The authors at this institution chose 0.25mg bevacizumab as this is lower than previous reported doses of 0.40mg to 0.75mg. Even though this a low dose, serum VEGF levels were not monitored so systemic effects of this dose are unknown. Although their results were very favorable this study has several limitations. It is noncomparative and retrospective. Sample size was small. Follow-up was limited. Although all the patients showed satisfactory results there were no eyes with posterior Zone 1 disease. The idea of combining treatment modalities for ROP certainly warrants further investigation.

9. STRABISMUS

Fusion can mask the relationships between fundus torsion, oblique muscle overaction/underaction, and A- and V- pattern strabismus

Deng H, Irsch K, Gutmark R, et al J AAPOS April 2013;17:177-183

The purpose of this study was twofold. The authors analyzed the correlation and relationship between the grade of objective ocular torsion, the grade of oblique muscle overaction/underaction, and the amplitude of A and V pattern. They also looked at the role of residual fusion in controlling these correlations. Patients were obtained from a 30-year retrospective chart review based on a diagnosis of abnormal fundus torsion or an A- or V-pattern strabismus. Three hundred ninety-six patients were included with a roughly equal distribution between esotropes and exotropes. A strong correlation existed between the size of the pattern, the degree of fundus torsion, and the degree of oblique over/underaction. The presence of stereopsis decreased the correlation while the absence of stereopsis increased it. The relationship between superior oblique overaction and an A-pattern, and inferior oblique overaction and a V-pattern were statistically significant. Lack of stereopsis increased the percentage of patients with a pattern strabismus who had oblique overaction and the presence of stereopsis diminished it. Fundus excyclotorsion was correlated with inferior oblique muscle overaction, and incyclotorsion was correlated with superior oblique muscle overaction. These correlations were statistically significant and increased or decreased based on the absence or presence of stereopsis, respectively. There was a strong correlation between oblique overaction and fundus torsion. There was a statistically significant correlation between pattern strabismus and fundus torsion. This relationship was lessened to a statistically significant degree if stereopsis was present in the V-pattern but not the A-pattern group. The correlation between pattern strabismus, oblique overaction, and fundus torsion has been well known, but the impact of the presence or absence of stereopsis on these relationships is of interest to the reader.

Diplopia after glaucoma drainage device implantation

Abdelaziz A, Capo H, Bannitt MR, et al J AAPOS April 2013;17:192-196

The authors estimate the incidence of diplopia after glaucoma drainage device (GDD) implantation using 15-year financial claims data of a large university hospital-based glaucoma practice. The accuracy of the claims data was verified through a retrospective review of the medical records. Of 2661 patients who underwent GDD surgery, 59 were coded as having diplopia or undergoing strabismus surgery. Diplopia developed in 1.4% of GDD patients. All cases developed within one year of GDD surgery, with the majority having an onset 2 weeks to 3 months after surgery. The majority of superotemporal GDD surgery cases developed exotropia and hypertropia; of the inferonasal GDD surgeries, almost half developed hypotropia. Slightly more than half of the diplopia cases were treated with prisms. Only 3 patients underwent surgery (2- altered drainage device or bleb, 1- strabismus surgery). Five patients had spontaneous resolution of their diplopia. This study is

limited by its retrospective nature and reliance on financial claims data. The true incidence of diplopia was most likely underestimated.

A computerized version of the Lancaster red-green test

Awadein A J AAPOS April 2013;17:197-202

Changes in vergence can cause fluctuations in the results of measured ocular misalignment on the Lancaster red-green test. Accurate plotting of the results on paper is subject to operator error. A new software program based on the Lancaster red-green test is compared to the original. Consecutive adult patients who complained of diplopia caused by incomitant strabismus were enrolled over a 9-month period. The software-based test was performed on a 40-inch monitor at a distance of 50cm (monitor version) and a second time with a projector and a screen at a working distance of 1 meter (projector version). Eighty-two patients were enrolled with a mean age of 34.3 years. Conventional testing results were comparable to computerized results for vertical and torsional deviations. For horizontal deviations, agreement was better between the traditional testing and the projector version than with the monitor version. Measured deviations for both computerized versions tended to be smaller than with conventional testing. Test timing averaged between 7 and 8 minutes for all three versions of testing. The computer monitor testing substituted blue for green because blue targets are more efficiently filtered on a computer monitor. Computerized results also have the advantage of being immediately stored and they can be transmitted electronically.

Quantifying Diplopia with a Questionnaire

Jonathan M. Holmes, Laura Liebermann, Sarah R. Hatt, Stephen J. Smith, *Ophthalmology* July 2013;120:1492-1496

This is a cross-sectional study. The purpose of this is to report a diplopia questionnaire (DQ) with a data-driven scoring algorithm. One hundred and forty-seven adults with double vision associated with strabismus completed both the diplopia questionnaire and the Adult Strabismus-20 quality-of-life questionnaire (HRQOL).

Conclusions: The authors state that they developed a data-driven scoring algorithm for the diplopia questionnaire. The diplopia questionnaire has excellent test-retest reliability and responsiveness and may be useful in both clinical and research settings.

Amblyopia and sensory features at initial presentation of Brown syndrome: an issue to recognize

H T Sekeroglu; E Muz; A S Sanac; E C Sener; et al. *Eye*. April 2013; 27(4):515-8

The study investigated the frequency of amblyopia and sensory features at initial presentation in patients with unilateral congenital Brown syndrome. This was a retrospective chart review from one Turkish institution, identifying 44 patients with Brown syndrome of ages 4-21 years, with median age of 5 years. The frequency of

amblyopia was 15.9% (seven patients) at initial presentation. The amblyopic eye was not necessarily the Brown syndrome eye. Absence of sensory fusion, assessed by the Worth 4 dot test, was associated with amblyopia.

Automated Analysis of Binocular Alignment Using an Infrared Camera and Selective Wavelength Filter.

Yang HK, Seo J-M, Hwang J-M, Kim KG. Invest Ophthalmol Vis Sci. April 2013; 54:2733-2737.

This study is a comparison of a computerized software that automatically quantifies the angle of strabismus from photographs based on a biometric 3-dimensional eye model with good reproducibility and minimal inter-observer variability. The software shows excellent agreement with the Krimsky test, but did not measure the latent component of strabismus, resulting in less correlation with the prism cover test. The authors developed an occluder made with a filter that blocks the subject's view and all visible light, but selectively transmits infrared light with wavelengths above 720nm. The photographs taken with the selective wavelength filter in front of the eye visualize the details of the eye completely behind the occluder, while blocking the subject's view. These infrared images may reveal the latent components of strabismus that are manifest only after disruption of fusion. They evaluated the efficacy of this system to estimate binocular alignment with the gold standard of the prism and alternate cover test (PCT). The 95% limit of agreement of inter-observer variability was + 4.8 prism diopters (D) for the PCT and + 4.3 PD for the selective wavelength filter analysis. The 95% limit of agreement of test-retest reliability between the PCT and selective wavelength filter analysis was + 8.5PD. Results of the PCT and selective wavelength filter analysis showed a strong positive correlation ($R=0.900$, $P<0.001$). This automated method is an accurate and reliable tool for measuring ocular deviation with minimal observer dependency.

Esotropia Greater at Distance: Children vs Adults

Erin P. Herlihy, James O. Phillips, Avery H. Weiss, JAMA Ophthalmol. March 2013;131(3):370-375.

Esotropia greater at distance than at near can be related to abducens palsy or to divergence insufficiency. This retrospective study of 32 patients examined the clinical and eye movement findings that distinguish abducens palsy from divergence insufficiency. Details regarding age, medical history, oculomotor and neurological examinations, and result of any neuroimaging studies were recorded. Eye movements were recorded in 2 subjects using binocular video-oculography. Fifteen children and 17 adults were identified; 93.3% of the children had an underlying central nervous system disorder that coincided with the onset of their esodeviation, and 23.5% of the adult patients had an underlying central nervous system disorder. Eye movement recordings in 2 pediatric patients revealed lateral incomitance suggestive of abducens palsy not detected by

clinical examination. Esotropia greater at distance pattern in an otherwise healthy adult is more likely due to age-related reduction in accommodation, increased ratio of accommodative vergence to accommodation, and relative divergence insufficiency.

Inferior Oblique Myokymia: A Unique Ocular Motility Disorder

Nicholas D. Chinskey, Wayne T. Cornblath, JAMA Ophthalmol. March 2013;131(3):404-405.

The authors describe a unique form of myokymia involving monocular, high frequency, low-amplitude contractions causing excyclotorsion, not incyclotorsion, induced by supraduction, suggesting an inferior oblique myokymia. This is the opposite of what is expected for superior oblique myokymia, in which infraduction triggers incyclotorsion. The etiology of superior oblique myokymia is uncertain, with reports suggesting vascular compression of the trochlear nerve, direct involvement of the muscle, and brainstem disorders. In our case, there was no abnormality of other oculomotor nerve functions, perhaps lending support to this being a primary muscle problem

Thromboembolism and Congenital Malformations From Duane Syndrome to Thalidomide Embryopathy

Cameron F. Parsa, Matthieu P. Robert, JAMA Ophthalmol. April 2013;131(4):439-447.

Fibrin emboli and focal hypoperfusion may explain the development of many sporadic congenital malformations. In their study, the authors apply inductive and deductive reasoning to study a pathophysiologic mechanism to unify a variety of disparate sporadic congenital malformations such as Duane syndrome, Peters anomaly, unilateral congenital cataracts, and the morning glory disc anomaly. All these share a vascular territory of the carotid arteries and a propensity for left-sided involvement in girls. Most aberrant misinnervation phenomena such as jaw-winking syndrome, crocodile tear syndrome, Brown syndrome, and congenital fibrosis syndrome and, by extrapolation, the hypoplasia or dysgenesis of noncephalic anatomical structures (including limbs) may be similarly explained. Such malformations will occur more frequently under thrombogenic conditions, such as those induced by thalidomide.

Divergence Insufficiency Esotropia Is a Misnomer

David Mittelman, JAMA Ophthalmol. April 2013;131(4):547.

In a commentary on Dr. Chaudhuri and Dr. Demer's article on sagging eye syndrome which describes the pathophysiology of non-neurologic causes of divergence paralysis esotropia, Dr. Mittelman emphasizes that the term divergence insufficiency esotropia is a misnomer and that the designation of divergence insufficiency esotropia should be reserved only for those patients with serious neurological disease. Instead, he proposes that the term "adult-onset age-related

distance esotropia” should be used to describe patients with acute onset esotropia in the distance which results from aging changes of orbital tissues and disruption of the LR-SR band.

Divergence Insufficiency Esotropia Is a Misnomer In Reply

Zia Chaudhuri, Joseph L. Demer, JAMA Ophthalmol. April 2013;131(4):547-548.

Dr. Chaudhuri and Dr. Demer agree with Dr. Mittelman that “age-related distance esotropia” (ARDE) should enter the lexicon to describe this non-neurologic condition

No, Not More Talk About Duane Syndrome

Creig S. Hoyt, JAMA Ophthalmol. April 2013;131(4):522-524.

In this editorial Dr. Creig Hoyt comments on the article by Parsa and Robert which suggests that thromboembolism during the perinatal period may be a causative factor in a number of congenital malformations, for example, Duane syndrome and benign sixth nerve palsy in childhood. The absence or hypoplasia of the sixth cranial nerve and innervation of the lateral rectus muscle by a branch of the third cranial nerve characterizes Duane syndrome. How this specific and stereotypic miswiring comes about in Duane syndrome remains a mystery. Rather than seeing it come about because of a genetic abnormality resulting in impaired axonal guidance, they assert that “Duane syndrome may develop following a focal vascular insult to the sixth nerve trunk with axonal degeneration, allowing for substitutive innervation from third nerve axons to the lateral rectus muscle.” Parsa and Robert suggest the possibility that the benign sixth nerve palsy of childhood and Duane syndrome have a common pathogenesis differentiated only by the timing of insult, being prenatal in Duane syndrome and postnatal in the benign sixth nerve palsy of childhood. Dr. Hoyt encourages further study of the proposal by Parsa and Robert that these features could be explained by emboli from the heart.

Sagging Eye Syndrome: Connective Tissue Involution as a Cause of Horizontal and Vertical Strabismus in Older Patients

Zia Chaudhuri, Joseph L. Demer, JAMA Ophthalmol. May 2013;131(5):619-625.

To avoid unneeded neurologic evaluation and neuroimaging, the authors stress the importance of recognizing the clinical features of this syndrome. Acquired vertical and horizontal strabismus may be the result of rupture of the LR-SR band causing horizontal rectus pulley displacement and EOM elongation. This is suggested on clinical exam by blepharoptosis and superior sulcus deficit.

Congenital Bilateral Aplasia of Medial Recti in a Family

Anirudh Singh, Anudeepa Sharma, Pradeep Sharma JAMA Ophthalmol. June 2013;131(6):798-800.

The authors present a father and 2 sons (non-sanguinous) with impaired adduction OU and large angle exotropia with preserved vertical ductions and no ptosis. MR of the orbits revealed hypoplastic medial rectus. At time of surgery, only a fibrous

capsule was visualized in the location where the medial rectus should be found. The authors hypothesize that the orbital layer of the medial rectus was intact, but the global layer was aplastic. A large lateral rectus recession and split vertical transposition with Foster modification gave improved alignment of less than 20 Δ exotropia on post-op exam. Genetic analysis was not performed to check for mutations in genes associated with cranial dysinnervation syndromes.

Intramuscular Hemangioma of the Inferior Oblique: A Rare Cause of Extraocular Muscle Enlargement

Norman C. Charles, Sonia Belliappa, Payal Patel, JAMA Ophthalmol. 2014;132(1):122-124. January 2014

The authors present a 25 year old male with a lower eyelid mass. The lesion elevated the globe and was firm and non-tender. Motility was fairly full but diplopia could be elicited in extreme downgaze. Neuroimaging revealed a circumscribed mass involving the inferior oblique muscle. Pathology confirmed a hemangioma. Differential diagnoses of enlarged muscle include thyroid disease, idiopathic orbital inflammation, lymphoma, amyloid, trichinosis, metastatic cancer and hemangioma.

Risk Factors and Genetics in Common Comitant Strabismus A Systematic Review of the Literature

Gail D. E. Maconachie, Irene Gottlob, Rebecca J. McLean, JAMA Ophthalmol. 2013;131(9):1179-1186. September 2013

The purpose of this study is to identify common genetic and environmental risk factors for common comitant strabismus. Literature search was performed using keywords gene, genetic environmental factor, inheritance, risk factor, esotropia, exotropia, strabismus, squint, convergent strabismus, and divergent strabismus. Exclusion criteria consisted of associated syndromes, strabismus not the primary outcome, poor study design or quality, and logarithm of the odds score less than 3. Forty-one articles fulfilled the inclusion criteria. Significant risk factors for strabismus included low birth weight, cicatricial retinopathy of prematurity, prematurity, smoking throughout pregnancy, anisometropia, hyperopia, and inheritance. Inheritance was further supported by twin and pedigree studies, which revealed the complexity of the inheritance pattern. At present the STBMS1 locus is the only gene location that has been supported; however, others have been reported

Functional Burden of Strabismus Decreased Binocular Summation and Binocular Inhibition

Stacy L. Pineles, Federico G. Velez, Sherwin J. Isenberg, Zachary Fenoglio, et.al. JAMA Ophthalmol. 2013;131(11):1413-1419. November 2013

The authors seek to highlight the binocular deficits in strabismus by comparing results of certain psychophysical tests performed on the better seeing eye with

results obtained with both eyes open. These tests, performed in a cohort of patients with strabismus and a control cohort of nonstrabismic patients, include visual acuity, Sloan low-contrast acuity, Pelli-Robson contrast sensitivity, and sweep visual evoked potential contrast sensitivity. Binocular summation is defined as the superiority of binocular over monocular performance on a visual threshold task. Binocular inhibition reflects destructive neural processes in which a subject has better visual functioning using one eye compared with both eyes open.

The Psychological Impact Of Strabismus: Does The Angle Really Matter?

Ailsa Ritchie, Patricio Colapinto, Saurabh Jain *Strabismus*. December 2013;21(4):203-208

The psychological impact of strabismus is well recognized and studies have shown that people with strabismus have problems with self-image and higher rates of generalized anxiety or distress compared with normal controls. However, few studies have evaluated the relationship between size of deviation and psychological impact. The authors prospectively studied 50 patients seeking treatment of their strabismus. All patients were assessed by an orthoptist and completed a Psychological Impact questionnaire. The average age was 48 years (range 15-84) and there were 26 females and 24 males. There was no correlation between psychological impact score and the maximum degree of horizontal deviation, the maximum angle of vertical deviation, presence of diplopia, visual acuity of the worse eye and direction of deviation ($p = 0.8$ for eso-deviations compared to exo-deviations, $p = 0.4$ for horizontal compared to vertical deviations). There was a slight negative correlation between psychological impact score and visual acuity of the better eye ($p = 0.04$).

The authors conclude that all patients can have a negative psychological impact from their strabismus, regardless of angle size, direction of deviation, age, sex, presence of diplopia, or visual acuity. Therefore, these factors should therefore not impact the decision to offer interventional treatments.

Changes in the Amygdala Produced by Viewing Strabismic Eyes

Jatta Berberat, Gregor P. Jaggi, Frederick M. Wang, Luca Remonda, *Ophthalmology* October 2013; 120(10):2125-2129

This is a prospective observational study of 31 healthy volunteers who underwent functional magnetic resonance imaging.

Methods: Functional magnetic resonance imaging, data and blood oxygen level-dependent signal changes were analyzed using the BrainVoyager QX software package.

Main outcome measures: Responses to viewing strabismus images were compared with those observed while reviewing normal eye images.

Results: Strabismus images lead to significant activation of the amygdale, hippocampus, parahippocampal and fusiform gyri in 30 of 31 subjects compared with normal eye images. This is indicative of a negative emotional response. Conclusion: These functional MRI results confirm that strabismus influences organically not only the patient with the nonparallel eyes but also observers. Treatment of strabismus therefore changes the interpersonal dynamic for patients with strabismus. Functional MRI confirms negative emotional response on the part of not only the patient but also people interacting with the patient with strabismus.

The use of prisms and botulinum toxin in the detection of binocular vision: a literature review

Kerry Hann, Fiona J. Rowe, Br Ir Orthopt J 2013; 10: 17–22

The aim of this review article is to compare the use of pre-operative prisms and pre-operative botulinum toxin injection in strabismic patients as two methods to determine binocular vision potential and to assess risk for post-operative diplopia despite good motor alignment. Five published uncontrolled studies were included in this review with samples range of 3 to 424 subjects. Diplopia testing using loose or trial frame prisms is helpful in confirming a low risk of post-operative diplopia if the patient senses no diplopia with full prism correction. The majority of patients who sense diplopia with full prism correction will not have diplopia post-operatively. Injection of botulinum toxin may temporarily provide good motor alignment and provide the patient a truer representation of the post-operative binocular state. The authors suggest an injection of botulinum toxin in patients who sense diplopia with full pre-operative prism correction. Botulinum toxin may also be preferred in cases with large angle strabismus as sensory assessment through bilateral large prisms is difficult. However, lower cost and lower risk of pre-operative assessment with prism makes prisms the preferred method and botulinum toxin injection reserved for select cases.

Vision therapy and computer orthoptics: evidence-based approach to use in your practice

Jennifer Lambert, Am Orthopt J 2013;63:32-35

This review article summarizes 5 clinical trials pertaining to convergence insufficiency treatments ranging in size from 46 to 221 subjects. Office-based therapy was more effective than home-based computer, pencil pushup treatments and placebo. Home-based computer orthoptics and pencil pushups yielded similar results. Office-based therapy had highest compliance at 91% whereas home-based computer orthoptics had the lowest compliance at 67%. Cost of office based therapy was highest at \$75-\$100 per visit whereas home-based pencil pushups was least expensive.

Vision therapy: are you kidding me? Problems with current studies

Sarah Whitecross, Am Orthopt J 2013;63:36-39

This review article serves as a counterpoint to the above article “Vision therapy and computer orthoptics: evidence-based approach to use in your practice” by Lambert published in the same issue of Am Orthopt J. The author cites multiple limitations in the 4 published studies performed by the Convergence Insufficiency Treatment Trial group. Only 1 study involved more than 100 subjects. Primary outcome varies among studies or is not stated. The metric called the Convergence Insufficiency Symptom Survey contains bias towards overdiagnosing convergence insufficiency. The office-based therapy group received more therapy than the home-based therapy group. There was no “no-treatment” control group to evaluate natural history of convergence insufficiency. The author concludes that the effectiveness of office-based or home-based therapy for convergence insufficiency has not been proved.

Fusional amplitudes: exploring where fusion falters.

The 43rd Richard G. Scobee Memorial Lecture
Katherine J. Fray , Am Orthopt J 2013;63:41-54

This prospective study involving 50 healthy adults sought to identify factors that influence fusional convergence and divergence measurements. The order of testing was significant in the measurement of divergence. Divergence break and recovery points were higher when tested before convergence and lower when tested after convergence. Encouraging the subject to maintain fusion had a significant effect on the convergence break and recovery points but not the divergence measurements. Alertness as measured by the Stanford Sleepiness Scale was not found to impact fusional vergence measurements. Near fixation as opposed to distance fixation yielded higher break and recovery points for convergence and divergence fusional amplitudes. For the clinician to improve fusional amplitude measurement reproducibility, the author recommends that patients should be given encouragement, that divergence should be measured before convergence, that measurement is performed with distance fixation before near fixation and that the patients' alertness level should be noted.

Incidence of strabismus and amblyopia in preverbal children previously diagnosed with pseudoesotropia

Ariel L. Silbert, Noelle S. Matta, David I. Silbert , Am Orthopt J 2013;63:103-106

This retrospective study of 253 patients diagnosed with pseudoesotropia found that 22 of the 207 patients under the age of 36 months subsequently developed strabismus. When stratified by refractive error of $\leq +1.50$ D and refractive error $> +1.50$ the rates of subsequent strabismus were 10% and 11%, respectively. None of the patients over 36 months of age at presentation developed strabismus. The authors conclude that children under the age of 36 months

diagnosed with pseudoesotropia are at increased risk for the development of true strabismus at a later time and therefore should be monitored.

Efficacy of modified cover testing for detection of incipient true strabismus with pseudostrabismus diagnosis

Cindy Pritchard , George S. Ellis, Am Orthopt J 2013;63:73-79

This prospective study of 53 pediatric subjects diagnosed with pseudostrabismus by standard cover testing were evaluated with a modified cover test in which one eye was covered for 15 seconds before moving the cover to the fellow eye for 15 seconds and repeating for a total of at least 5 cycles. Seven subjects had positive or suspicious findings for esodeviation and 6 of the 7 were found to have esotropia by standard cover testing at a subsequent visit. Five subjects were found to have positive or suspicious findings for exodeviation and 1 of the 5 was found to have exotropia by standard cover testing at a subsequent visit. The time between the initial diagnosis of pseudostrabismus and diagnosis of true strabismus ranged from 1 to 27 months. The authors conclude that some patients diagnosed with pseudostrabismus actually have incipient strabismus and that the modified “occlusive” cover test described improves detection of patients at risk of developing manifest strabismus, particularly esotropia.

Assessing abnormal head posture: a new paradigm. Halachmi-Eyal O, Kowal L. Curr Opin Ophthalmol. 2013 Sep;24(5):432-7.

The authors review examination techniques used to assess a patient with an anomalous head posture (AHP). Assessment of the AHP with both eyes open, both eyes closed, left and right eye occluded separately and while in the upright and supine position differentiate visually driven AHP from orthopedic and vestibular abnormalities. Identification of the three T's (head tilt, head turn and head tip) can help to further classify the etiology of visually driven AHP. The most common causes of a head tilt include congenital nystagmus and vertical misalignment secondary to superior oblique palsy. Face turn is most commonly associated with congenital nystagmus, neurogenic strabismus, refractive errors and visual field defects. Head tip postures are most commonly caused by incomitant strabismus, nystagmus, neurologic conditions and ptosis. A combination of head tilt, turn and tip may be present in one individual, but one is usually preferred and dictates the AHP.

Outcomes in patients with esotropic duane retraction syndrome and a partially accommodative component

Ramesh Kekunnaya, Federico G. Velez, Stacy L. Pineles

Indian J Ophthalmol 2013;61:701-4.

This short series of six cases highlights the association of accommodative component in esotropic Duane syndrome.

Conclusion of this paper is as follows, Patients with Duane syndrome can have an accommodative component to their esotropia, which is crucial to detect and correct prior to surgery to decrease the risk of long-term over-correction. Occasionally, torticollis in Duane syndrome can be satisfactorily corrected with spectacles alone.

Differentiating bilateral superior oblique paresis from sensory extorsion

Muthusamy B, Chang H-Y, Irsch K, et al
J AAPOS October 2013;17:471-476

This study evaluates the difference between the 'immediate-onset' (IO) torsional diplopia, seen after a head trauma, with 'gradual-onset' (GO) torsional diplopia. The authors question whether these two types of strabismic patients represent two different disease entities. The authors compared degrees of subjective torsional misalignment in upgaze versus downgaze. Thirty-eight patients were included. Definite head trauma and immediate diplopia (IO) were seen in 27 patients, while 11 patients had gradual onset diplopia (GO). The IO group had a mean age of 31.6 years, while the GO group had a mean age of 52.6 years. 33% of the patients in the IO group had a chin-down head posture while no one in the GO group displayed this. 27% of the GO group patients displayed a chin-up head posture but none of the IO group displayed this. The IO group had an increase in extorsion from up- to down-gaze of 6.7' to 24.3'. The GO group showed no change from up-gaze to down-gaze. The authors hypothesize that the IO group represents bilateral superior oblique paresis, whereas the GO group represents 'sensory extorsion' (a defect in the pathways subserving binocular function). As a result of this difference in etiology the surgical interventions were somewhat different. 20/23 patients in the IO group with complete surgical information, underwent Harada-Ito surgery while the remaining three underwent inferior-oblique weakening procedures. In the GO group, of the patients with complete surgical information, 4 underwent Harada-Ito surgery while 3 underwent inferior-oblique weakening procedures. Both groups experienced significant improvement in net extorsion in primary gaze. Bilateral Harada-Ito surgery improved the discrepancy in excyclotorsion from upgaze to downgaze whereas bilateral inferior-oblique weakening procedures actually worsened it. Thus differentiating the type of torsional diplopia may help in the decision on the best surgical management technique. The authors comment that the GO group was often associated with exotropia more commonly than the IO patients (45% vs 22%) and therefore the GO group may represent patients with excyclotorsion in the setting of central fusion disruption. The authors also state that Lancaster red-green test is better at differentiating torsion in upgaze vs downgaze than Double Maddox rod testing. This was a small, retrospective study with a small number of surgical patients in the GO group.

Lateral Rectus Superior Compartment Palsy

R. Clark, J. Demer. Am J Ophthal Feb 2014; 157(2): 479-486.

This was a prospective observational case control study. MRI was used to find evidence for compartmental lateral rectus atrophy. The abducens nerve is divided into superior and inferior branches. This study attempted to see if there was evidence of compartmental affects with specific lesions. By using MRI testing they were able to identify a subgroup of patients with selective atrophy of the superior compartment of the lateral rectus. These patients appeared to have some minimal abduction present and slight hypotropia due to the inferior branch still functioning. 12 patients in the study showed superior and inferior compartment size change. 6 patients had only superior compartment volume reduction. They also suggest that differentiating between the two types of palsy may affect surgical outcomes.

The Stability of the Monofixation Syndrome

M. Ing, K. Roberts, A. Lin, J. Chen. Am J of Ophthal 2014; 157(1); 248- 253.

This study was a chart review of 63 patients with monofixation syndrome (MFS). These patients were followed for 3 years and were monitored for stability. The etiology was predominantly esotropia. 57 patients remained stable without decompensation for 13.9 years. Only 6 decompensated and required surgery. All of these patients were esotropic. Over 90% of patients had gross stereoacuity. This study concluded that decompensation was rare and could be surgically corrected.

The Effect of Ocular Rigidity upon the Characteristics of

Saccadic Eye Movements. Mohammed Alhazmi, Dirk Seidel and Lyle S. Gray. Invest. Ophthalmol. Vis. Sci. March 4, 2014 vol. 55 no. 3 1251-1258.

Purpose. To determine whether variation in ocular rigidity (a quantity that describes the elastic properties of the globe) affects the characteristics of horizontal saccadic eye movements.

Methods. Thirty-three young, visually healthy subjects participated with informed consent in the study. Axial length was measured using the IOLMaster ocular biometer. Ocular rigidity coefficients were determined using Schiottz tonometry. Horizontal saccades were stimulated randomly to 40° in 10° steps. Eye movements were recorded continuously at a sampling rate of 60 Hz using the Viewpoint video-eyetracker.

Results. Peak velocity increased significantly with increasing ocular rigidity ($F [2,263] = 30.635, P < 0.001$). Time to peak velocity ($F [2,263] = 27.723, P < 0.001$) and total response time ($F [2,263] = 21.133, P < 0.001$) decreased

significantly with increasing ocular rigidity. Ocular rigidity was significantly positively correlated with peak velocity ($R^2 = 0.67$, $P < 0.001$), and significantly negatively correlated with time to peak velocity ($R^2 = 0.64$, $P < 0.001$), and total response time ($R^2 = 0.62$, $P < 0.001$).

Conclusions. The known relationship of ocular rigidity with myopia can be extended to shorter hyperopic eyes, which are found to have higher ocular rigidity. The dynamic characteristics of saccadic eye movements are found to vary systematically with ocular rigidity. These findings suggest that the structural characteristics of the eye are an important factor in determining dynamic characteristics of eye movements.

Synopsis: The authors investigated the effect of ocular rigidity upon saccadic eye movements. We found that eyes with high ocular rigidity (hyperopic) move significantly faster than those with low ocular rigidity (myopic). These findings suggest that the characteristics of saccades vary with refractive error.

Vertical and Oblique Saccade Disconjugacy in Strabismus. Mark M. G. Walton, Seiji Ono, and Michael Mustari. *IOVS January 2014 55:275-290.*

Purpose. Previous studies have shown that horizontal saccades are disconjugate in humans and monkeys with strabismus. The present study was designed to extend these results to vertical and oblique saccades. A major goal was to assess the conjugacy in terms of both amplitude and direction.

Methods. Saccadic eye movements were recorded binocularly in three adult monkeys. One had normal eye alignment, one had exotropia resulting from a bilateral medial rectus tenotomy in the first week of life, and one had esotropia resulting from prism rearing during the first 3 months of life. We assessed the conjugacy of saccades in various directions by comparing both amplitude and direction.

Results. Saccades in the strabismic monkeys were disconjugate in terms of both amplitude and direction. These effects were as large for vertical and oblique saccades as for horizontal ones. However, the pattern of disconjugacy often varied as a function of saccade direction. In some cases, saccades that appeared to be conjugate in terms of amplitude differed substantially when direction was taken into account.

Conclusions. These data indicate that the assessment of saccade disconjugacy in strabismus may yield misleading results if direction is not considered. The complex pattern of disconjugacy suggests that strabismus is associated with substantial abnormalities within the circuitry controlling saccades. Neurophysiological studies are needed to identify the specific neural substrates for these behavioral effects.

Synopsis: The authors quantified the conjugacy of saccades in various directions in three monkeys (one normal, one exotrope, and one esotrope). For both strabismic animals, saccades in the two eyes often differed notably, in terms of both amplitude and direction.

Crouzon Syndrome: Relationship of Rectus Muscle Pulley Location to Pattern Strabismus. Avery H. Weiss, James Phillips, and John P. Kelly. *IOVS January 2014 55:310-317.*

Purpose. Investigate the relationship between the extorsion of the rectus muscle pulleys and the V-pattern exotropia and “overelevation in adduction” observed in Crouzon syndrome.

Methods. Twenty children with Crouzon syndrome had assessment of eye alignment. The horizontal and vertical positions of the four rectus muscle pulleys were estimated from coronal CT images. Eye alignment was simulated in Orbit 1.8 software by shifting the corresponding location of the rectus muscle pulley array.

Results. Eleven of the 20 patients had a V-pattern exotropia with displacements of each rectus muscle pulley ranging from 2 to 7 mm. The remaining nine patients were orthotropic with <2 mm displacement of the rectus muscle pulleys. Simulated displacements (>2 mm) of either the horizontal or vertical rectus muscle pulleys produced a similar strabismus pattern. The amount of V-pattern exotropia observed clinically was highly correlated with the amount predicted by pulley displacements in Orbit 1.8 ($r^2 = 0.63$; $P < 0.0001$). The displacement of vertical and horizontal rectus muscle pairs was significantly higher for patients having overelevation in adduction.

Conclusions. Rotation of the four rectus muscle pulleys relative to the corresponding rotation planes of the globe changes the direction and magnitude of their active and passive pulling forces in a gaze-dependent manner. Extorsion of the horizontal and vertical rectus muscle pulleys in Orbit 1.8 reproduces the pattern strabismus observed in Crouzon syndrome. The high correlation between the predicted magnitude of the V-pattern exotropia and observed exotropia indicates that extorsion of the rectus muscle pulleys primarily accounts for the pattern strabismus.

Synopsis: Extorsion of the horizontal and vertical rectus muscle pulleys can account for the V-pattern exotropia and “overelevation in adduction” in Crouzon syndrome.

Exotropia-Hypotropia Complex in High Myopia

Monga S, Kekunnaya R, Sachdeva V J *Pediatr Ophthalmol Strabismus* 2013;50(6):340-346

The goal of this paper was to highlight the association of exotropia-hypotropia complex in cases of high myopia in contrast to the more frequently reported esotropia-hypotropia complex (heavy eye syndrome). This is a retrospective review of 15 patients diagnosed with having high myopia (axial length ≥ 27) and exotropia-hypotropia. The majority of the patients had unilateral high myopia with dense amblyopia. All orbits were scanned using MRI or CT. The mean axial length of the deviated eye (29.60 mm) was significantly more than the axial length of the fellow, or control, eye (24.69 mm). No specific radiologic findings were identified to explain the etiopathogenesis of the exotropia-hypotropia complex unlike the displacement of extraocular muscle paths seen in heavy eye syndrome. The authors suggest that future research using high resolution advanced imaging protocols may contribute to a better understanding of the exotropia-hypotropia complex in high myopia.

10. STRABISMUS SURGERY

Surgical results after one-muscle recession for correction of horizontal sensory strabismus in children

Hopker LM and Weakley DR *J AAPOS* April 2013;17:174-176

The authors evaluate one-muscle recession for the treatment of sensory strabismus in children. This was a retrospective review of surgeries over a 7-year period. Thirty-three patients met inclusion criteria. Approximately 1/3 (n=12) were esotropic. The mean follow-up was 39 months. Successful postoperative alignment was achieved in 75% of the esotropes and 90% of the exotropes. The authors did not specifically look to see if lateral incomitance was induced. No patients reported postoperative diplopia. The dose-response curve was similar between esotropes and exotropes. The authors felt this procedure has utility up to a preoperative deviation of 25-30 prism diopters.

Choice of conjunctival incisions for horizontal rectus muscle surgery- a survey of American Association for Pediatric Ophthalmology and Strabismus members

Mikhail M, Verran R, Farrokhyar F, and Sabri K *J AAPOS* April 2013; 17:184-187

This paper reports results of a worldwide questionnaire on conjunctival incision preference for adult and pediatric strabismus surgery (primary and reoperation). The questionnaire was distributed to all AAPOS members. The net overall response rate was 27.8% (301/1022). For primary surgeries, the fornix incision was the most popular with both pediatric (58%) and adult (53%) usage. For reoperations, the

limbal incision was preferred in both children (58%) and adults (63%). Respondents cited less pain and inflammation postoperatively as the reasons to use the fornix incision. Better exposure and better teaching opportunity were cited for the use of the limbal incision. Limbal incision was preferred for adjustable sutures 3:1. This study is limited by a low response rate and no evaluation of risk of ASI in the decision-making process.

The effect of previous orbital decompression on results of strabismus surgery in patients with Graves' ophthalmopathy

Kim MH, Park K and Oh SY J AAPOS April 2013;17:188-191

The authors evaluated the effect of strabismus surgery on proptosis and compared the surgical outcomes of patients with and without previous orbital decompression. A retrospective review of 14 years of consecutive patients with surgery for Graves ophthalmopathy was performed. A minimum of 6 months of follow-up was required postoperatively (mean followup was 25 months). Fifty-six patients were included. There was a statistically significant difference in the age between decompression patients (48.7 years) and nondecompression patients (40.2 years). Preoperative strabismus measurements were comparable between the groups. Exophthalmometric measurements improved minimally post-strabismus surgery in both groups. Strabismus surgical success (defined as no diplopia in primary and downgaze or no diplopia with prisms within 8PD horizontally and 4PD vertically) was achieved in over 90% of both the decompression and nondecompression groups. There was a 10.7% reoperation rate. Other studies have shown strabismus surgery success is lower after decompression surgery but this is not validated in this study. This discrepancy may be because in this study the indication for decompression was cosmetic in 22 of 27 patients (not for neuropathy). The medial bony strut was preserved in all patients, which may have improved strabismus surgery outcomes. Recessions of 1 or 2 muscles did not significantly affect proptosis results. This study was retrospective with no control group.

Self-Grading Effect of Inferior Oblique Recession

Jun Ho Yoo, Seung-Hyun Kim, Ji Won Seo, Hae Jung Paik, et al, J Pediatr Ophthalmol Strabismus 2013; 50:102-105 (March/April)

The study determine the effects of a 10mm inferior oblique recession versus a 14mm inferior oblique recession. A retrospective study reviewed 43 patients with inferior oblique overaction associated with congenital unilateral superior oblique palsy. 17 patients had a 10mm IO recession whereas 26 had a 14mm IO recession. The study found that both IO recession procedures were self grading and no significant differences were evident at 3 months postoperatively.

Clonidine Premedication Versus Placebo: Effects on Postoperative Agitation and Recovery Time in Children Undergoing Strabismus Surgery

Laura J. Heinmiller, Leonard B. Nelson, Marc B. Goldberg, Adam R. Thode, J Pediatr Ophthalmol Strabismus 2013; 50:150-154 (March/April)

The purpose of this article is to evaluate the effects of using clonidine preoperatively to avoid postoperative agitation. The article also discusses recovery time when using clonidine versus placebo postoperatively. The article is well written and does a very good job to keep the study double blinded. The study shows that although clonidine does reduce postoperative agitation, the recovery time for patients who receive clonidine prior to surgery is longer and patients remain in the post-anesthesia care unit later than placebo. In addition, parents are also questioned to evaluate parental satisfaction. Parents were overall more satisfied with a reduction in postoperative agitation and were happier to take home a slightly sleepier child.

Determinants of Ocular Deviation in Esotropic Subjects Under General Anesthesia

Vincent Daien, Chloé Turpin, François Lignereux, Riadh Belghobsi, et al, J Pediatr Ophthalmol Strabismus 2013; 50:155-160 (March/April)

The study aimed to identify determinants of ocular deviation in patients with esotropia while under general anesthesia. Forty esotropic patients were evaluated for their ocular deviation in the awaked stated as well as under general anesthesia. The study concluded that the ocular position under general anesthesia was most influenced by preoperative ocular deviation and patient age; the older the patient, the less the ocular deviation under general anesthesia.

Changes in Sagging Extraocular Muscle Following Surgical Recession of the Superior Rectus Muscle in Rabbit Eyes

Won Yeol Ryu, Jeong Bum Bae, J Pediatr Ophthalmol Strabismus 2013; 50:162-168 (March/April)

The study evaluates whether central muscle sag has an effect on recession on rabbit models. The authors created central muscle sag in one eye purposely and in the other eye recessed the superior rectus muscle without any central muscle sag. The purpose was to determine if the effects of a muscle recession are increased when central muscle sag is created. The authors concluded that the effects of a recession were exaggerated in an eye where central muscle sag was created because there seems to be posterior migration of the nasal and temporal edges.

Decrease in the rate of esotropia surgery in the United Kingdom from 2000 to 2010 S. Jacob Heng, Caroline J. MacEwen. Br J Ophthalmol May 2013; 97: 598-600.

This study evaluated the annual incidence of strabismus surgery in children aged 0-14 years in the United Kingdom over 10 years. There appeared to be a steady

decline in both the incidence and frequency of strabismus surgery from 2000 to 2006. England showed a decrease of 19.7%, Scotland 29.7%, and Wales 17.3%. 2006 to 2010, the incidence of surgery only decreased by 2.1% in England, 3.3% in Scotland, and 4% in Wales. Authors suggest that the decrease in surgery may be due to a true decrease in the incidence of strabismus, earlier detection with more successful conservative treatment or an increased threshold in performing surgery.

Postoperative minimal overcorrection in the surgical management of intermittent exotropia Yoonae A. Cho, Seung-Hyun Kim. Br J Ophthalmol July 2013; 97: 866-869.

This was a retrospective study evaluating the outcome of 111 patients who underwent surgery for exotropia. All patients were followed for 5 years. Patients may have had unilateral or bilateral surgery. The mean age was 7.3 years. 16 patients underwent unilateral surgery, and 95 underwent bilateral surgery. Mean preoperative deviation was 27.7 diopters. The patients were divided into 4 groups based on postoperative outcome at day 1: ortho group, minimally overcorrected group, usually overcorrected group, and highly overcorrected group. The success rate in the ortho group was 43%, 60% in the minimally overcorrected, 58% in the usually overcorrected, and 56% in the highly overcorrected. There was no difference statistically in the success rate of the 4 groups. However, the overcorrection rate was 0% in the ortho group and minimally overcorrected, and was 8% and 16% respectively for the other two groups. It appeared that the minimally overcorrected group had a lower recurrence rate than the ortho group and also had a lower overcorrection rate.

Contralateral lateral rectus recession versus recess-resect for recurrent exotropia after unilateral recess-resect. Joo Hyun Kim, Hae Jin Kim, Dong Gyu Choi. Br J Ophthalmol June 2013; 97: 752-756.

This retrospective study looked at 39 subjects who underwent recurrent surgery for exotropia. Initially, the patient underwent primary surgery for exotropia with a unilateral recess-resect. The second procedure was then assigned to either a contralateral lateral rectus recession (9-10 mm recession) vs. contralateral recess-resect (5-6 mm recess, 4-5 mm resect). Mean follow up after the reoperation was 32 months. Success rate was 73% in the LR group and 80% in the RR group. The difference was not significant. Rate of stereopsis was similar in both groups. The author suggests that lateral rectus recession is adequate to correct 20-25 diopters of recurrent exotropia.

Preoperative Factors Predicting the Surgical Response of Bilateral Lateral Rectus Recession Surgery in Patients With Infantile Exotropia

Jason C. S. Yam, Gabriela S. L. Chong, Patrick K. W. Wu, Ursula S. F. Wong, et al
J Pediatr Ophthalmol Strabismus 2013; 50:245-250 (July/August)

A retrospective study of 50 patients with infantile exotropia who had bilateral lateral rectus recessions was performed. The study analyzed preoperative parameters such as age of onset, age at surgery, interval between onset and surgery, preoperative deviation, refractive error, anisometropia, amount of surgery performed, intermittent or constant exotropia, presence of A or V pattern. The authors concluded that surgical response decreases over time due to an exotropic drift. When applying the surgical dose, one should consider both the exotropic drift and the preoperative deviation.

Comparison of bilateral lateral rectus recession and unilateral recession resection for basic type intermittent exotropia in children.

Lihua Wang, Qizheng Wu, Xiangyun Kong, Zhiwei Li. Br J Ophthalmol July 2013; 97: 870-873.

This study retrospectively evaluated 85 patients between the ages of 3-15 years with basic type exotropia who underwent surgery, either bilateral lateral rectus recession or recession resection surgery. Based on binocular fixation preference testing, patients with alternative fixation were selected for BLR surgery; otherwise the non-fixating eye was selected for R&R surgery. Thirty eight patients had BLR surgery and 47 patients in the R&R group. Outcomes early did not vary between the two groups. Long term success was higher in the R&R group; the undercorrection rate was lower in the R&R group; the overcorrection rate was the same between the two groups. The limitations of this study include the fact that it is retrospective and the sample size is small as well as a short followup period.

Inferior oblique myectomy for upshoots mimicking inferior oblique overaction in Duane retraction syndrome

Awadein A, J AAPOS June 2013 17;3:253-258

Typically the upshoot seen in the adducting eye of a patient with Duane syndrome is not treated with inferior oblique surgery. This study was a prospective, interventional study of consecutive patients over a 5-year period with Duane syndrome, who underwent an inferior oblique myectomy to treat upshoot. Eleven patients were included. The patients had to display a gradual elevation of the eye in adduction or have a hypertropia in primary position, to be included. Patients who displayed abrupt movements, which suggest possible muscle slippage, were not included. Minimum followup was six months (mean 8.6 months). Two patients underwent bilateral inferior oblique surgery and four simultaneously had medial rectus recessions. At final follow-up, 10/11 (91%) displayed no residual upshoot. No patient developed

prolonged inferior oblique underaction. V-patterns also improved. Mean pre- and postoperative hypertropia measured 5 prism diopters and 1 prism diopter respectively. It is important to note that only 17 of 59 (29%) of patients with Duane syndrome and upshoot who were seen during the study period met the inferior oblique criteria for inclusion (six families declined surgery). Therefore preoperative selection is critical when considering this surgical technique to correct Duane syndrome upshots.

Bilateral lateral rectus muscle recession with medial rectus pulley fixation for divergence excess intermittent exotropia with high AC/A ratio

Choi HY and Jung JHJ, AAPOS June 2013 17:3;266-268

Over a four-year period, seven consecutive patients with an exodeviation ≥ 10 prism diopters (PD) more at distance than at near and with a high AC/A ratio underwent bilateral lateral rectus muscle recessions and pulley posterior suturing on both medial rectus muscles. Five of the seven patients achieved successful results (shrinking of the distance-near disparity to < 10 PD and a near or distance angle < 10 PD). One patient required a bifocal to correct a postoperative esotropia at near. Followup was at least 1 year. The preoperative evaluation included a 1 hour patch test, and near measurements with +3.00 D lenses. This study had a small sample size and was nonrandomized. Also all patients had a residual exophoria or intermittent exotropia. These could potentially worsen over time.

Changes in refractive error and anterior segment parameters after isolated lateral rectus muscle recession

Noh JH, Park KH, Lee JY et al, J AAPOS June 2013 17:3;291-295

The authors evaluated the short-term effect of isolated lateral rectus muscle recession on refractive error, corneal measurements, anterior chamber depth, and volume. This was a 9-month prospective study of consecutive patients. Measurements were performed before surgery, and 1 week and 1 month after surgery. Patients with prior eye surgery were excluded, as were those with sensory strabismus or an inability to maintain reliable fixation. The study includes 24 eyes of 24 patients with a mean age of 8 years. The article states that the conjunctival incision was on the muscle insertion. One week after surgery, there were statistically significant changes in spherical equivalent, horizontal and mean keratometry, corneal astigmatism, anterior chamber volume, and both central and peripheral anterior chamber depth. At the one month followup, these changes became progressively smaller, with the exception of spherical equivalent which persisted. Flattening in corneal power in the horizontal meridian with a myopic shift was found at 1 week after surgery. At one month after surgery there was subsequent steepening of corneal power in the vertical meridian. The authors speculate these changes are based on scleral malleability but that this would not explain the transient nature of the findings. Anterior chamber depth and volume were shallowed. Alteration of ciliary body circulation and lenticular curvature are postulated as the

cause. The authors suggest longer followup to see if the myopic shift completely returned to baseline. Future studies might also look at the type of conjunctival incision to see if this plays any role in these changes. Muscle reattachment technique, and the tightness of suture tying might also play a role.

Surgical Outcomes of Medial Rectus Recession in Esotropia with Cerebral Palsy

Dae Joong Ma, Hee Kyung Yang, Jeong-Min Hwang, *Ophthalmology* April 2013;120:663-667

This is a retrospective cohort study involving 30 patients with esotropia and cerebral palsy and 60 age-matched esotropes without cerebral palsy (CP) who underwent a unilateral or bilateral medial rectus muscle resection.

The purpose of the study is to determine the outcome of a reduced amount of medial rectus muscle recession in esotropes with cerebral palsy and to compare the surgical outcomes with that of normal controls. The surgical amount of medial rectus muscle recession was reduced by 1mm per muscle in patients with CP. Research was performed at the Seoul National University College of Medicine, Seongnam, Korea.

Conclusions: The main outcome measures were success rates, surgical response, cumulative probabilities of success, and factors affecting surgical responses evaluated by generalized linear mixed models. Even with reduced amount of recession, esotropes with CP show a greater surgical response to medial rectus muscle recession than did those without cerebral palsy. The incidence of late overcorrection was significantly higher compared with that of patients without CP.

Outcomes of surgery in children with early-onset exotropia

S Y Suh; M J Kim; J Choi; S-J Kim *Eye*; July 2013; 27(7): 836–40

This was a retrospective chart review of o evaluate the sensory and motor outcomes of patients undergoing surgery for early-onset exotropia, and to compare differences between constant (XT) and intermittent exotropia (X(T)) at presentation. The medical records of 45 patients with a reported onset of exotropia before 1 year of age were reviewed. The mean age of onset of exodeviation was 9.3 ± 3.8 months. Mean age at first visit was 3.7 ± 2.3 years and mean age at first surgery was 4.5 ± 2.4 years. The mean postoperative follow-up was 17.3 months (range, 6–37 months). Of the 45 patients, 67% showed alignment within ± 10 PD at the final visit. Gross stereopsis on the Titmus fly was achieved in all 34 testable patients, and stereopsis of at least 60 seconds of arc was achieved in 10 patients (29%). Eleven patients were included in the XT group and 34 patients in X(T) group. Of the seven XT patients who could have sensory testing performed, 1 of 7 (14%) had stereopsis greater than 60 seconds of arc. The authors conclude that patients with a history of exotropia presenting in infancy can achieve reasonable motor and sensory outcomes after strabismus surgery. Please note that these patients may have had intermittent exotropia in infancy, not (constant) infantile exotropia, and patients with neurological disease were excluded. A critique of this study was that parental reporting was used to determine age of exodeviation onset.

Botulinum toxin injections combined with or without sodium hyaluronate in the absence of electromyography for the treatment of infantile esotropia: a pilot study

J Chen; D Deng; H Zhong ; X Lin, et al. *Eye*. March 2013;27(3):382-6.

In this prospective randomized study, the authors evaluate the feasibility and safety of botulinum toxin type A (BTA) injections with or without sodium hyaluronate for the treatment of infantile esotropia. Forty-seven patients with infantile esotropia who were ages 12-81 months were randomly divided into two groups. In both groups, the patients received 2.5- 3.75 units BTA into both medial rectus muscles, injected 5-10 mm posterior to the muscle insertion. Injections were performed under general anesthesia without electromyography. In one group, the BTA was mixed with sodium hyaluronate. Alignment and complications were compared at 6 months. Alignment within 10 PD of orthotropia was present in approximately one-third of patients 6 months after injections (30.4% in the BTA+ sodium hyaluronate group vs 37.5% in the BTA group). Ptosis of 2-3 mm was present more often in the BTA group (20.8%) than in the BTA + sodium hyaluronate group (2.2%; $P=0.008$). The authors conclude that the addition of sodium hyaluronate decreases the frequency of complicated ptosis, and they speculate that sodium hyaluronate decreases diffusion of BTA to other muscles.

Three Horizontal Muscle Surgery for Large-Angle Infantile or Presumed Infantile Esotropia Long-term Motor Outcomes

Klio I. Chatzistefanou; Ioannis D. Ladas, Konstantinos D. Droutsas, Cryssanthi Koutsandrea, et.al. *JAMA Ophthalmol*. August 2013;131(8):1041-1048.

In this study, the authors analyzed the short and long term motor outcomes of bimodal rectus recession and one lateral rectus resection for large angle esotropia, defined as 50Δ or greater. The short-term (8 weeks) and long-term motor outcomes of one hundred ninety four consecutive patients with presumed congenital esotropia were studied. Motor success was defined as within $\pm 10 \Delta$ of orthotropia. The median age of patients at surgery was 2.7 years and the median follow-up was 4.5 years. The mean preoperative deviation was 68.2Δ . Seventy nine percent were successfully aligned at the 8-week postoperative evaluation and successful alignment decreased to sixty two percent at the last follow-up visit or prior to reoperation. Early versus late outcomes were compared and revealed a higher rate of late overcorrections (5.15% vs 24.1%, respectively; $P = .001$) but the same rate of undercorrections (15.4% vs 15.1%; $P = .85$). The presence of amblyopia, high hyperopia, or the total amount of millimeters of surgery did not influence surgical outcome but the presence of inferior oblique overaction and the magnitude of the preoperative esodeviation were associated with poor outcome. Delayed consecutive exotropia was more prevalent in the 50Δ to 69Δ range of preoperative esodeviation.

Botulinum Toxin as a Postoperative Diplopia Test – It Can Also Reduce the Angle of Deviation Prior to Surgery

Zoe Ockrim, Clifford R. Weir, James Li Yim, Marie Cleary
Strabismus. December 2013;21(4):199-202

The surgical treatment of strabismus in adults can result in intractable postoperative diplopia in a small percentage of patients. Those at risk are often identified preoperatively using prisms to simulate the postoperative deviation, however, some clinicians prefer to use botulinum toxin to reduce the angle of deviation temporarily to assess post-operative diplopia. The purpose of the study is to investigate how frequently botulinum toxin, when used as a postoperative diplopia test, reduces the angle of deviation prior to subsequent strabismus surgery.

The authors conducted a retrospective study of 39 adult patients with constant concomitant horizontal strabismus (32 had exotropia and 7 had esotropia) who had undergone botulinum toxin injections (5 units) to assess the risk of postoperative diplopia. Approximately one-third of patients (14/39) sustained a reduction of ≥ 15 prism diopters for near or distance or both, for at least 4 months when comparing the pre-injection angle with the preoperative angle of deviation. This was more common in the esotropia group (4/7 patients) than the exotropia group (10/32 patients), however the numbers particularly in the esotropia group are small. These findings suggest that when botulinum toxin is given as a postoperative diplopia test, it could also be used as an adjunct prior to strabismus surgery, particularly in patients with large angles of deviation who may not wish to have their fellow (often “better”) eye operated on.

Strabismus surgery outcomes after scleral buckling procedures for retinal reattachment

Jee Ho Chang, Amy K. Hutchinson, Monica Zhang, Scott R. Lambert,
Strabismus. December 2013;21(4):235-241

When planning surgery to correct strabismus after a scleral buckling procedure, the question arises whether to remove the scleral buckle. If the buckle is the obvious cause of the strabismus, removal of the buckle is viewed as helpful; however, removal is controversial when it is not the obvious cause of the strabismus.

The authors retrospectively investigated the strabismus surgery outcomes after scleral buckling procedure for retinal reattachment. Scleral buckles were removed from 8 patients, with no retinal redetachments occurring after removal. Success, defined as ≤ 10 prism diopters (PD) residual horizontal and/or ≤ 4 PD residual vertical deviations, was achieved in 6 of 18 eyes (33%). Scleral buckle removal was the most significant factor associated with successful surgical alignment (62.5% success with buckle removal vs. 10.0% success without buckle removal). Scleral buckle removal may have improved ocular alignment by: (1) allowing the rectus muscles to attach directly to the sclera, (2) lengthening muscles that were splayed over bulky implants, (3) lessening muscle restriction

by dissection and lysis of adhesions during removal of the buckle, (4) permitting the muscles to move more freely during the adjustment procedure; and (5) freeing an oblique tendon or muscle inadvertently incorporated in the scleral buckle. Although the success rate was higher in the adjustable suture group (50% in adjustable group vs. 14.3% in non-adjustable group), this difference was not statistically significant. The authors suggest that scleral buckles can be safely removed in select patients and their removal may improve ocular alignment following strabismus surgery.

Role of Inferior Rectus Botulinum Toxin Injection in Vertical Strabismus Resulting from Orbital Pathology

Howard J. Bunting, Emma L. M. Dawson, John P. Lee, and Gillian G. W. Adams
Strabismus. September 2013;21(3):165-168

The study consists of a retrospective review of 13 patients undergoing inferior rectus botulinum toxin injection for vertical strabismus due to orbital pathology: 6 with idiopathic orbital inflammatory syndrome (IOIS) including myositis, 3 with previous orbital wall fractures, 1 post-optic nerve sheath Schwannoma resection, 1 with lymphoma, 1 with metastasis, and 1 post-superior ophthalmic vein hemorrhage. A beneficial effect with inferior rectus botulinum toxin was obtained in 9/13 (69%) patients. Resolution or improvement occurred in 4/6 (67%) patients with IOIS. Resolution was obtained in the patients with optic nerve sheath Schwannoma resection, and superior ophthalmic vein hemorrhage. Improvement was noted in the patients with lymphoma and with a metastasis. However, in patients with orbital wall fractures, only 1 of 3 patients obtained improvement. Benefit appeared independent of the size of vertical deviation, with 4/6 (67%) showing improvement with a pre-toxin angle 4-12 PD, and 5/7 (71%) improving with a pre-toxin angle 16-25 PD. Eleven patients received only 1 injection, one patient received 2, and another had 8 injections. At final follow-up functional cure with botulinum toxin was achieved in 5/13 (38%) patients, functional improvement was evident in 4/13 (31%), and the remaining 4 patients (31%) gained minimal or only temporary amelioration of diplopia.

The authors conclude that vertical strabismus secondary to a range of orbital conditions, particularly inflammatory, often can be successfully managed by inferior rectus botulinum toxin injections.

Improvements in patients' quality-of-life following strabismus surgery: evaluation of postoperative outcomes using the Adult Strabismus 20 (AS-20) score.

P. Glasman, R. Cheeseman, V. Wong, J. Young, et al.
Eye (Basingstoke). 2013 November;27(11):1249-53

The authors utilized the AS-20 questionnaire, an instrument developed to measure the quality of life in adult patients with strabismus. The questionnaire involves twenty questions answered on a five-point scale. The investigators use

this instrument to study the quality of life improves following strabismus surgery in eighty-six patients. They found that strabismus surgery gives a highly significant improvement in the quality of life scores. Larger changes in deviation were associated with higher gains in quality of life in smaller post-operative angles were also correlated with greater improvement in the quality of life scores. This instrument is readily available and can be used to quantify the quality of life improvement in all of our post-operative patients.

Resolution of hypertropia with correction of intermittent

exotropia Michael C Struck, Timothy J Daley,,*British Journal of Ophthalmology* 2013;97:10 1322-1324 October 2013

The authors report on the spontaneous resolution of hypertropia in a subset of patients with preoperative exotropia and hypertropia who underwent surgery for exotropia alone. The study is a retrospective case series. Charts were reviewed for a single surgeon to identify all patients less than 18 years of age who underwent surgical treatment for intermittent exotropia from 1/2002 to 12/2012. 17 patients with intermittent exotropia noted to have 5 prism diopters or greater of vertical deviation in primary position on their preoperative evaluation were included in the study. Exclusion criteria included previous strabismus surgery, dissociated vertical deviation, paretic or restrictive strabismus, neurologic disorders, visual acuity worse than 20/30, anisometropia greater than 2.75 diopters, and hypermetropia greater than 3.75 diopters. Preoperative measurements were significant for a relative absence of a vertical deviation at near. Surgical treatment included bilateral lateral rectus recession (n=4) or unilateral lateral rectus recession and medial rectus resection (n=13). All patients were found to have a complete resolution of any vertical deviation in any field of gaze. The authors propose that the measured distance hypertropia is not created by a true vertical or cyclovertical muscle imbalance. They believe the reduction in the hypertropia at near fixation predicts its resolution with horizontal muscle surgery. Therefore these patients should not have vertical surgery to address the coincident vertical deviation.

Fibrin Glue for Closure of Conjunctival Incision in Strabismus Surgery A report by the American Academy of Ophthalmology

Michael B. Yang, Michele Melia, Scott R. Lambert, Michael F. Chiang,
Ophthalmology September 2013; 120:1935-1941

The purpose of this study is to evaluate the severity of postoperative inflammation, degree of patient discomfort, and adequacy of wound closure associated with using fibrin glue as compared with sutures.

Literature searches of PubMed and Cochrane Library were performed. Five studies compared fibrin glue with sutures for closure of limbal conjunctival incisions in fornix incisions during strabismus surgery.

Conclusions: Studies in the literature suggest that the off-label use of fibrin glue to close limbal conjunctival incisions in strabismus surgery resulted in less postoperative inflammation and required shorter operating time compared with sutures; however, THE USE OF FIBRIN GLUE INCREASED THE PERCENTAGE OF WOUNDS REQUIRING SUBSEQUENT REPAIR WITH SUTURES. Comments: Figure 1, page 1936 shows a nice view of the blood coagulation cascade and where the fibrin factor fits in the cascade.

Surgical correction of superior oblique palsy: a case series and guideline for surgical choice

Gillian Coyle, Caroline J. Macewen, Br Ir Orthopt J 2013; 10: 23–27

The aim of this retrospective case series is to simplify decision-making for surgical management of superior oblique palsy. Forty-four patients having a total of 50 procedures were included. Regardless of the amount of hypertropia in primary gaze, each patient underwent a single muscle procedure except in cases of bilateral superior oblique palsy. A simple algorithm was used to determine which muscle procedure to perform. Inferior oblique disinsertion was performed for hypertropia in primary gaze and inferior oblique overaction. Superior oblique tuck was performed for hypertropia and underaction of the superior oblique. Inverse Knapp procedure was performed for hypertropia and limited depression in adduction and abduction. Harada-Ito was performed for cases primarily involving torsion. The range of hypertropic correction was 4-28^Δ. Six patients required a second surgery and there were no overcorrections. Torticollis was not addressed in this study. The authors advocate for surgery on 1 muscle for hypertropia in unilateral cases of superior oblique palsy regardless of the size of the hyperopia in primary gaze.

The efficacy of botulinum toxin treatment for children with persistent esotropia

Scott R. Lambert, Marla J. Shainberg, Am Orthopt J 2013;63:24-28

This retrospective study reports results botulinum toxin injection of one extraocular muscle as a third intervention for the treatment of persistent esotropia following bilateral medial rectus recession and bilateral lateral rectus resection. Four of the 5 patients identified had infantile esotropia and the 5th patient had partial accommodative esotropia. Each patient received an injection of 3-5 units of botulinum toxin in 1 medial rectus muscle. At last follow-up (range 14-79 months), 2 of the 5 patients had $\leq 8^{\Delta}$ of residual esotropia. Two of the other 3 patients with 18-35^Δ of persistent esotropia underwent a 3rd eye muscle surgery and developed consecutive exotropia. This is a small sample size. The author concludes that although only a minority of patients had successful motor

alignment with botulinum toxin, there were no overcorrections which may occur with further incisional eye muscle surgery.

Selection of patients and results of 25 years of topical anesthesia and adjustable suture surgery

Malcom L. Mazow, Jack Fletcher , Am Orthopt J 2013;63:85-91

This retrospective study compares the lead author's results with two techniques of adjustable suture extraocular muscle surgery. Group 1 was comprised of 123 patients who underwent surgery using topical anesthetic plus IV sedation/analgesia (monitored anesthesia care) and suture adjustment was performed in the operating room during the primary procedure. Group 2 was comprised of 60 patients who underwent surgery with general or retrobulbar anesthetic and suture adjustment was performed after the primary procedure either on the same day or 1-day post-operatively. Patients considered good candidates for Group 1 had acquired restrictive strabismus (excluding previous scleral buckle and thyroid with poor "spring back muscle force"), good ductions, good fixation with each eye and no previous extraocular muscle surgery. The protocol used for Group 1 included small IV doses of versed and fentanyl and a dose of topical xylocaine gel in the pre-operative holding area followed by IV propofol and additional xylocaine gel in the operating room during the incisional surgical procedure. The propofol was stopped 5-8 minutes before suture adjustment. A fixation target was mounted on the ceiling of the operating room so that patients could remain supine except for cases involving torsion in which the patient sat upright in the operating room for suture adjustment. Successful alignment to within 10^Δ of orthophoria in primary gaze was achieved in 86.2% of patients in Group 1 and 86.7% of patients in group 2. Statistical analysis to determine statistical significance was not performed, but the means of the surgical results appear to be clinically similar between the 2 groups.

Effectiveness of medial rectus advancement alone or in combination with resection or lateral rectus recession in the management of consecutive exotropia

Kasi SK, Tamhankar MA, Pistilli M, et al, J AAPOS October 2013;17:465-470

There is no consensus as to the optimal surgery for consecutive exotropia. The authors evaluated the effectiveness of medial rectus advancement alone or in combination with resection or lateral rectus recession or both. Consecutive patient with at least 3 months of followup were included. The mean age of the 46 patients was 43 +/- 15.5 years. The mean exotropia was 32 +/- 18 PD at distance and 38 +/- 15 PD at near. The general surgical principle was that medial rectus strengthening would collapse the distance/near disparity while total dosing was based on the distance deviation. At a mean follow-up of 2.5 years, 33 patients (72%) achieved good postoperative alignment (within 10 PD of orthophoria). A

pseudotendon was encountered intraoperatively in 13%. There was a trend towards preoperative adduction deficits being associated with prior medial rectus recessions ≥ 5 mm. Improvement in the adduction deficit was noted in 91% (30/33). Over half of the patients (57%) received a postoperative adjustment. The larger the preoperative deviation, the greater the risk of patient's having a poor result (1.8x greater risk of a fair or poor result for every increase of 10 PD in the preoperative deviation). Questionnaire results showed psychosocial improvement, which interestingly did not correlate with surgical outcomes, but did correlate with the magnitude of change in the deviation.

Esotropia surgery in children with Down syndrome

Perez CI, Zuazo F, Zanolli MT, et al, J AAPOS October 2013;477-479

Surgical treatment of children with esotropia and Down syndrome was compared with age-matched controls. A retrospective review of 11 years of charts was performed and 3 age-matched controls were selected for every 2 patients with Down syndrome. Data from 17 children with Down syndrome and esotropia who underwent medial rectus recessions OU was evaluated. There was a mix of congenital and acquired esotropia patients in both the Down syndrome and age-matched controls (n=27). Results were similar in the two groups in terms of age at surgery, followup, preoperative esotropia, surgical dosing, & preoperative cycloplegic correction. At six months follow-up, surgical success was achieved in 76% of patients with Down syndrome and 85% of control patients. At final followup, surgical success in Down syndrome patients remained the same, while the success in the control group decreased to 78%. Many studies lump Down syndrome patients with other neurodevelopmental disorders and report that these patients are often overcorrected surgically. The authors feel that Down syndrome patients have comparable results to the general surgical population. This was a small retrospective study with possible selection bias.

Rectus muscle plication using an adjustable suture technique

Velez FG, Demer JL, Pihlblad MS, et al, J AAPOS October 2013;17:480-483

Muscle plication is less invasive than resection, more easily reversible, eliminates the need for rectus muscle disinsertion, and may compromise anterior segment circulation to a lesser degree. The authors report a novel technique to combine a rectus muscle plication with an adjustable suture. Five adult patients underwent surgery with a mean follow-up of 3.4 months. The lateral rectus was plicated in 3 patients and the superior rectus in 2 patients. Two of the five patients required adjustment. All had satisfactory alignment postoperatively (within 6 PD of orthotropia for horizontal deviations and 2 PD for vertical deviations). No cosmetic deformity such as a conjunctival lump was noted. The authors note that reoperation on plicated muscles does not allow separation of the plicated portion because it joins in a fibrous union with the overlying muscles. This study was not

randomized, was small, and did not follow patients for a lengthy period. The study purpose was mainly to describe a new surgical technique.

The effect of a temperature-sensitive poloxamer-alginate-CaCl₂ mixture after strabismus surgery in a rabbit model

Ryu WY, Jung HM, Roh MS et al, J AAPOS October 2013;17:484-489

Using a rabbit model, the authors evaluated the effectiveness of a poloxamer-alginate mixture (PA) as an antiadhesive agent. It has a high molecular biocompatibility, and its temperature-sensitive characteristics allow it to form a solution at room temperature and then change immediately into a gel at body temperature. The authors operated on the superior recti of 36 eyes (18 rabbits). One eye received application of the PA mixture (PA group) between the recessed superior rectus and the conjunctiva, and between the superior rectus and the sclera, and the other eye received normal saline subconjunctivally after the recession. The pathologist was masked to treatment group. At 1 week after surgery, adhesions between the superior rectus and both the conjunctiva and sclera were significantly less in the PA group than in the control group. This persisted to 4 weeks post-surgery but not to a statistically significant degree. However the differences were not statistically significant. Inflammation was similar between the two groups on day 1 and 1 week postop, but the PA group inflammation was significantly less at week 4. The PA group also showed less degree of late fibrosis. Rabbit eyes have anatomical differences when compared to human eyes, such as less subconjunctival tissue, so future human trials would be needed to see if similar results were obtained.

Three-muscle surgery for very large-angle constant exotropia

Li JH and Zhang LJ, J AAPOS December 2013;17:578-581

The authors report their results of surgery on only three horizontal muscles to treat very large exotropias. Consecutive patients with exotropia ≥ 120 prism diopters were included. An R&R was performed on the nonfixing eye, combined with a lateral rectus recession on the fixing eye. Twenty-three patients were included. No patient had restrictions on forced duction testing and some adjustable sutures were used. Mean followup was 8.1 \pm 1.4 months. The goal of 10 PD esotropia was achieved in 19/23 (82.6%). There were no cases of consecutive esotropia greater than 10 PD. All residual deviations were exotropic. The final outcome averaged 5 PD exotropia at near and distance. Limitation of abduction was only seen significantly on the day of surgery and improved by day 1. At last followup the abduction limitation averaged 0.8mm in the fixing eye and 1.3mm in the nonfixing eye. No patient had binocular vision before or after surgery and no patient developed diplopia in primary gaze. Two patients had diplopia on extreme lateral gaze. 22/23 patients were satisfied with their cosmetic outcome. Postoperative measurements were unmasked.

Management of large V-pattern exotropia with minimal or no inferior oblique overaction

Awadein A and Fouad HM, J AAPOS December 2013;17:588-593

For patients with V-pattern exotropia and minimal or no inferior oblique overaction, the authors compared bilateral lateral rectus recessions with superior transposition one full tendon width (BLRup), versus BLR recess with inferior oblique myectomy OU (BLRIO). Consecutive patients over a six-year period were reviewed retrospectively. During the study period, the surgical option was not randomized. More patients underwent BLRIO in the later part of the study. 34 patients had sufficient follow-up to be included in the study. 16 underwent BLRup and 18 underwent BLRIO. The mean age at surgery was 10.6 +/- 3.7 years. The mean follow-up was 8.2 +/- 3.1 months. In the BLRup group, 56% of patients had success at follow-up, 31% had undercorrections and 13% had overcorrections. In the BLRIO group, 72% had a successful outcome, 22% had overcorrections and 6% had undercorrections. These differences were statistically significant. BLRup group had a greater drift at six months (P = 0.04). The BLRup group collapsed the V-pattern in 44% of cases and no cases developed an A-pattern (overall 16 PD reduction). In the BLRIO group 78% of patients had collapse of the V-pattern, but the other 22% developed a consecutive A-pattern (overall 25 PD reduction). In both groups, the amount of V-pattern correction was significantly correlated to the size of the preoperative V-pattern. Continued improvement in collapsing the V-pattern was noted out to 3-6 months. Two patients in the BLRIO group developed bilateral inferior oblique underaction. Fundus excyclotorsion was seen in 8 patients postoperatively in the BLRup group (compared with 2 preoperatively). Five patients in the BLRIO group developed fundus incyclotorsion postoperatively. A formal deviometer or orthopedic goniometer was not used to measure up- and downgaze positions, which would have made measurements more precise. The study had small groups and surgical groups were not randomized.

Risk factors influencing the outcome of strabismus surgery following retinal detachment surgery with scleral buckle

Rabinowitz R, Velez FG and Pineles SL, J AAPOS December 2013;17:594-597

The authors looked at factors that contribute to successful motor outcome in the primary position after strabismus surgery in patients with a scleral buckle. The authors reviewed 15 years of surgical records retrospectively. 25 patients were included. Four had prior strabismus surgery. Most underwent adjustable suture surgery. The average time between retinal detachment repair and onset of diplopia was 4 months. 19 patients had mixed vertical and horizontal surgery. 13 of the 25 patients underwent additional strabismus surgery. 9 of the 25 patients had a successful outcome after one surgery and another 9 had a successful motor outcome after additional procedures. Of the 21 patients with fusion potential, 13 obtained a good sensory outcome and 8 had persistent diplopia. Smaller total deviations, smaller horizontal deviations, and less restriction on forced duction testing were associated with a better motor outcome after the first

surgery. Removal of the scleral buckle did not improve motor success results. This retrospective study included patients from multiple different surgeons. There was a wide range of ages and follow-up. Some patients who needed additional surgeries declined which would affect final results.

Biomechanics of superior oblique Z-tenotomy

Shin A, Yoo L and Demer JL, J AAPOS December 2013;17:612-617

The authors investigated the biomechanical effect of various doses of Z-tenotomy of the superior oblique tendon in a bovine tendon model. They created a custom, horizontally mounted microtensile load cell. Each specimen was subjected to increasing tension until it ruptured. Z-tenotomy was performed at 0%, 20%, 40%, 50%, 60% and 80% tendon width from each tendon margin. The control material was isotropic latex rubber. For the controls, there was a linear trend of decreasing maximum force with increasing percentage Z-tenotomy due to the combined effect of tensile and shear forces. For the 30 superior oblique specimens tendon failure declined with a parabolic shape for Z-tenotomy less than 50%. For more than 50% Z-tenotomy, superior oblique force transmission was reduced to a roughly constant value of nearly zero. These results suggest that the superior oblique tendon is not an isotropic material like latex. Tenotomy over 50% is mechanically very nearly the same as complete, unguarded tenotomy. An extraocular tendon has strong parallel fibers aligned longitudinally with thin transverse fibers and a small amount of viscous extrafibrillar matrix filled between fiber bundles in the transverse direction. Extraocular muscles appear to have poor transfer of shear forces with substantial force decoupling between transfer layers. This explains why a >50% Z-tenotomy leaves only a minimal shear force mechanism to transmit forces. These experiments are in vitro and do not account for sheaths or other tissues present in vivo. Although according to this study any tenotomy of >50% would be equivalent, clinical results do not necessarily support this data in other papers.

Analysis of Risk Factors for Consecutive Exotropia and Review of the Literature

Yurdakul NS, Ugurlu S. J Pediatr Ophthalmol Strabismus 2013; 50(5):268-273

This retrospective study reviewed 101 patients charts who underwent comitant esotropia surgery to look for possible risk factors for the development of consecutive exotropia. The results were compared to previous studies found in the literature. Risk factors in this study found to be associated with consecutive exotropia included limitation of adduction postoperatively, amblyopia, and asymmetric surgery. Limitation of adduction was found in 29.8% of the exotropia group; none in the no exotropia group. Assymmetric surgery had been performed in 61.7% of the exotropia group and only 9.3% of the no exotropia group. It was observed that consecutive exotropia may take months or years to develop. The

mean interval between initial surgery and the onset of consecutive exotropia was 11 months (range 0 to 126 months). The authors recommend treatment of amblyopia prior to surgical intervention and tailoring of the type and amount of surgery to avoid postoperative limitation of adduction.

Surgical Results of Consecutive Exotropia

Rajavi Z, Feizi M, Mughadasifar H, et al., J Pediatr Ophthalmol Strabismus 2013; 50(5):274-281

This interventional case series study of 40 patients with consecutive exotropia aimed to determine success rates of different surgical procedures. Risk factors of surgical failure was also examined. Surgical methods were based on medial rectus function: Lateral rectus weakening for normal function, medial rectus strengthening for limited function (-1 to -3), or a combined procedure when correction of each of these surgeries was less than the amount of deviation. Satisfactory alignment (8 prism diopter or less) was achieved in 83% of the medial rectus strengthening, 81% of lateral rectus weakening and 57% of combined procedure patients. More preoperative exodeviation was the only risk factor of surgical failure.

Risk Factors Predicting the Need for Additional Surgery in Consecutive Esotropia

Choi, YM, Lee JY, Jung JH, Kim SH, Cho YA, J Pediatr Ophthalmol Strabismus 2013;50(6):335-339

The goal of this study was to evaluate risk factors predicting surgical treatment of consecutive esotropia after surgery for intermittent exotropia. Surgery for esotropia was performed in patients with more than 10 prism diopters esodeviation persisting a minimum of 6 months. A retrospective chart review was performed of patients who underwent exotropia surgery. 52 patients with consecutive esotropia were included in the study of which 35 were in the nonsurgical group and 17 patients were in the surgery group. Age, gender, lateral incomitancy, and vision were not found to be risk factors for future surgery in these patients. A larger esodeviation at one month postoperatively was a risk factor for requiring surgery for consecutive esotropia.

Bupivacaine Injection Remodels Extraocular Muscles and Corrects Comitant Strabismus

Joel M. Miller, Alan B. Scott, Kenneth K. Danh, Dirk Strasser,
Ophthalmology December 2013; 120(12):2733-2740

This is a prospective, observational clinical series. This study was designed to evaluate the clinical effectiveness and anatomic changes resulting from bupivacaine injection into extraocular muscles to treat comitant horizontal strabismus.

Participants: Thirty-one comitant horizontal strabismus patients.

Methods: Nineteen patients with esotropia received bupivacaine injections in the lateral rectus muscle, and 12 patients with exotropia received bupivacaine injections in the medial rectus muscle. Sixteen of these, with large strabismic angles, also received botulinum type A toxin injections in the antagonist muscle at the same treatment session. A second treatment was given to 13 patients who had residual strabismus after the first treatment.

Conclusions: Bupivacaine injection alone or together with botulinum toxin injection in the antagonist muscle improves eye alignment in comitant horizontal strabismus by inducing changes in the rectus muscle structure and length.

11. ANTERIOR SEGMENT

Intraobserver reliability of contact pachymetry in children

Weise KK, Kaminski B, Melia M, et al *J AAPOS* April 2013;17:144-148

This study evaluated intraobserver reliability of a handheld contact measurement of central corneal thickness. The cohort of children was normal and ranged in age from newborn to 17 years. There were 1933 subjects (3494 eyes) with a mean age of 7.5 years. The mean CCT was 559 μm with a mean absolute value of the test-retest difference of 6.1 μm . In-office measurements were more variable than those taken under anesthesia, but this difference did not persist, after adjusting for the difference in CCT magnitude in the two groups. More younger children, (with thinner OCTs) were measured under anesthesia. As the CCT increased, the test-retest difference increased, as did the coefficient of repeatability. There was no evidence of an effect on testing order for the 3 measurements taken. Age, sex, race, and examination setting did not affect the magnitude of test-retest differences, after adjusting for laterality. Thinner cornea measurements were more reliable, probably because of off-center measurements. Off-center measurements are more likely to be thicker, causing greater variability. Thicker measured CCT values had larger test-retest differences than thinner measured CCT values. The authors recommend disregarding measurements when the reported standard deviation is $>5\mu\text{m}$. Also when the first measurement is $>575\mu\text{m}$, a second measurement should be taken.

Corneal thickness measured by Scheimpflug imaging in children with Down syndrome

Aslan L, Aslankurt M, Yuksel E, et al. J AAPOS April 2013;17:149-152

Corneal changes are more common in Down syndrome patients. Accurate corneal thickness measurements can be obtained with the Pentacam Scheimpflug imaging system. This system captures dozens of images quickly. The entire cornea is measured. This system was used to measure full corneal thickness, including central and paracentral areas in healthy individuals and Down syndrome patients. Prospective evaluation of 31 Down syndrome and healthy age-matched controls was performed. Four Down syndrome patients were excluded because of poor image results. CCT values were thinner in Down syndrome patients. CCT values of $<500\mu\text{m}$ (59.2%) and $<450\mu\text{m}$ (18.5%) in Down syndrome patients were obtained, versus 37.8% and 5.4% respectively in controls. Thinnest point (TP) values were also less in the Down syndrome patients (62.9%/21.1% versus 43.2%/10.8%). Down syndrome patients had CCT measurements, which averaged $45\mu\text{m}$ less and TP values which averaged $51\mu\text{m}$ less than controls. Mean corneal volume was less as well ($56.2\mu\text{m}^3$ versus $61.3\mu\text{m}^3$). Pentacam software analysis revealed subclinical keratoconus in 21.1% of Down syndrome eyes versus 1.35% of eyes in the control group. Down syndrome eyes showed the TP most commonly centrally (52%) and inferotemporally (38%). CCT measurements are important because they can affect IOP measurements. Not only are CCT measurements often abnormal in Down syndrome patients, but these patients are at higher risk for keratoconus. Early detection can lead to potential earlier cross-linkage treatment. This rapid non-contact method of corneal evaluation may have utility, especially in low cooperation individuals, such as Down syndrome patients.

Clinical Correlations of Dry Eye Syndrome and Allergic Conjunctivitis in Korean Children

Tae hyung Kim, Nam ju Moon, J Pediatr Ophthalmol Strabismus 2013; 50:124-127 (March/April)

Children with dry eyes and allergic conjunctivitis were investigated their clinical patterns were evaluated. The study found that children with allergic conjunctivitis had shorter tear breakup time, and those with multiple allergens had shorter times than those with single allergens. Children do not often complain of dry eyes so its important to remember that this can occur and treat children appropriately.

Corneal Cross-Linking as a Treatment for Keratoconus Four-Year Morphologic and Clinical Outcomes with Respect to Patient Age

Riccardo Vinciguerra, Mario R. Romano, Fabrizio I. Camesasca, Paolo Vinciguerra, *Ophthalmology* May 2013;120:908-916

This is a retrospective, single-center, nonrandomized clinical study that takes place in Italy. The purpose of the study is to report the four-year outcome of corneal cross-

linking (CXL) for progressive keratoconus in a population of different age groups. Four hundred consecutive eyes treated with corneal cross-linking for progressive keratoconus in April 2006 and April 2010 are included in this study.

Intervention: After removal of corneal epithelium, the cornea was irrigated for 30 minutes with a solution of 0.1% riboflavin and 20% dextran, followed by irradiation with an ultraviolet A light for 30 minutes.

Comparative analysis included 400 eyes of 301 patients. The patients studied were stratified in 3 groups; Group A: patients younger than 18 years of age, group B: patients 18-29 years of age, group C patients 30-39 years of age, group D patients greater than 40 years.

Conclusions: Outcomes stratified by age indicate the efficacy of corneal cross-linking in stabilizing the progression of ectatic disease and keratoconus in all age groups. The results indicated better functional and morphologic results in the population between 18 and 39 years of age.

Comment: Today, most corneal cross-linking research has been done in Europe and South America. Randomized trials are being developed in the United States.

Evaluation of Moxifloxacin 0.5% in Treatment of Nonperforated Bacterial Corneal Ulcers: A Randomized Controlled Trial

Namrata Sharma, Manik Goel, Shubha Bansal, Rasik B. Vajpayee, *Ophthalmology* June 2013;120:1173-1178

This is a randomized, controlled, equivalence clinical trial performed primarily in New Delhi, India. The purpose of the study is to compare the equivalence of Moxifloxacin 0.5% with a combination of fortified cefazolin sodium 5% and Tobramycin sulfate 1.3% eye drops in the treatment of moderate bacterial corneal ulcers.

Microbiologically proven cases of bacterial corneal ulcers were enrolled in the study and were allocated randomly to 1 of 2 treatment groups. Group A was given a combination of therapy of fortified cefazolin and tobramycin. Group B was given monotherapy of moxifloxacin 0.5%. The primary outcome variable for this study was percentage of the ulcers healed at 3 months. The secondary outcome variables were best-corrected visual acuity and resolution of infiltrates.

Conclusions: Corneal healing using 0.5% moxifloxacin monotherapy is equivalent to that of combination therapy using fortified cefazolin and Tobramycin in the treatment of moderate bacterial corneal ulcers.

Transepithelial corneal collagen crosslinking for progressive keratoconus in a pediatric age group

Abdelrahman G. Salman *J Cataract Refract Surg.* August 2013;39(8):1164-70

The purpose of the study was to evaluate the effectiveness of transepithelial corneal collagen crosslinking (CXL) in children with keratoconus. In this prospective study, the right eye was treated with transepithelial corneal collagen crosslinking whereas the comparison left eye was treated with topical lubricants and standard care.

Transepithelial riboflavin administration spares the patient corneal epithelial debridement, but requires a special riboflavin formulation to penetrate into the

corneal stroma. After riboflavin application, the treated eye was exposed to UVA light for 30 minutes. Twenty-two patients were enrolled, ranging in age from 13 to 18 years, with a mean age of 15.7 years \pm 2.1 (SD). Eighteen of the 22 patients were boys. Five patients required conscious sedation for treatment. Prior to the study, the right and left eyes were well matched in terms of visual acuity and keratoconus parameters. Mean follow up was 12.0 \pm 3.4 months. After transepithelial CXL, the mean uncorrected distance visual acuity improved by 2.7 lines (from 0.95 \pm 0.34 logMAR to 0.68 \pm 0.45 logMAR) ($P < .05$). There was no improvement in the control group ($P > .05$). The mean simulated keratometry (K) decreased by a mean of 2.03 diopters (D); ($P < .05$), whereas the simulated K increased by a mean of 0.59 D ($P > .05$) in the control group. Preliminary results of transepithelial CXL in children with keratoconus were encouraging, with no evidence of progression of keratoconus over 12 months in the treated eyes.

Management of pediatric keratoconus – Evolving role of corneal collagen cross-linking: An update Vardhaman P Kankariya, George D Kymionis, Vasilios F Diakonis, Sonia H Yoo, Indian Journal of Ophthalmology Aug 2013 Vol. 61 No. 8

The above article is a review article detailing the role of corneal collagen cross-linking.

Table 1: Chief characteristics of published studies regarding outcomes of corneal collagen cross linking in pediatric keratoconus

Authors (year)	Subjects (eyes)	Age range (years)	Design	Documented progression	CXL technique	Outcomes	Follow-up
Soeters <i>et al.</i> (2011) ^[11]	4 (5)	10-16	Case series	Yes	Standard protocol	4 eyes were stabilized, 1 eye ended up in PKP	1 year
Arora <i>et al.</i> (2012) ^[23]	15 (15)	10-15	Prospective	No (other eye with advanced keratoconus)	Standard protocol	Stabilization	1 year
Bakshi <i>et al.</i> (2012) ^[30]	9 (9)	11-17	Retrospective	Yes	Standard protocol	Stabilization	2 years
Vinciguerra <i>et al.</i> (2012) ^[4]	40 (40)	9-18	Prospective	Yes	Standard protocol	Stabilization	2 years
Caporossi <i>et al.</i> (2012) ^[53]	77(152)	10-18	Prospective	Yes	Standard protocol	Stabilization	3 years
Chatzis <i>et al.</i> (2012) ^[61]	52 (59)	9-19	Retrospective	Yes	Standard protocol	Initial stabilization, and late progression	3 years
Magli <i>et al.</i> (2013) ^[7]	29 (37)	12-18	Retrospective, comparative	Yes	Epi on and Epi off (2 groups)	Stabilization for both groups	1 year
Buzzonetti <i>et al.</i> (2012) ^[8]	13 (13)	8-18	Prospective	No	Transepithelial CXL	No stabilization	18 months
Zotta <i>et al.</i> (2012) ^[9]	4 (8)	11-16	Case series	Yes	Standard protocol	Stabilization	3 years

With limited evidence CXL can be considered in children with progressive keratoconus. Standard epithelium of CXL protocol should be followed. Parents should be informed about the off-label nature, possibility of short lasting effect and need for re-treatment especially in very aggressive forms.

CURRENT OPHTHALMOLOGIC TREATMENT STRATEGIES FOR ACUTE AND CHRONIC STEVENS JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS

Jessica B. Ciralsky et al Current Opinion in Ophthalmology July 2013 24(4) p.321-328

Review of the ophthalmologic treatments for acute Stevens-Johnson syndrome (SJS) as well as the emerging treatment options for patients with chronic, severe ocular surface damage from the disease. Amniotic membrane transplantation (AMT) applied to the eyes and eyelids in the acute phase, preferably within the first week, of SJS can prevent scarring and visual problems that characterize the chronic phase of the disease. The severity of ocular inflammation in the acute phase does not always correlate with severity of skin and systemic involvement. It is crucial that all patients with SJS be urgently evaluated by an ophthalmologist familiar with the current management of the disease, and offered the option of AMT. Although challenging, the severe, chronic ocular problems of SJS can be at least be partially alleviated with autologous serum drops, mucous membrane grafting to replace scarred tarsal conjunctiva, specialized contact lenses (PROSE), conjunctival replacement surgery (COMET), limbal stem cell transplantation and keratoprotheses. Emerging treatments offer increased hope for those who have already suffered damage from SJS, but emphasis on preventing damage in the acute phase is most crucial.

UPDATE ON MANAGEMENT OF HERPES KERATITIS IN CHILDREN

Karen Revere et al Current Opinion in Ophthalmology July 2013 p. 336-342

Summary of the articles published in 2012 pertaining to the clinical presentation, diagnosis, and treatment of herpetic keratitis, with specific attention to the pediatric population. Herpetic keratitis has higher recurrence rate in children than adults. Recurrences are more likely to occur as stromal disease. Vision loss in children is from corneal scarring leading to deprivation and/or refractive amblyopia. Acyclovir is safe and well tolerated in children, and preferable to difficult and toxic eye-drop regimens. Immunochromatographic assay is an effective diagnostic tool to confirm diagnosis of herpes simplex virus-1 (HSV) in corneal scrapings with high specificity but poorer sensitivity. Real time PCR can be employed to follow changes in HSV viral load in patients where resistance is suspected. Delays in treatment related to misdiagnosis, as well as resistance to current antiviral therapeutics, can lead to visually devastating corneal opacification. In the pediatric population, already at risk for amblyopia, this can be especially damaging. Children are unique with regards to the way in which they manifest herpetic keratitis, making rapid diagnosis and treatment even more challenging.

Conjunctival Papilloma: Features and Outcomes Based on Age at Initial Examination

Swathi Kaliki, Sruthi Arepalli, Carol L. Shields, Kendra Klein, et.al. JAMA Ophthalmol. May 2013;131(5):585-593.

Conjunctival papilloma is a benign epithelial tumor occurring in both children and adults with varying clinical features and outcomes. This study evaluated the clinical features, treatment, and outcomes in patients with conjunctival papilloma based on age at initial examination. Ten children and adolescents and 63 adults with conjunctival papilloma. Interventions included excisional biopsy, cryotherapy, oral cimetidine, topical or injection interferon alfa-2b, and photodynamic therapy. Conjunctival papillomas are larger and more likely to be multiple in children and adolescents than in adults. Excisional biopsy and cryotherapy with or without adjuvant oral cimetidine and/or topical interferon alfa-2b provide satisfactory tumor control. Papilloma recurrence is more common in children and adolescents than in adults.

The non-invasive tear film break-up time in normal children

Sophie M Jones, Ken K Nischal, *British Journal of Ophthalmology* 2013;97:9 1129-1133 September 2013

This study evaluates the non-invasive tear break-up time (NITBUT) and lipid layer interferometry in normal children. The study examined children with no history of ocular surface disease or anterior segment abnormalities. A Keeler tearscope mounted on a slit lamp was used to measure NITBUT and lipid layer interferometry. The time from eye opening to the first distortion of the grid was noted and an average of 3 was used to calculate NITBUT. 36 children/72 eyes were included. Mean NITBUT was 21.76 ± 4.06 s (range 14.9 – 30.95). This is significantly higher than recent studies on adult patients. 24 children underwent tearscope lipid layer interferometry. 18 demonstrated grade 1 and 6 demonstrated grade 2, both of which are within the normal range. The authors note the increase in NITBUT compared with adult studies and hope this study can be used as normative data for future research on tear film instability in children.

Diagnostic Potential of Iris Cross-sectional Imaging in Albinism Using Optical Coherence Tomography

Viral Sheth, Irene Gottlob, Sarim Mohammad, Rebecca J. McLean, *Ophthalmology* October 2013; 120(10):2082-2090

This is a prospective cross-sectional study comparing 55 individuals with albinism and 45 healthy controls. The purpose of the study was to characterize

“in vivo” anatomic abnormalities of the iris in albinism compared with healthy controls using anterior segment optical coherence tomography (AS-OCT) and to explore the potential of using this technique to make the diagnosis of albinism. Main Outcome Measures: Iris anterior segment optical coherence tomography (AS-OCT) measurements included 1) total iris thickness, 2) stroma/anterior border layer thickness (SAB) and 3) posterior epithelial layer thickness (PEL). These instrument measurements were compared with phenotypical measurements including 1) iris transillumination, 2) retinal layer measurements at the fovea, 3) nystagmus intensity, 4) best corrected visual acuity, 5) visual evoke potential asymmetry, 6) skin pigmentation and 7) hair pigmentation of the head, lashes and brow.

Results: The mean iris thickness of control patients was 10.7% thicker compared with the iris thickness of the albinism patients. There is a particular difference in the posterior epithelial layer thickness (PEL), which was 44% thicker in control patients compared with the albinism group.

Conclusions: The authors feel that anterior segment ocular coherence tomography and iris measurements are significantly correlated to best corrected visual acuity and nystagmus intensity in contrast to iris transillumination grading. FURTHERMORE, THE AUTHORS FEEL THAT THE SIGNIFICANT REDUCTION IN THE POSTERIOR EPITHELIAL LAYER THICKNESS CAN BE CONSIDERED A PATHOGNOMONIC FINDING FOR ALBINISM.

Study limitations: The authors feel that a possible weakness of the study is that diagnosis was based on phenotype rather than genotype mainly because of the significant proportion of unknown mutations leading to albinism. This meant that the sensitivity and specificity of the measurements could not be compared with a genetically determined albino population.

Effectiveness of Nonpharmacologic Treatments for Acute Seasonal Allergic Conjunctivitis

Paramdeep S. Bilkhu, James S. Wolffsohn, Shehzad A. Naroo, Louise Robertson, *Ophthalmology* January 2014; 121(1):72-78

This article comes from Ophthalmic Research Group, Aston University, Birmingham, United Kingdom. This is a randomized, masked clinical trial designed to investigate whether artificial tears and cold compresses alone or in combination provide a treatment benefit and whether they were as effective as or could enhance topical antiallergic medications.

Participants: Eighteen subjects (mean age 29.5 years) allergic to grass pollen.

Intervention: Controlled exposure to grass pollen using an environmental chamber to stimulate an ocular allergic reaction followed by application of 1) artificial tears (ATS), 2) 5 minutes of cold compresses (CC), 3) artificial tears combined with cold compresses or 4) no treatment applied at each separate visit in random order. A subset of 11 subjects also had epinastine hydrochloride (EH) applied alone and epinastine combined with CC in random order or instillation of a volume-matched saline control.

Main outcome measures: Bulbar conjunctival hyperemia, ocular surface temperature and ocular symptoms repeated before and every 10 minutes after treatment for 1 hour.

CONCLUSIONS: AFTER CONTROLLED EXPOSURE TO GRASS POLLEN, COLD COMPRESSES AND ARTIFICIAL TEAR TREATMENT SHOWED A THERAPEUTIC EFFECT ON THE SIGNS AND SYMPTOMS OF ALLERGIC CONJUNCTIVITIS. COLD COMPRESSES ENHANCE THE USE OF EPINASTINE ALONE AND WAS THE ONLY TREATMENT TO REDUCE SYMPTOMS TO A BASELINE WITH 1 HOUR OF ANTIGENIC CHALLENGE. SIGNS OF ALLERGIC CONJUNCTIVITIS GENERALLY WERE REDUCED MOST BY A COMBINATION OF COLD COMPRESSES IN COMBINATION WITH ARTIFICIAL TEARS OR EPINASTINE HYDROCHLORIDE.

Reviewers Comment: This article underlines the importance of cold compresses, artificial tears and appropriate hydration in the treatment of allergic conjunctivitis.

Anterior segment photography in pediatric eyes using the Lytro light field handheld noncontact camera

Marcus I, Tung IT, Dosunmu EO, et al, J AAPOS December 2013;17:572-577

This study compares anterior segment findings identifiable on digital photographic images taken with the Lytro light field camera (LLTFC) to those obtained from the clinical anterior segment eye examination. The authors conducted a prospective study of consecutive patients under age 9 with one or more abnormal anterior segment findings. 157 eyes of 80 children were included (3 eyes were excluded because of poor patient cooperation). The mean age was 4.36 years. Seven subjects (9%) had poor quality photographs that were of insufficient quality. Masked review of LLTFC photographs correctly identified 133 of 206 abnormalities (65%). Lens abnormalities in the setting of a dilated iris were identified best (79%) and anterior chamber abnormalities were identified at the lowest rate (50%). The camera is non-threatening to young children and easily held with one hand. It is small and can be held comfortably next to the slit lamp. The cost is less than a RetCam and lacks a flash. The software can refocus images on areas of interest after capture. This study was not designed to determine the LLTFC utility as a screening tool. It cannot capture video or image the posterior segment. Clinical documents were often needed to assist interpretation of images. Complete masking could not be achieved. Tear film caused some reflection artifacts.

Corneal Topography and Corneal Thickness in Children

Reddy SP, Bansal R, Vaddavalli PK. , J Pediatr Ophthalmol Strabismus 2013; 50(5): 304-310

The goal of this study was to evaluate corneal thickness, topography and elevation in children. 100 eyes of 100 patients (age 5-15) with no significant ocular history, complaints or history of contact lens use underwent evaluation

with the Orbscan corneal topography system. The study aimed to provide normative data of corneal topography measurements in children. A trend towards thinner corneas in children compared to adults was noted. The thinnest point on the entire cornea was an average of $531 \pm 34.41 \mu\text{m}$ thick. The thinnest point of the cornea was most commonly located in the inferotemporal quadrant followed by the superotemporal quadrant. The central cornea had an average thickness of $540 \pm 34.03 \mu\text{m}$. Normal standards for elevation and curvature topography was also provided. The most common anterior and posterior corneal elevation pattern was the incomplete ridge. The authors conclude these data may prove useful in future comparative studies of different corneal diseases in children.

12. CATARACT

Juvenile Cataract Morphology in 3 Siblings Not Yet Diagnosed with Cerebrotendinous Xanthomatosis

Arif O. Khan, Mohammed A. Aldahmesh, Jawaher Y. Mohamed, Fowzan S. Alkuraya, *Ophthalmology* May 2013;120:956-960

This is a prospective case series involving 4 siblings and their 2 parents who are first cousins. The purpose of the study is to evaluate the treatment with oral chenodeoxycholic acid as a prevention of cataracts and neurologic deterioration associated with cerebrotendinous xanthomatosis.

Children with clinically undiagnosed cerebrotendinous xanthomatosis (CTX) frequently demonstrate early lenticular changes heralding the disease. This study highlights the morphology of lens opacities in a family with genetically confirmed disease. CYP27A1 is a candidate gene associated with cerebrotendinous xanthomatosis.

Conclusions: An unusual pattern of fleck lenticular deposits along the Y-sutures characterized the lenticular findings in this condition. Findings are best seen on page 958, volume 120, number 5, May 2013. FLECK OPACITIES AND POSTERIOR CAPSULAR CATARACT OPACITY CAN BE APPRECIATED IN MANY OF THESE PATIENTS. FURTHERMORE, THE PUNCTATE OPACITIES TEND TO FOLLOW ALONG THE Y-SUTURE.

The authors emphasize that such juvenile lenticular findings should raise suspicion of this treatable metabolic storage disease especially when in the context of recurrent diarrhea during early childhood. Asymptomatic fleck-like opacities at or near the anterior Y-suture may be assigned a carrier status.

Comment: This is a rare disorder not frequently seen in the United States. It is caused by a recessive CYP27A1 mutation that is characterized by abnormal deposition of cholestanol and cholesterol in multiple tissues including the lens and brain.

13. CATARACT SURGERY

Reanalysis of refractive growth in pediatric pseudophakia and aphakia Whitmer S, Xu A, and McClatchey S J AAPOS April 2013;17:153-157

The logarithmic model of the rate of refractive growth for aphakic children is flawed at the youngest ages. A newer model (RRG2) was developed with 'adjusted age' to account for in utero eye growth. RRG2 is based on refractions at the spectacle plane. In highly hyperopic young children, this produces artificially large differences between an aphakic refraction at the natural lens plane versus the spectacle plane. The authors have developed a new model the RRG3 based on an aphakic refraction at the natural lens plane. This was a retrospective observational case series to develop and test the model. The primary outcome measures were the mean values of rate of refractive growth for pseudophakic and aphakic eyes calculated with the RRG3. Factors that might affect the RRG3 were also evaluated.

Seventy-eight pseudophakic eyes and 70 aphakic eyes were included. There was a mean follow-up time of 9.5 years. RRG3 values did not differ for pseudophakic or aphakic patients, when comparing surgery before or after 6 months of age. This stands in contradistinction to when the RRG or RRG2 model is applied. Therefore all further analysis grouped ages. The mean RRG3 value for pseudophakic and aphakic eyes was -13 ± 6 D and -16 ± 10 D respectively. Other factors such as sex, presence of glaucoma, and bilateral or unilateral surgery were not found to contribute significantly. LogMAR best corrected visual acuity, presence of an IOL, and calculated initial adjusted aphakic refraction had a mild effect on the RRG3. The RRG3 eliminates the optical effect of vertex and distance therefore eliminates previously observed age-related differences when using the RRG or RRG2. This study was retrospective and not randomized. All children in this study had surgery at or after 3 months of age so the data may not be applicable to earlier surgeries. A large, prospective, randomized study could help validate these results.

Glaucoma after pediatric cataract surgery in a population with limited access to care

Baden C, Shija F, Lewallen S et al J AAPOS April 2013;17:158-162

This study evaluates the incidence of postoperative glaucoma after pediatric cataract surgery in a resource-constrained setting in Africa. This paper was a retrospective three-year chart review. Inclusion criteria, were met by 136 patients (222 eyes). Primary IOLs were placed in 211/222 but data was not available on the remaining 11 eyes. Mean diagnosis of the cataract was at 6 months of age. Surgery was performed at a median age of 6.6 years. Median follow-up was 7.8 months. The short follow-up may lower secondary glaucoma estimates. Eyes operated on prior to 9 months of age were more likely be microphthalmic, less likely to have received an IOL, more likely to have bilateral cataracts, more likely to have preoperative nystagmus, and have received longer follow-up. Six eyes of 5 patients developed glaucoma during follow-up. The study cohort had a 2 cases per 100 operated annual glaucoma incidence rate. Primary IOL implantation was associated with a lower risk

of glaucoma development, whereas longer followup was associated with a higher risk. Long-term followup rates were improved if the patient presented for their one-year followup and if spectacles were prescribed at the most recent visit. Only ¼ of patients were still attending follow-up by 3 years post surgery. The low rate of glaucoma in this study could be due to underdiagnosis, older average age at the time of surgery, patient loss to follow-up, or small sample size of glaucoma cases, preventing the use of multiple logistic regression analysis. The small number of glaucoma cases prevents comment on risk factors. Efforts must be made in the future to increase followup rates.

Visual Outcome and Changes in Corneal Endothelial Cell Density Following Aphakic Iris-Fixated Intraocular Lens Implantation in Pediatric Eyes With Subluxated Lenses

Sorath Noorani Siddiqui, Ayesha Khan, J Pediatr Ophthalmol Strabismus 2013; 50:178-182 (March/April)

The study determines the safety of artisan lenses in children with subluxed lenses. A prospective study followed children who had an artisan lens placed in their eye after lensectomy for subluxed lenses. The children were followed for approximately a year and the lens was found to have minimal side effects. The corneal endothelial density was not adversely affected in the first year following lens implantation and the vision was good postoperatively. The article does state that (as it is obvious) that one year is not a sufficient amount of time to determine efficacy of the lens as this lens will be in the child's eye for a very long time, so although the concept is interesting and definitely worth studying, more time is needed to determine the safety of these lenses.

Long-term Risk of Glaucoma After Congenital Cataract Surgery

Scott Lambert, Amitabh Purohit, Hillary M. Superak, Michael J. Lynn, et al. Am J of Ophthalm August 2013; 156(2): pg. 355-360.

This retrospective study analyzed the occurrence of glaucoma after cataract extraction on children less than 7 months of age. Sixty-two eyes of 37 children who had undergone surgery with a minimum of 3 years follow up were reviewed. Six eyes had IOL implantation while 56 were left aphakic. Nine eyes developed open angle glaucoma. The probability of developing glaucoma was estimated to be 19.5% by 10 years. If patients classified as glaucoma suspect were included in the statistics, 2/3 of patients would have developed disease. It is important to monitor children in this young age group for a prolonged time for glaucoma development.

Posterior Iris-claw Aphakic Intraocular Lens Implantation in

Children Johannes Gonnermann, Necip Torun, Matthias Klamann, Ann-Karina Maier, et al. Am J Ophthalm August 2013; 156(2): pg. 382-386.

This study reviewed the implantation of iris-claw lens implantation (Artisan PCIOL, Verisyse VRS54) in 7 eyes in 4 children who were aphakic without adequate posterior capsular support as a viable alternative to angle supported IOL, scleral fixated PCIOL, iris fixated PCIOL, or intrascleral fixated PCIOL. Mean follow up was

31 months. There was mean endothelial cell loss of 6.4% (3013 cells/mm³ to 2831 cells/mm³). One dislocation occurred. Six of the 7 eyes achieved BCVA of 0.1 logMAR or better. Postoperative IOP was similar to preoperative measurements. The authors suggest that iris-claw IOL is a viable option for lens implantation in children without capsular support.

Corneal Endothelial Cell Characteristics After Pediatric Cataract Surgery

Aparna Ramasubramanian, Iason Mantagos, Deborah K. Vanderveen, J Pediatr Ophthalmol Strabismus 2013; 50:251-254 (July/August)

The study described corneal endothelial cell characteristics after pediatric cataract surgery. Using specular microscopy, endothelial cell features were correlated with clinical and surgical features. The authors concluded that there is endothelial cell loss along with polymegathism and pleomorphism in children who underwent cataract surgery and that this is an important aspect of the ophthalmic examination when the child is old enough to perform a specular microscopy to determine corneal changes and if there is a risk for corneal decompensation.

One-Year Strabismus Outcomes in the Infant Aphakia Treatment Study

Erick D. Bothun, Julia Cleveland, Stephen P. Christiansen, Scott R. Lambert, *Ophthalmology* June 2013;120:1227-1231

This is a secondary outcome analysis in a prospective, randomized clinical trial known as the Infant Aphakia Treatment Study (IATS). All participants in this study were randomized in multiple institutions. The purpose of the study was to compare treatment of aphakia with primary intraocular lens or contact lenses in 114 infants with unilateral congenital cataract.

The main outcome measures included a portion of patients in whom strabismus developed during the first 12 months of follow-up comparing the intraocular lens group versus the contact lens group.

Conclusions: Intraocular lens placement does not prevent the early development of strabismus after congenital cataract surgery. However, strabismus was less likely to develop in infants whose cataract was removed at an early age.

Uncorrected visual acuity in children with monofocal

Pseudophakia Bharti R. Nihalani; Deborah K. VanderVeen *J Cataract Refract*

Surg. March 2013;39(3):419-24

In this single institution retrospective chart review, the authors report on uncorrected distance and near visual acuity in pediatric eyes treated with primary monofocal intraocular lens (IOL) implantation. Records of children older than 5 years who had uneventful monofocal IOL implantation targeted for emmetropia within ± 1.00 diopter (D) spherical equivalent were reviewed. Eyes with secondary IOL placement and

sulcus-fixated IOLs were excluded. The main outcome measure was uncorrected visual acuity at distance and near. Good visual acuity was defined as 20/40 or better. Forty-one eyes of 25 children had uncorrected distance and near visual acuity recorded in the early postoperative period. The mean age was 11.2 years \pm 3.6 (SD). Twenty eyes (49%) had good visual acuity at distance and near, 11 had good visual acuity at distance only, 6 had good visual acuity at near only, and 4 had worse than 20/40 at distance and near. In children with bilateral pseudophakia, 12 (75%) of 16 had 20/40 or better uncorrected acuity at distance and near, with approximately symmetric refractive error (0.2 \pm 1.2 D), meaning that monovision was neither targeted nor present.

In summary, monofocal IOL placement resulted in good uncorrected distance and near visual acuity in almost 50% of pediatric eyes and in 75% of patients with bilateral pseudophakia. This study brings into question whether multifocal IOLs are truly needed to obtain good uncorrected distance and near vision in young eyes. Young eyes may pseudoaccommodate better than older eyes.

Vitrectorhexis versus forceps posterior capsulorhexis in pediatric cataract surgery. Kochgaway L, Biswas P, Paul A, Sinha S, Biswas R, Maity P, et al. *Indian J Ophthalmol* July 2013;61:361-4.

Fifty eyes with congenital and developmental cataract were included in this study. The posterior capsulorhexis was created using ultrata forceps in 17 eyes or through a vitrector in 33 eyes. Forceps capsulorhexis was performed before IOL implantation, while vitrectorhexis was performed after IOL implantation in the bag. The results of both the surgery were compared using the following criteria: incidence of extension of rhexis, ability to achieve posterior rhexis of appropriate size, ability to implant the IOL in the bag, the surgical time, and learning curve. Vitrectorhexis after IOL implantation was an easy to learn alternative to manual posterior continuous curvilinear capsulorhexis in pediatric cataract surgery. It was more predictable and reproducible, with a short learning curve and lesser surgical time.

Implantation of phakic intraocular lens in 3 patients with oculocutaneous albinism.

Gwyneth A. van Rijn, Colette Snoek, Maurits Joosse, et al.
J Cataract Refract Surg. October 2013;39:1604-8.

The authors describe 3 *adult* patients with oculocutaneous albinism type 1A who underwent successful implantation of an Artisan phakic intraocular lens. The indication was high refractive error and difficulties with contact lens wear/spectacles. There was follow up of 8-14 years. In these 3 patients, there was stable to improved corrected distance visual acuity, endothelial cell loss of approximately 1% per year, and no lens subluxation. The authors provide preliminary evidence that the irides of oculocutaneous albinism patients can support an iris-fixated lens for one decade. Pediatric ophthalmologists may wish to discuss phakic iris-fixated IOL as a possible

future refractive option, pending additional data, for albinism patients with very high refractive errors.

Surgical outcomes after intraocular lens implantation for posterior lenticonus-related cataract according to preoperative lens status.

BJ Lee, JH Kim, YS Yu. ,*J Cataract Refract Surg.* February 2014;40:217-23. The study was a retrospective chart review from a single surgeon of 43 pediatric patients (47 eyes) with posterior lenticonus-related cataract who lensectomy, posterior capsulectomy and anterior vitrectomy. Primary intraocular lens implantation was performed in patients over the age of 24 months. In younger patients, intraocular lens implantation was performed after 24 months. The authors compared visual outcomes between two groups of patients with posterior lenticonus: total cataract and cataract localized to the posterior pole. Interesting results include:

1. The majority of posterior lenticonus cataracts were unilateral (39 of 47 eyes).
2. Intraocular lens placement in the sulcus or the bag was achieved in all 47 eyes.
3. Most eyes with total cataracts (11 of 12 eyes) had preexisting posterior capsular defects, which were discovered at the time of cataract removal.
4. More than half of the patients achieved final visual acuity of 20/40 or better (26 of 47 eyes).
5. Eyes with total cataract had slightly better visual outcomes than eyes with cataract localized to the posterior pole, which was of borderline statistical significance ($P=0.05$). One possible explanation for this trend is that total cataracts presented at a slightly younger age and were operated on at a younger age, limiting amblyopia.

Surgical outcomes after application of a liquid adhesive ocular bandage to clear corneal incision during cataract surgery. Harvey S. Uy, Kenneth R. Kenyon.*J Cataract Refract Surg.* November 2013;39:1668-74.

This prospective randomized clinical trial of 90 *adult* eyes undergoing phacoemulsification compared the anatomic and refractive outcomes of three clear corneal incision closure methods: wound hydration, a single 10-0 nylon suture, and a liquid adhesive ocular bandage. The liquid adhesive ocular bandage resulted in improved wound-edge closure (compared to hydration), reduced surgically-induced astigmatism (compared to suturing), and diminished foreign-body sensation (compared to suturing). This was a study performed on adult eyes, but it opens the door for the study of liquid adhesive ocular bandages in pediatric ophthalmic surgery. In our field, wound leak avoidance is paramount, and minimizing suturing could decrease foreign body sensation and trips to the operating room for suture removal.

Predictability of Intraocular Lens Power Calculation Formulas in Infantile Eyes with Unilateral Congenital Cataract: Results from the Infant Aphakia Treatment Study

D. Vanderveen, R. Trivedi, A. Nizam, M. Lynn, S. Lambert, for the Infant Aphakia Treatment Study Group. *Am J Ophthalmol* December 2013, 156 (6): pgs. 1252-1260.

The Aphakia Treatment Study randomized 57 of 114 patients to receive an IOL; 56 patients were successfully implanted. Thirteen eyes were excluded from the study, so data was evaluated based upon 43 eyes. The mean age at surgery was 2.5 \pm 1.5 months. Mean axial length was 18.1 \pm 1.1 mm. The IOL power was determined in the OR based upon A-scan and K readings. According to the study protocol, IOL power was selected to result in a +8.0 postoperative refraction for infants 4-6 weeks of age, and +6.0 diopters for infants older than 6 weeks. All patients had SN60AT lens model implanted with posterior capsulotomy and anterior vitrectomy. Formulas used included the Hoffer Q, Holladay 1, Holladay 2, SRK/T, and the SRK II. Overall mean refraction for the younger group was +6.8 \pm 2 diopters. The older group was +5.6 \pm 1.7 diopters. The Holladay 1 and SRK/T formulas gave equally good results and had the best predictive values.

Traumatic pediatric cataract in southern Ethiopia- results of 49 cases

Kinori M, Tomkins-Netzer O, Wygnanski-Jaffe T, et al
J AAPOS October 2013;17:512-515

This study extends a previous report on treatment of pediatric cataracts in rural Ethiopia with followup of at least 12 months. This was a retrospective review of patients treated over 13 months. 49 of 65 children were included because the rest were lost to follow-up. 44/49 were boys. Two-thirds of the cases were caused by blunt trauma. Half of the blunt trauma cases were caused by donkey kicks. One-third of the cases were perforating eye injuries. 32/49 had scleral tunnels and the rest were performed through a clear corneal incision. Six children were left aphakic, 41 received a PCIOL and 2 received an ACIOL. There were no cases of endophthalmitis but 7 cases had complications (hypotony/RD, IOL subluxation, aphakic glaucoma, pupil opacification (n=2), posterior capsule opacification (n=2). At presentation only 5 children had an acuity of CF or better. After surgery 43 children (88%) had an acuity of CF or better. Blunt trauma cases and cases where an IOL was implanted, were more likely to achieve this level of acuity. The authors comment that the goals of surgery in this part of the world must be more 'modest', but improvement in acuity can occur.

Visual Outcome Of Cataract In Pediatric Age Group: Does Etiology Have A Role

Mehul A. Shah, Shreya M. Shah, Ashit H. Shah, Jaimini S. Pandya
Eur J Ophthalmol January-February 2014; 24(1): 76 - 83

A total of 128 eyes in children under 5 years of age were retrospectively evaluated in Dahod, India with unilateral cataract. A total of 85 (66.4%) were traumatic cataracts (group 1) and 43 (33.3%) nontraumatic (group 2). Patients underwent surgery with intraocular lens implantation with 22 (51.1%) of group 1 patients and 40 (47.1%) of group 2 patients achieving visual acuity > 20/200.

14. GLAUCOMA

Late-Recognized Primary Congenital Glaucoma

David S. Walton, Karina Nagao, Helen H. Yeung, Steven A. Kane, J Pediatr Ophthalmol Strabismus 2013; 50:234-238 (July/August)

The purpose of the study is to describe a cohort of children with later recognized primary congenital glaucoma (LRPCG). The medical records of children who were diagnosed with primary congenital glaucoma after age 1 were reviewed. The study determined the age of onset, diagnostic signs, intraocular pressures, visual acuity. Interestingly enough, corneal clouding was not an initial sign for any of the patients. The authors concluded that an awareness of the diagnostic signs can assist in early diagnosis of LRPCG and prevent vision loss.

Caregiver Burden Assessment In Primary Congenital Glaucoma

Tanuj Dada, Ashutosh Aggarwal, Shveta Jindal Bali, Meenakshi Wadhvani
Eur J Ophthalmol May-June 2013; 23(3): 324 – 328

Caregivers of patients with primary congenital glaucoma have significant emotional and psychological burden. One-third of these primary care givers suffer from moderate to severe depression. This study used a Caregiver Burden Questionnaire (CBQ) and the depressive symptomatology was evaluated using a Patient Health Questionnaire–9 (PHQ-9) on 55 primary caregivers, of which 2 were males.

Online-Only Article: Ophthalmic Technology Assessment: Rebound Tonometry in Children: A Report by the American Academy of Ophthalmology

Scott R. Lambert, Michele Melia, Angela N. Buffenn, Michael F. Chiang,
Ophthalmology April 2013;120:657-662

Rebound tonometry in children is better tolerated by young children than applanation tonometry.

Polypropylene vs silicone Ahmed valve with adjunctive mitomycin C in paediatric age group: A prospective controlled study

Y El Sayed; A Awadein *Eye*. June 2013; 27:728–34.

The authors prospectively compared silicone and polypropylene Ahmed glaucoma valves implanted in children ages 10 and under who had already failed other glaucoma procedures. 50 eyes of 33 patients with pediatric glaucoma were followed for two years after implanting either a polypropylene or silicone Ahmed valve. In eyes with bilateral glaucoma, one eye was implanted with polypropylene and the other eye was implanted with silicone, and this assignment was made at random. In eyes with unilateral glaucoma, patients were matched on the basis of glaucoma type and the number of prior operations. Twenty five eyes received a polypropylene valve, and 25 eyes received a silicone valve. Eyes implanted with silicone valves achieved a significantly lower intraocular pressure (IOP) compared with the polypropylene group at 6 months, 1 year, and 2 years postoperatively. The average survival time was significantly longer ($P=0.001$ by the log-rank test) for the silicone group than for the polypropylene group and the cumulative probability of survival by the log-rank test at the end of the second year was 80% (SE: 8.0, 95% CI: 64–96%) in the silicone group and 56% (SE: 9.8, 95% CI: 40–90%) in the polypropylene group. The difference in the number of postoperative interventions and complications between both groups was statistically insignificant. The authors conclude that silicone Ahmed valves can achieve better IOP control, and longer survival with fewer antiglaucoma drops compared with polypropylene valves in children younger than 10 years. They suspect that there is less encapsulation with the silicone valves than the polypropylene valves. There were more smaller eyes and thus more pediatric sized implants placed in the silicone group than in the polypropylene group, but if anything, this makes the better results in the silicone group more convincing.

Based on the results of this study and the authors' review of other retrospective literature, silicone rather than polypropylene Ahmed valves seem like the better choice for pediatric glaucoma cases that have failed other surgical procedures.

CYP1B1 genotype influences the phenotype in primary congenital glaucoma and surgical treatment

X. Chen, Y. Chen, L. Wang, D. Jiang, W. Wang, M. Xia, L. Yu, X. Sun. *Br. J Ophthalmol* 2014; 98: 246-251.

This study evaluated gene mutation in patients of Han Chinese ethnicity with primary congenital glaucoma and look at operative effects. 238 patients were examined. 192 patients went through their first operative treatment were analyzed for their relationship between clinical characteristics and surgical effect. It was found that these patients had a higher operative success rate with better IOP control.

15. REFRACTIVE SURGERY

16. GENETICS

Null CYP1B1 Genotypes in Primary Congenital and Nondominant Juvenile Glaucoma

Maria-Pilar Lopez-Garrido, Cristina Medina-Trillo, Laura Morales-Fernandez, Julian Garcia-Feijoo, *Ophthalmology* April 2013;120:716-723

This is a CYP1B1 genotyping, segregation analysis, and functional evaluation of mutations in a cohort 177 probands clinically diagnosed with primary congenital glaucoma (PCG) and nondominant juvenile glaucoma (ndJG).

Methods: Automatic DNA sequencing of the promoter gene region and 3 CYP1B1 exons. This study was performed in Madrid and Albacete, Spain. The main outcome measures were based on slit lamp examinations, measurements of intraocular pressures, gonioscopy, and fundus examinations.

Conclusions: This is reported to be the largest of analysis of CYP1B1 mutations performed in European patients with primary congenital glaucoma. The study shows that complete absence of the CYP1B1 gene activity frequently lead to severe phenotypes of glaucoma. The results of this study support CYP1B1 glaucoma is not a simple monogenic disease and that CYP1B1 activity levels could influence the clinical/phenotypic expression of the disease.

Genome engineering using the CRISPR-Cas9 system.

Ran FA, Hsu PD, Wright J, Agarwala V, Scott DA, Zhang F. *Nat Protoc.* 2013 Nov;8(11):2281-308. doi: 10.1038/nprot.2013.143. Epub 2013 Oct 24

A revolution in treating genetic diseases may have just started! CRISPR stands for **clustered regularly interspaced short palindromic repeats**. It is a part of the bacterial immune system which has been discovered to be useful in correcting DNA mutations; with this system it may be possible to excise and correct many errors in DNA that cause human disease. The authors describe the tools needed for RNA-guided Cas9 mediated genome editing. They are not the first authors to describe this (although the first reports are also very recent), but they are the first to modify it to minimize off-target cleavage. In brief, with the CRISPR technique an RNA-guide is used to get a Cas9 nuclease to a specific spot in the genome where there is a disease-causing mutation. The nuclease cuts the DNA at this spot and the DNA can then repair itself using a template. Unlike gene therapy, now used for one type of LCA, in which a viral vector with a new copy of the defective gene must be delivered with only genes small enough to be packaged eligible for the most well studied vector, with CRISPR even large genes could be amenable to “gene therapy” by directly fixing the defective region of DNA.

Characterisation of retinoblastomas without RB1 mutations: genomic, gene expression, and clinical studies.

Rushlow DE, Mol BM, Kennett JY, Yee S, et al. *Lancet Oncol.* 2013 Apr;14(4):327-34. doi: 10.1016/S1470-2045(13)70045-7. Epub 2013 Mar 13.

Retinoblastoma (Rb) is a malignant ocular tumor of childhood. When a child presents with Rb it is of critical importance to determine whether it is caused by a germline mutation, present in all of the child's cells, predisposing them to other ocular and non-ocular tumors and also implying risk to other family members, or a spontaneous mutation which is an isolated event carrying no other risks. For many years this has been determined by sending a portion of the tumor and the patient's blood for genetic testing to look for mutations in the RB1 gene, the only known cause of Rb. In this extremely important paper, Brenda Gallie's group describes their discovery of another gene that can cause Rb, the MYCN gene. This is of vital importance in the work up of children with retinoblastoma.

The authors analysed 1068 samples from unilateral Rb patients and studied genomic copy number, RB1 gene expression and protein function, retinal gene expression, histological features, and clinical data, and they compared this information between those in which RB1 mutations had been found versus those with no mutation found. They had 29 tumors in which no RB1 mutation was found. 15 of the 29 RB1(+/+) tumours had high-level MYCN oncogene amplification (28-121 copies; RB1(+/+)MYCN(A)), whereas none of 93 RB1(-/-) primary tumours tested showed MYCN amplification ($p < 0.0001$). Two more MYCN amplification patients were subsequently identified. Median age at diagnosis of the 17 children with RB1(+/+)MYCN(A) tumours was 4.5 months (IQR 3.5-10), compared with 24 months (15-37) for 79 children with non-familial unilateral RB1(-/-) retinoblastoma.

The take-home message: A portion of children with unilateral retinoblastoma develop it as a result of MYCN amplification, not sporadic RB1 mutation. These children have a very young age of onset (such as we usually associate with hereditary Rb) and aggressive histologic features. This new cause of retinoblastoma should be considered in patients with retinoblastoma.

Pax6 downregulation mediates abnormal lineage commitment of the ocular surface epithelium in aqueous-deficient dry eye disease.

Chen YT, Chen FY, Vijmasi T, Stephens DN, Gallup M, McNamara NA. *PLoS One.* 2013 Oct 15;8(10):e77286. doi: 10.1371

Keratinizing squamous metaplasia of the ocular surface can cause blindness and is found in systemic autoimmune disease. It is also a feature of aniridia. The authors had previously established the autoimmune regulator-knockout (Aire KO) mouse as a model of autoimmune keratoconjunctivitis sicca and identified an essential role for autoreactive CD4+ T cells in squamous metaplasia pathogenesis. They had also noted the down-regulation of paired box gene 6 (Pax6) in both human patients with Sjögren's syndrome and Aire KO mice. Pax6 encodes a pleiotropic transcription factor guiding eye morphogenesis during development. They hypothesized that the role of Pax6 in maintaining ocular surface homeostasis was disrupted in the inflamed eye and that loss of Pax6 played a functional role in the development and progression of surface disease. Adoptive transfer of autoreactive T cells from Aire

KO mice to immunodeficient recipients confirmed CD4+ T cells as the cause of Pax6 downregulation in Aire KO mice. They then treated the mice with adenovirus vector forcing Pax6 expression in corneal epithelial cells, and it reversed the squamous metaplasia! This could be a novel treatment for inflammatory ocular surface disease, and possibly for aniridia related cornea opacity.

Small-interfering RNAs (siRNAs) as a promising tool for ocular therapy. Guzman-Aranguez A, Loma P, Pintor J. Br J Pharmacol. 2013 Oct;170(4):730-47

Genetic eye diseases which are caused by lack of a normal protein are the best targets for subretinal gene replacement therapy. This encompasses many autosomal recessive disorders. But what about autosomal dominant disorders where the problem is not the lack of enough normal protein but instead the toxicity of an abnormal protein product? For these disorders small-interfering RNAs are promising. This review nicely discusses how interfering RNAs work, and why the eye seems to be a very good target for this type of treatment for glaucoma, retinitis pigmentosa, and neovascular eye diseases, among others.

Patient-specific iPSC-derived photoreceptor precursor cells as a means to investigate retinitis pigmentosa.

Tucker BA, Mullins RF, Streb LM, Anfinson K, et al Elife. 2013 Aug 27;2:e00824.

The authors demonstrate that it is possible to take a skin biopsy from patients with retinitis pigmentosa, grow them in a dish, de-differentiate them into pluripotent stem cells, then drive differentiation to photoreceptor precursor cells. These cells can be studied to determine which gene is causing the RP. Then a normal copy of that gene can be placed into a viral vector and used to treat the cells in vitro. In this study these treated cells were then injected subretinally into a mouse without photoreceptors and photoreceptors formed from the transplanted cells. This is proof of concept that a strategy might be developed for humans in which patients with retinal degeneration could have their own skin cells made into photoreceptors, corrected by gene therapy in a dish, then transplanted into their own eyes to restore vision when all photoreceptors have been lost.

This study describes using next-generation and Sanger sequencing to identify disease-causing USH2A mutations in an adult patient with autosomal recessive RP. Induced pluripotent stem cells (iPSCs), generated from the patient's keratinocytes, were differentiated into multi-layer eyecup-like structures with features of human retinal precursor cells. The inner layer of the eyecups contained photoreceptor precursor cells that expressed photoreceptor markers and exhibited axonemes and basal bodies characteristic of outer segments. Analysis of the USH2A transcripts of these cells revealed that one of the patient's mutations causes exonification of intron 40, a translation frameshift and a premature stop codon. Western blotting revealed upregulation of GRP78 and GRP94, suggesting that the patient's other USH2A variant (Arg4192His) causes disease through protein misfolding and ER stress. Transplantation into 4-day-old immunodeficient Crb1 (-/-) mice resulted in the formation of morphologically and immunohistochemically recognizable photoreceptor

cells, suggesting that the mutations in this patient act via post-developmental photoreceptor Degeneration.

Subretinal gene therapy of mice with Bardet-Biedl syndrome type 1.

Seo S, Mullins RF, Dumitrescu AV, Bhattarai S, Gratie D, Wang K, Stone EM, Sheffield V, Drack AV. *Invest Ophthalmol Vis Sci.* 2013 Sep 11;54(9):6118-32. doi: 10.1167/iovs.13-11673.

Bardet Biedl syndrome usually presents with loss of vision in the first decade and may produce complete blindness due to retinal degeneration between the second and third. There are 17 known genetic subtypes, but the most common is BBS1 and the most common mutation is M390R. A mouse model of this disorder has been created and recapitulates the human phenotype. Subretinal gene therapy was attempted in this mouse as a pre-clinical study for humans. An AAV2/5 vector with a normal copy of the gene was created, and was injected subretinally in the right eye of affected mice, while the same viral vector with a reporter molecule, Green Fluorescent Protein (GFP), which can be seen as a green fluorescent glow, was injected subretinally in the fellow eye. Unaffected mice were also treated. It was discovered that while the treatment rescued formation of the protein complex of BBS proteins, called the BBSome, it did not rescue the ERG of treated animals. The reason was over-expression toxicity of the BBS1 protein. That is, just as too little of the BBS1 gene protein product is toxic to the retina, so is too much. In normal mice receiving a subretinal injection of the viral vector there was retinal degeneration. In BBS1 mice there was no worsening of retinal function, but neither was there improvement in most cases. None of the eyes treated with the same vector carrying the reporter molecule showed toxicity. One small group of BBS mice did show a small improvement in ERG function—this was the group given the smallest volume of vector. The conclusion is that for this gene the expression of the delivered normal gene will have to be titrated carefully, but that treatment of BBS1 retinal degeneration by subretinal gene therapy may be possible.

AAV-mediated gene therapy for choroideremia: preclinical studies in personalized models.

Vasireddy V, Mills JA, Gaddameedi R, Basner-Tschakarjan E, Kohnke M, et al *PLoS One.* 2013 May 7;8(5):e61396. doi: 10.1371

The authors report that Choroideremia (CHM) is an X-linked retinal degeneration that is symptomatic in the 1(st) or 2(nd) decade of life causing nyctalopia and loss of peripheral vision. The disease progresses through mid-life, when most patients become blind. It may be amenable to subretinal gene therapy because it is due to loss of function of a protein, REP1, and the gene is of the size that can be packaged in AAV which is already in a successful clinical trial for treating RPE65 LCA. There is no animal model to test it, however. Therefore the authors used cells from CHM patients, namely lymphoblasts and induced Pluripotent Stem Cells (iPSCs) from human patients and treated them in vitro. It restored the REP1 enzymatic activity and restored protein trafficking! They also did subretinal gene therapy in normal mice

with their vector, and it was not toxic. This bodes well for a future treatment of human choroideremia with gene therapy.

Gene therapy for blindness.

Sahel JA, Roska B *Annu Rev Neurosci.* 2013 Jul 8;36:467-88. doi: 10.1146/annurev-neuro-062012-170304. Epub 2013 May 31.

This is an excellent review of gene replacement and neuroprotection and also new avenues such as optogenetic therapies.

Novel Mutation in BEST1 Associated With Retinoschisis

Ruwan A. Silva, Audina M. Berrocal, M, Byron L. Lam, Thomas A. Albini, *JAMA Ophthalmol* June. 2013;131(6):794-798.

Best vitelliform macular dystrophy is caused by mutations in BEST1 on the long arm of chromosome 11. An array of BEST1 phenotypes have been characterized, including microcornea, rod cone dystrophy, early-onset cataract, posterior staphyloma, vitreoretinopathopathy, and adult-onset foveomacular vitelliform dystrophy.

BEST1 encodes bestrophin, a 585–amino acid protein with more than 120 described mutations. The authors present 2 siblings with bilateral retinoschisis and electroretinography consistent with Best's disease. The siblings demonstrated bilateral symmetric multifocal macular lesions and a normal full-field ERG with an abnormal electrooculogram. The children also had subretinal fluid and retinoschisis associated with a novel mutation in BEST1.

De Novo Splice Mutation in the Versican Gene in a Family With Wagner Syndrome

Pierre-Raphael Rothschild, Isabelle Audo, Brigitte Nedelec, Tiffany Ghiotti, et.al. *JAMA Ophthalmol.* June 2013;131(6):805-807.

Wagner syndrome (WS) is a rare inherited vitreoretinopathy caused by mutations in the versican gene (VCAN). Clinically, Wagner syndrome is characterized by an optically empty vitreous with no systemic features. The risk of retinal detachment is high. The authors present a patient with asymptomatic parents and de novo VCAN mutation with clinical features typical for Wagner syndrome. De novo VCAN mutations have not been reported to date. This case report highlights the importance of VCAN screening in isolated individuals with a WS phenotype.

Mutation of GNAQ in a Cytologically Unusual Choroidal Melanoma in an 18-Month-Old Child

Steve Daniel Levasseur, Katherine E. Paton, Catherine D. Van Raamsdonk, Manraj K. S. Heran, *JAMA Ophthalmol.* June 2013;131(6):810-812.

Fewer than 1% of uveal melanomas occur in patients younger than 20 years. The

authors report a histologically unusual uveal melanoma in an 18 month old girl that was confirmed by the presence of a GNAQ somatic mutation. The authors note that only 5 cases of congenital uveal melanoma have been reported. Their patient presented with an abnormal red reflex at 6 months of age, so the author believe this case may be congenital. The clinical and histopathologic features of pediatric uveal melanoma are usually similar to those found in adults. They are typically unilateral, occur in the choroid with no sex predilection, and are usually of spindle cell type.

Clinical whole-exome sequencing for the diagnosis of Mendelian disorders. Y Yang, DM Muzny, JG Reid, et al.

N Engl J Med. October 2013; 369(16):1502-11.

Whole-exome sequencing is a diagnostic approach for the identification of molecular defects in patients with suspected genetic disorders. The authors performed whole-exome sequencing in a certified clinical laboratory on 250 probands, who were referred with a range of phenotypes suggesting potential genetic causes. Approximately 80% were children with neurologic phenotypes. Whole-exome sequencing identified 86 mutated alleles that were highly likely to be causative in 62 of the 250 patients, achieving a 25% molecular diagnostic rate (95% confidence interval, 20 to 31). Among the 62 patients, 33 had autosomal dominant disease, 16 had autosomal recessive disease, and 9 had X-linked disease. Many were de novo mutations: 83% of the autosomal dominant mutant alleles and 40% of the X-linked mutant alleles. This study suggests that whole-exome sequencing may identify an underlying genetic defect in approximately 25% of patients with suspected genetic disease, and this is especially applicable to children with neurologic phenotypes. This technique may replace traditional methods and enhance the success of finding that elusive genetic diagnosis.

Early-Onset Foveal Involvement in Retinitis Punctata Albescens With Mutations in RLBP1

Elodie Dessalces, Béatrice Bocquet, Jérôme Bourien, Xavier Zanlonghi, et.al. *JAMA Ophthalmol.* 2013;131(10):1314-1323. October 2013

Retinitis punctata albescens (RPA) is an autosomal recessive form of retinitis pigmentosa characterized by white dotlike deposits in the fundus, in most cases caused by mutations in RLBP1. The authors studied the visual function and disease progression in 11 patients with RPA. Patients were screened for mutations by polymerase chain reaction sequencing of the 9 RLBP1 exons. Patients underwent standard ophthalmic examination, fundus imaging, autofluorescence testing, Goldmann visual field measurement, optical coherence tomography, adaptive optics-based infrared fundus ophthalmoscopy, dark adaptometry, and electroretinography. All patients had nyctalopia from a young age. No specific refractive errors were identified. Visual acuity varied widely from 20/20 to count fingers. Electroretinography revealed rod dysfunction. Optical coherence tomography revealed decreased foveal thickness and progressive decrease in cone

density with age in several patients. The authors emphasize that early foveal cone death may be a feature of this disease.

RYR1 Mutations as a Cause of Ophthalmoplegia, Facial Weakness, and Malignant Hyperthermia

Sherin Shaaban, Leigh Ramos-Platt, Floyd H. Gilles, Wai-Man Chan, et.al. JAMA Ophthalmol. 2013;131(12):1532-1540. December 2013

Family members from 2 pedigrees, one consanguineous, one not, with atypical Moebius or congenital fibrosis of the extraocular muscles were examined and next gen sequencing performed. Affected members had homozygous or compound heterozygous mutations in the RYR1 gene. Mutations in this gene are also associated with malignant hyperthermia. The authors emphasize that patients with ophthalmoplegia may be associated with increased risk of malignant hyperthermia.

Peripapillary Chorioretinal Lacunae in a Girl With 3q21.3 to 3q22.1 Microdeletion With Features of Aicardi Syndrome

Eileen Broomall, Deborah Renaud, Rafif Ghadban, Ralitza Gavrilova, et.al. JAMA Ophthalmol. 2013;131(11):1485-1487. November 2013

Aicardi syndrome is characterized by the classic triad agenesis of the corpus callosum, seizures, and peripapillary chorioretinal lacunae. Aicardi syndrome occurs exclusively in girls and XXY boys. Although the inheritance pattern is X-linked dominant, the causative genes have not been identified. The authors present a 3 year old girl with peripapillary chorioretinal lacunae and dysplastic optic disc with an interstitial microdeletion on the long arm of chromosome 3. Revised clinical criteria allow for a diagnosis of Aicardi syndrome with 2 of the classic features plus 2 other associated findings, such as muscular hypotonia and cerebral migration anomalies, as seen in the authors' patient. The authors advocate using a chromosomal microarray in girls with chorioretinal lacunae when the neurological and systemic features do not fully correspond to those of Aicardi syndrome.

Genetic Testing for Inherited Eye Disease Who Benefits?

Janey L. Wiggs, Eric A. Pierce, JAMA Ophthalmol. 2013;131(10): 1265-1266. October 2013

The authors discuss how advances in gene sequencing technology, such as next generation sequencing, facilitates the rapid detection of possible disease causing gene mutations responsible for diseases such as congenital and juvenile glaucoma, inherited retinal degenerations and inherited optic neuropathies. Rapid sequencing should lead to development of clinical tests and facilitate the development of targeted therapies for such diseases. The most benefit will be realized by patients whose treatment options and disease risk assessment are dependent on the specific mutation causing their disease, and for these disorders, genetic tests should be routinely considered as part of the clinical evaluation.

Cone Dystrophy with Supernormal Rod Response Novel KCNV2 Mutations in an Underdiagnosed Phenotype

Lina Zelinger, Bernd Wissinger, Dalia Eli, Susanne Kohl, *Ophthalmology*
November 2013; 120(11):2338-2343

This article comes from ophthalmology study centers in Jerusalem, Israel, and Tübingen, Germany. This is a case series involving patients with cone-dominated disease in unaffected relatives with a purpose/objective to study the clinical variability in KCNV2 mutation spectrum in cone dystrophy with supernormal rod response (CDSRR) in the Israeli population.

Participants: Two-hundred and twenty families including 447 affected individuals were clinically classified as manifesting a retinal degeneration with predominant involvement of the photopic system. This included the clinical diagnosis of a cone-rod dystrophy or CRD, cone dystrophy (CD) and maculopathy. Genomic DNA was extracted and Sanger sequencing was performed on polymerase chain reaction products (PCR). Whole genome single nucleotide polymorphism analysis was performed using Affymetrix platforms.

Main outcome measures: Single nucleotide polymorphisms microarray and homozygosity analysis, DNA sequence analysis, visual function testing and electroretinography were used.

Conclusions: This is the first report of genetic and clinical analysis of cone dystrophy with super-normal rod response (CDSRR) in the Israeli population leading to the identification of 4 novel/new KCNV2 mutations. The results of this study support recent studies showing that CDSRR can be misdiagnosed and therefore, screening of KCNV2 for mutations should be considered in patients with cone-dominated diseases, particularly when dark-adapted responses are delayed.

Outcome of ABCA4 Disease-Associated Alleles in Autosomal Recessive Retinal Dystrophies: Retrospective Analysis in 420 Spanish Families

Rose Riveiro-Alvarez, Miguel-Angel Lopez-Martinez, Jana Zernant, Jana Aguirre-Lamban *Ophthalmology* November 2013; 120(11):2332-2337

This is a case series of a total of 420 unrelated Spanish families; 259 with autosomal recessive Stargardt's disease; 86 with autosomal recessive cone-rod dystrophy; 75 with autosomal recessive retinitis pigmentosa. The purpose of this study is to provide a comprehensive overview of all detected mutations in the ABCA4 gene in Spanish families for autosomal recessive retinal disorders including Stargardt's disease (arSTGD), cone-rod dystrophy (arCRD) and retinitis pigmentosa (arRP), and to assess genotype-phenotype correlation and disease progression in 10 years by considering the type of variants in the age of onset.

Methods: Spanish families are analyzed through a combination of ABCR400 genotyping microarray, denaturing high performance liquid chromatography and

high-resolution melting scanning. Direct sequencing was used as a confirmation technique for identified variants.

Main outcome measures: DNA sequence variants, mutation detection rates, haplotypes, age at onset, central or peripheral vision loss and night blindness.

Results: This study detected 70.5% ABCA4 mutations in autosomal recessive Stargardt's disease and 36.6% of all expected ABCA4 mutations in autosomal recessive cone-rod dystrophy patient cohort.

Conclusions: An increasing understanding of causal ABCA4 alleles and autosomal recessive Stargardt's disease and autosomal recessive cone-rod dystrophy facilitates disease diagnosis and prognosis and also is important in selecting patients for emergent clinical trials of therapeutic interventions.

Reviewers Comment: The authors suggest genetic testing (specifically, ABCR400 genotyping microarray, denaturing high-performance liquid chromatography and high-resolution scanning to be included) before making diagnoses in a patient. Finally, the authors state that patients' with classic autosomal recessive retinitis pigmentosa phenotypes should be screened first for mutations in the known autosomal recessive RP genes and not in the ABCA4 disease-associated alleles.

Ocular Manifestations of 22q11.2 Microduplication

Jose A. Cordovez, Jenina Capasso, Michelle D. Lingao, Karthikeyan A. Sadagopan, *Ophthalmology* January 2014; 121(1):392-398

This study comes from the Ocular Genetics and Glaucoma Service of Thomas Jefferson University, Philadelphia, Pennsylvania.

This is a case series designed to report a new ocular manifestations of the duplication 22q11 syndrome and explore involved genes that may offer insight to mechanisms of pathogenesis.

Main outcome measures: Microarray results and identification of candidate genes within the duplicated segment.

Results: The patients in this case demonstrated Marcus Gunn jaw winking, Duane's retraction syndrome and other abnormal eye movements consistent with a congenital cranial dysinnervation disorder (CCDD), retinal vascular tortuosity, and primary infantile glaucoma.

Conclusions: This case expands the ocular phenotype for duplication of 22q11 and serves to identify potential candidate genes for the development of congenital cranial dysinnervation disorder (CCDD).

Phenotypic Conservation in Patients With X-Linked Retinitis Pigmentosa Caused by RPGR Mutations

Sarwar Zahid, Naheed Khan, Kari Branham, Mohammad Othman, et.al. *JAMA Ophthalmol.* August 2013;131(8):1016-1025.

The purpose of this study was to evaluate the clinical findings in patients with X-linked retinitis pigmentosa with 13 distinct RPGR mutations and assess for

phenotypic concordance or variability. This retrospective review, spanning 25 years, identified 42 such patients with a median follow up of 5.5 years. Clinical data assessed for concordance included visual acuity, Goldmann visual fields, and full-field electroretinography. Visual acuity and ERG phenotypes are concordant in some patients carrying identical mutations but assessment of Goldmann visual field phenotypes revealed stronger phenotypic conservation. Phenotypic concordance is important for establishing proper counseling of patients as well as for establishing accurate patient selection and efficacy monitoring in therapeutic trials.

Retinal gene therapy in patients with choroideremia: initial findings from a phase 1/2 clinical trial.

Maclaren RE, Groppe M, Barnard AR, Cottrill CL et al, *Lancet*. 2014 Jan 15. (13)62117-0.

Choroideremia is an X-linked recessive retinal degeneration. It is caused by mutations in the *CHM* gene which encodes the REP1 protein. It causes peripheral vision loss first, leaving a small island of central vision for many years. Retina, choroid and RPE are lost first in the periphery and later in the center. Central vision corresponds to this visibly present preserved central retina. In this phase I study, 6 male patients with choroideremia due to *CHM* mutations predicted to be null (i.e. to completely lack the protein of interest) were recruited to have subretinal gene therapy. Age ranged from 41 to 63 years. AAV2 with a chicken Beta actin promoter was used as the vector; this combination has been successfully used in the LCA gene therapy trial. The authors also added a Woodchuck hepatitis post-translational regulatory element (WPRE) to enhance AAV-mediated transgene expression. Yes, you read that correctly, **Woodchuck hepatitis virus!**

Because of the difficulty in making retinal blebs with only a small area of remaining retina, a retinal detachment was first made through a retinotomy, then a second injection with the vector in it was placed under the detached retina. Overall mean gain in visual acuity was 3.8 letters and in all patients retinal sensitivity increased in the treated eye over a time period in which the untreated eye decreased slightly. Two patients gained 2-4 lines of vision despite retinal detachment of the macula being part of the procedure. Four other patients with near normal acuity pre-op lost 1-3 letters.

In conclusion, this trial showed safety and some exciting efficacy in quite advanced choroideremia patients. It remains to be seen if the most important effect—halt of progression—will be demonstrated.

Next generation sequencing-based molecular diagnosis of retinitis pigmentosa: identification of a novel genotype-phenotype correlation and clinical refinements Feng Wang · Hui Wang · Han-Fang Tuan et al, *Hum Genet* (2014) 133:331–345

123 patients with retinitis pigmentosa in whom no genetic cause could be found

with typical genetic testing had next generation sequencing performed with a special gene capture panel covering 163 known retinal genes including 48 known RP genes.

61 mutations were identified in 45 probands including 38 mutations never reported before. Clinical diagnosis was changed in 6 patients based on the new genetic information.

Of note, 5 patients had recessive mutations in *CLN3*, the gene which causes juvenile Batten Disease. It was previously thought that all patients with functional mutations in this gene would develop neurodegeneration, but in this cohort the patients found apparently had only RP. The authors did a good job of following up on these patients to be sure they only had RP. One child is only 10 years old, still in the age of developing Juvenile Batten, and another 20 years old, so these mutations are still suspect in my mind. However there were 3 probands who had other family members with the same mutations and same retina-only phenotype who were in their 40's and 50's! None of the patients identified have the common Batten disease deletion in *CLN3* that occurs in about 80% of patients with Juvenile Batten Disease. Most were novel and missense and there was one recurring mutation, c.1213C>T, p.(R405 W).

In conclusion, next generation sequencing may aid in diagnosis of patients with RP in whom traditional gene directed testing has been negative, however of the 123 patients tested only 45 had genes found, so it is not perfect. *CLN3* may be a "new" isolated RP gene, adding to our growing understanding that genes that cause syndromes may often cause isolated features of those syndromes when the mutations are mild.

DNA Variations in Oculocutaneous Albinism: An Updated Mutation List and Current Outstanding Issues in Molecular Diagnostics

Dimitre R. Simeonov, Xinjing Wang, Chen Wang, Yuri Sergeev et al, *Hum Mutat* 34:827–835, 2013

Albinism is a common cause of nystagmus in children, and it may be difficult to diagnose partial forms. Genetic testing is available but because the carrier frequency is 1/100 individuals and because some true disease causing mutations still cannot be found in affected people, genetic testing can be complex. An up to date list of mutations and their status is vital. The controversial R402Q variant is discussed.

Induced pluripotent stem cells as custom therapeutics for retinal repair: Progress and rationale.

Wright LS1, Phillips MJ1, Pinilla I2, Hei D3, Gamm DM4 *Exp Eye Res.* 2014 Feb 14.

Using induced pluripotent stem cells, which can be produced from skin biopsies, may be a way to repair and/or replace ocular tissues without the ethical issues of embryonic stem cells.

Trial End Points and Natural History in Patients With G11778A Leber Hereditary Optic Neuropathy : Preparation for Gene Therapy Clinical Trial.

Lam BL, Feuer WJ, Schiffman JC, Porciatti V, Vandenbroucke R, Rosa PR, Gregori G, Guy J., JAMA Ophthalmol. 2014 Feb 13.

A clinical trial using gene therapy for LHON is planned but has not started. The authors sought to study what the endpoints should be, especially is spontaneous recovery, which could be confused with treatment efficacy, common. They did a prospective observational study including 44 individuals with G11778A LHON. Follow up was 6-36 months. 13 eyes of 8 patients (18%) improved, but 24 months after the onset of symptoms, any further improvements were to no better than 20/100. Acuity recovery occurred in some patients despite continued marked retinal nerve fiber layer thinning indistinguishable from that in patients who did not recover visual acuity. Spontaneous improvement of visual acuity in patients with G11778A LHON is not common and is partial and limited, so improvements in vision with gene therapy with the ND4 subunit it should be possible to detect. Visual acuity appears to be the most suitable primary end point for the planned clinical trial.

ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing

Robert C. Green, Jonathan S. Berg, Wayne W. Grody, Sarah S. Kalia, etal, Genet Med . 2013 July ; 15(7): 565–574

Now that whole exome sequencing is being used as a type of genetic testing, it is apparent that all of us have many mutations without realizing it. Mutations in a gene not being directly tested for the clinical disorder the patient complains of may have health implications. Should patients be told about these “incidental findings” or will it cause anxiety without any actionable plan? The American College of Medical Genetics has made recommendations for which types of incidental findings should be reported.

In summary they recommend:

1. Constitutional mutations found in the genes on the minimum list (see Table) should

be reported by the laboratory, regardless of the indication for which the clinical sequencing was ordered.

a. Additional genes may be analyzed for incidental (secondary) variants, as deemed appropriate by the laboratory.

b. Incidental (secondary) variants should be reported regardless of the age of the patient.

c. Incidental (secondary) variants should be reported for any clinical sequencing conducted on a constitutional (but not tumor) tissue. This includes the normal sample of a tumor-normal sequenced dyad and unaffected members of a family trio.

2. The Working Group recommends that laboratories seek and report only the types of variants within these genes that we have delineated (see Table).

a. For most genes, only variants that have been previously reported and are a recognized cause of the disorder or variants that are previously unreported but are of the type which is expected to cause the disorder, as defined by prior ACMG guidelines,²⁰ should be reported.

b. For some genes, predicted loss of function variants are not relevant (e.g., COL3A1 and most hypertrophic cardiomyopathy genes).

c. For some genes (e.g., APOB), laboratories should only report variants for certain conditions.

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Genet Med. Author manuscript; available in PMC 2014 January 01.

3. It is the responsibility of the ordering clinician/team to provide comprehensive preand post-test counseling to the patient.

a. Clinicians should be familiar with the basic attributes and limitations of clinical sequencing.

b. Clinicians should alert patients to the possibility that clinical sequencing may generate incidental findings that could require further evaluation.

c. Given the complexity of genomic information, the clinical geneticist should be consulted at the appropriate time that may include ordering, interpreting, and communicating genomic testing.

4. These recommendations reflect limitations of current technology, and are therefore

focused on disorders that are caused by point mutations and small insertions and deletions, not those primarily caused by structural variants, repeat expansions, or copy number variations.

5. The Working Group recommends that the ACMG, together with content experts

and other professional organizations, refine and update this list at least annually.

fMRI of Retina-Originated Phosphenes Experienced by Patients with Leber Congenital Amaurosis.

Ashtari M, Cyckowski L, Yazdi A,

Viands A, Marshall K, et al. (2014)

PLoS ONE 9(1)

Functional MRI can be used to elucidate visual phenomena and visual function in LCA patients.

Immunosuppressive Treatment for Retinal Degeneration in Juvenile Neuronal Ceroid Lipofuscinosis (Juvenile Batten Disease).

Drack AV, Mullins RF, Pfeifer WL, Augustine EF, Stasheff SF, Hong SD. *Ophthalmic Genet.* 2014 Feb 19.

Immunosuppression over 2 years in a child with Juvenile Batten Disease did not stop the retinal degeneration, but may have slowed it. A short tolerability clinical trial using Cellcept in patients with this disorder is currently underway.

Clinical interpretation and implications of whole-genome sequencing.

Dewey FE, Grove ME, Pan C, Goldstein BA, et al. *JAMA.* 2014 Mar 12;311(10):1035-45.

Ordering genetic testing for single genes or panels of genes known to directly cause a genetic disorder has become standard of care in ophthalmology and most other fields of medicine. However the role of whole-genome sequencing (WGS), i.e. sequencing one individual's entire genome to provide "personalized medicine," is less clear. The authors of this paper sought to determine whether whole-genome sequencing is a clinically and/or personally useful test for physicians and patients.

12 adults had whole-genome sequencing performed by Illumina, Inc., and 9/12 had the same testing by another company, Complete Genomics, Inc. These are commercially available fee for service laboratories, however all 12 participants received the testing as part of a research study. None of the participants had a known genetic disease at the time of recruitment. A multidisciplinary team reviewed the genetic findings, and a team of 5 physicians made recommendations for follow up of these findings.

The authors found that 10-19% of known inherited disease genes were not appropriately covered to pick up single nucleotide disease-causing variants.

Concordance between the two different testing labs was excellent (99-100%) for the known disease-causing genes they did cover, but poor for small insertions and deletions of genes (53-59%).

Each of the 12 adult participants had 90 to 127 genetic variants that could possibly be disease-causing. Each one of these variants required, on average, 54 minutes of work to determine whether it was disease-causing. 69% of the variants found which had formerly been reported as disease-causing were found to be benign or of uncertain significance.

Each of the 12 participants had 2-6 personal disease-risk findings. One patient had a frameshift mutation in BRCA1, predisposing to breast and ovarian cancer. Physicians proposed a median of 1-3 further diagnostic tests and/or referrals per patient based on the findings.

In conclusion, the authors noted that for 12 adult volunteers WGS had incomplete coverage of disease-causing genes, low reproducibility between labs for finding deletions or duplications, and uncertainty about the clinical usefulness of many of the variants found. In at least one case a clinically actionable genetic mutation was found. The authors recommend considering these limitations when considering whole genome sequencing for "screening" of patients at this time.

Ocular Manifestations of 22q11.2 Microduplication

Jose A. Cordovez, Jenina Capasso, Michelle D. Lingao, Karthikeyan A. Sadagopan, *Ophthalmology* January 2014; 121(1):392-398

This study comes from the Ocular Genetics and Glaucoma Service of Thomas Jefferson University, Philadelphia, Pennsylvania.

This is a case series designed to report a new ocular manifestations of the duplication 22q11 syndrome and explore involved genes that may offer insight to mechanisms of pathogenesis.

Main outcome measures: Microarray results and identification of candidate genes within the duplicated segment.

Results: The patients in this case demonstrated Marcus Gunn jaw winking, Duane's retraction syndrome and other abnormal eye movements consistent with a congenital cranial dysinnervation disorder (CCDD), retinal vascular tortuosity, and primary infantile glaucoma.

Conclusions: This case expands the ocular phenotype for duplication of 22q11 and serves to identify potential candidate genes for the development of congenital cranial dysinnervation disorder (CCDD).

17.TRAUMA

Protective Eyewear Use as Depicted in Children's Television Programs

Michael E. Korchak, Robert U. Glazier, Rebecca S. Slack, Michael W. Plankey, Hylton R. Mayer, *J Pediatr Ophthalmol Strabismus* 2013; 50:102-105 (March/April)

The study analyzes popular television programs to evaluate use of protective eye wear and depiction of eye injuries and found that for the most part children's television programs do not treat ocular injuries as seriously as it should be treated. There were several scenes where eye protection should have been used and was not. In addition, when eye injuries did occur (mostly chemical injuries), the consequences were not major and were often resolved by itself in the following scene. As many eye injuries can be prevented by better education, appropriate protective eyewear use and avoidance of risk factors, children's television programs are at a unique position to assist in this as many children watch an average of 3-5 hours of television a day. The study found that the use of protective eyewear and eye injuries are rarely shown on scripted children's television programs

Incidence of Retinal Hemorrhages in Abusive Head Trauma

Majida A. Gaffar, ; Debra Esernio-Jenssen, Sylvia R. Kodsi, *J Pediatr Ophthalmol Strabismus* 2013; 50:169-172 (March/April)

The authors did a retrospective review of 48 cases of abusive head trauma to determine whether there is a correlation between retinal hemorrhages and cases

where the perpetrator was identified versus if the perpetrator was not identified. In addition, if the perpetrator was identified, the authors further evaluated if the perpetrator confessed versus when the perpetrator did not confess. The study concluded that there was a statistically significant difference if the perpetrator was identified (whether there was a confession or not) versus if there was no identified perpetrator.

Patterns of Retinal Hemorrhage Associated With Increased Intracranial Pressure in Children

Gil Binenbaum, David L. Rogers, Brian J. Forbes, Alex V. Levin
PEDIATRICS Vol. 132 No. 2 August 2013 pp. 430 -434.

This is a study that analyzes the incidence and patterns of retinal hemorrhages associated with non-traumatic raised intracranial pressure (> 20 cm H₂O). This incidence and pattern is compared to retinal hemorrhages noted in raised intracranial pressure seen in abusive head trauma.

One hundred children were evaluated prospectively and retrospectively (mean age: 12 years; range: 3–17 years). Mean opening pressure was 35 cm H₂O (range: 20–56 cm H₂O); 68 (68%) children had opening pressure >28 cm H₂O. The most frequent etiology was idiopathic intracranial hypertension (70%). Seventy-four children had papilledema. Sixteen children had retinal hemorrhages: 8 had superficial intraretinal peripapillary retinal hemorrhages adjacent to a swollen optic disc, and 8 had only splinter hemorrhages directly on a swollen disc. All had significantly elevated OP (mean: 42 cm H₂O).

In this study, only a small proportion of children with nontraumatic elevated ICP have retinal hemorrhages. When present, retinal hemorrhages are associated with markedly elevated OP, intraretinal, and invariably located adjacent to a swollen optic disc. This peripapillary pattern is distinct from the multilayered, widespread pattern of retinal hemorrhages in abusive head trauma. When retinal hemorrhages are numerous, multilayered, or not near a swollen optic disc (eg, elsewhere in the posterior pole or in the retinal periphery), increased ICP alone is unlikely to be the cause.

Epidemiology of infant ocular and periocular injuries from consumer products in the United States, 2001-2008

Chen AJ, Linakis JG, Mello MJ, and Greenberg PBJ June AAPOS 17;3:239-242

Data for this study was derived from the National Electronic Injury Surveillance System. One hundred sample hospitals are representative of the estimated 5300 hospitals with 24-hour emergency departments in the United States. Over a seven-year period, there were an estimated 21,000 visits to US emergency departments by patients aged 0-12 months for consumer product related eye injuries. The majority (63%) involved infants 9-12 months old and there was a slight preponderance of males (54%). Chemical (46%) and household items (24%) were the most likely causative agents. Over $\frac{3}{4}$ of the injuries occurred in the home. The leading injuries were contusions and abrasions, followed by conjunctivitis. Patient acuity and long-

term follow-up data were not determined. Also this data only represents emergency room visits., and may not represent across the board injury percentages.

Visual Outcomes after Blunt Ocular Trauma

Richard J. Blanch, Peter A. Good, Peter Shah, Jon R.B. Bisho *Ophthalmology*
August 2013;120:1588-1591

This is a study from Birmingham, United Kingdom. The purpose of the study is to describe the prognosis and retinal location in patients presenting with acute traumatic maculopathy and extramacular retinal injuries. This is a retrospective, noninterventional case series. All patients presented with commotio retinae or sclopetaria retinae to the Birmingham Midland Eye Centre Eye Casualty from October 1, 2007, to February 23, 2011. The main outcome measures were assessed by visual acuity.

Conclusions: After macular injury, 26% of patients were left with a visual acuity of less than 20/30. Reduced visual acuity after extramacular commotio retinae may represent occult macular injury or previously undiagnosed visual impairment in the affected eye. Extramacular commotio occurs mostly in an inferotemporal to temporal location, consistent with direct trauma to the sclera overlying the injured retina.

'Toy' Laser Macular Burns in Children.

N Raoof, TKJ Chan, NK Rogers, W. Abdullah, et al.,*Eye (Lond)*. 2014
Feb;28(2):231-4

The authors present a case series of five children, all who developed macular injury following exposure to laser 'toys' purchased online. Most children had vision in the 20/40 range and one patient had a choroidal in the neovascular membrane. The authors state that the power of these lasers exceeds the standards accepted for class 2 lasers, that which are not supposed to cause injury when exposed to the eye.

Demographic and Clinical Profile of Ocular Chemical Injuries in the Pediatric Age Group

Rasik B. Vajpayee, Himanshu Shekhar, Namrata Sharma, Vishal Jhanji,
Ophthalmology January 2014; 121(1):377-380

This study comes from the All India Institute of Medical Sciences, New Delhi, India, and the Centre for eye Research Australia, University of Melbourne, Melbourne, Australia.

This is a retrospective hospital-based study designed to review risk factors, management and visual outcomes of pediatric chemical eye injuries in a tertiary care hospital in North India.

Main outcome measures: Demographic profile, nature of chemical injury, complications and visual outcomes after chemical injury.

Conclusions: Chemical injuries in pediatric patients are more commonly encountered in the preschool age group and are associated with severe visual

loss. Alkali injury from bursting of chuna packets was the most common mode of injury in pediatric patients in this study.

Reviewers Comment: Lime was the most commonly involved chemical in 88 cases. The lime came from “chuna packet” injury, which is commonly used as an additive to tobacco chewing in this part of the world. Other chemicals include toilet cleaner, caustic soda, organic acids and other unknown chemicals.

Pediatric hyphema: a review of 138 consecutive cases

SooHoo JR, Davies BW, Braverman RS, et al, J AAPOS December 2013;17:565-567

The authors performed an 8-year retrospective medical record review of consecutive cases of traumatic hyphema in children. Children with an open globe injury or severe systemic injury that prevented ophthalmic evaluation were excluded. Of the 138 cases, 122 occurred in boys. The overwhelming majority (n=123), occurred in the home. The most common mechanisms for injury were general play (27%), projectiles from guns (paintball, airsoft, pellet) (26%), and sports (23%). 97% recovered vision of at least 20/40. The three cases that did not occur sustained choroidal rupture, retinal scarring, or optic neuropathy. No rebleeding episodes occurred. Initial IOP measurements were available for 88% of the patients, and they averaged 19.9mm Hg (range 6-51mm Hg). Six patients required medical treatment >1 month for persistent elevated IOP, and 4 patients required surgical intervention (2 A/C washouts and 2 glaucoma filtration surgeries). The average initial IOP of patients requiring surgery was 35mm Hg. Two patients developed hypotony 2' to cyclodialysis clefts. Surgical cohorts in this study were small and the study had no standardized treatment protocols.

Retinal hemorrhage and brain injury patterns on diffusion-weighted magnetic resonance imaging in children with head trauma

Binenbaum G, Christian CW, Ichord RN et al, J AAPOS December 2013;17:603-608

Diffusion-weighted MRI is an excellent technique to evaluate hypoxic-ischemic injury (HII) in pediatric head trauma. This technique can identify brain tissue damage much earlier than T2-weighted sequences. It is especially helpful in infants. This study evaluated the associations between retinal hemorrhage severity and HII patterns as identified on DW-MRI in young children with accidental and inflicted head trauma. Children were <3 years old, admitted over a 3-year period, and had a brain DW-MRI within 1 week of injury. A primary analysis of this cohort of patients was already published but did not include ocular findings. Five patterns of brain injury were identified. Forty-five children met inclusion criteria (16 accidental head trauma, 29 inflicted head trauma). The median age was 4.5 months for accidental cases and 2.3 months for inflicted injuries. Traumatic injury lesions on DW-MRI were present on 14 of 16 accidental injuries and all 29 inflicted injuries. HII lesions were found in none of the

accidental traumas and 10/29 abusive head trauma cases. Retinal hemorrhages were found in 2/16 accidental cases and 11/29 inflicted cases. Moderate to severe retinal hemorrhages were seen more frequently if HII was present. Retinal hemorrhage severity was not however correlated with traumatic injury severity. Based on these results, the HII pattern seems distinct to inflicted trauma, and its presence may be helpful in determining the etiology of head trauma.

18. RETINA

Clinical Phenotypes and Prognostic Full-Field Electroretinographic Findings in Stargardt Disease Sarwar Zahid, Thiran Jayasundera, William Rhoades, Kari Branham et al. Am J Ophthalmol March 2013; 155(3): pg 465-473.

This retrospective review of 198 patients with Stargardt's Disease evaluated the relationship between clinical and full-field ERG findings with progressive loss of visual function. This study found that the majority of patients with Stargardt's do not exhibit progressive scotoma. A smaller subgroup did progress more quickly and they appeared to have significantly worse scotopic B-wave amplitudes at presentation. In addition, there was a correlation between full field ERG values at presentation and clinical stage with respect to fundusoscopic examination.

Evaluation of Retinal Nerve Fiber Layer Thickness in Patients With Anisometropic and Strabismic Amblyopia Using Optical Coherence Tomography

Ismail Ersan, Nazmi Zengin, Banu Bozkurt, Ahmet Özkagnici J Pediatr Ophthalmol Strabismus 2013; 50:113-117 (March/April)

Retinal nerve fiber layer thickness was evaluated in strabismic amblyopic eyes, anisometropic amblyopic eyes and control eyes using optic coherence tomography. OCT measurements found no significant difference in RNFL thickness between strabismic, anisometropic and control eyes; however, the RNFL thickness seemed to be related to refraction.

Macular and Retinal Nerve Fiber Layer Thickness in Unilateral Anisometropic or Strabismic Amblyopia

Dima Andalib, Alireza Javadzadeh, Reza Nabai, Yashar Amizadeh, J Pediatr Ophthalmol Strabismus 2013; 50:218-221 (July/August)

The purpose of the article is to compare macular and nerve fiber layer (NFL) thickness in amblyopic versus nonamblyopic eyes by optical coherence tomography (OCT). A prospective cross sectional descriptive study was performed. Fifty patients

were evaluated and the macular thickness as well as the peripapillary nerve fiber layer thickness. In anisometropic amblyopia, the macula was found to be thicker. This was not the case in strabismic amblyopia. There was no significant difference in NFL thickness in strabismic or anisometropic amblyopia.

Hypertensive Retinopathy in Severely Hypertensive Children: Demographic, Clinical, and Ophthalmoscopic Findings From a 30-Year British Cohort

Katie M. Williams, Anish N. Shah,; Danny Morrison, Manish D. Sinha, *J Pediatr Ophthalmol Strabismus* 2013; 50:222-228 (July/August)

A retrospective chart review of 53 British children with severely hypertensive disease with or without renovascular disease was performed. 39 children received an ophthalmic exam; of these, only 7 had hypertensive retinopathy, 6 were severe disease. The trend was for children with renovascular disease to have more severe retinopathy but the difference was not significant. Also, children with hypertensive retinopathy had higher blood pressure than those without.

Comparison Of Anatomic And Functional Results After Retinotomy For Retinal Detachment In Pediatric And Adult Patients

Marcin Stopa, Jaroslaw Kociecki, Piotr Rakowicz, Anna Gotz-Wieckowska, *Eur J Ophthalmol* May June 2013; 23(3): 410 – 416

This was a retrospective, nonrandomized, interventional study involving 20 pediatric patients and 25 adult patients operated with vitrectomy and retinectomy due to retinal detachment. The study observed that in the pediatric population, reattachment was less (60%) than adults (88%), a higher number of further reoperations ($p=0.008$) was required and postoperative proliferative vitreoretinopathy was significantly more frequent ($p=0.003$). Statistically significant improvement in visual acuity was observed in adults ($p<0.001$) but not in children ($p=0.360$) due to large proportion of anatomic failure. The clinical features and prognosis for pediatric retinotomies and retinectomies are different from those for adults. Even though the overall visual acuity was worse in children than in adults, 25% of pediatric eyes achieved 5/50 or better vision.

Topographic Correlation between β -Zone Parapapillary Atrophy and Retinal Nerve Fiber Layer Defect

Bum-Joo Cho, Ki Ho Park, *Ophthalmology* March 2013;120:528-534

This is a retrospective, cross-sectional study involving 128 eyes from 128 consecutive patients with primary open angle glaucoma (POAG) and a single localized retinal nerve fiber layer (RNFL) defect performed in Seoul, Korea. This involved the use of digital optic disc photographs involving topographic

measurements of localized retinal nerve fiber layer (RNFL) and β -zone parapapillary atrophy (PPA). (This is very well-defined in figure 1, page 529.)

The main outcome measures were angular location and angular extent of β -zone parapapillary atrophy and retinal nerve fiber layer defect, angular location of the point of maximal radial extent (PMRE) of the β -zone parapapillary atrophy and the β -zone parapapillary atrophy-to-disc ratio.

Conclusions: 64.1% of the 120 eyes with single localized retinal nerve fiber layer defect had β -zone parapapillary atrophy. The angular location of the retinal nerve fiber layer defect showed a linear correlation of those with the β -zone parapapillary atrophy. Comments: In primary open angle glaucoma a localized retinal nerve fiber layer defect is correlated spatially with β -zone of parapapillary atrophy. This study involved some new concepts including β -zone parapapillary atrophy. This is an extension of traditional analysis of cup-to-disc measurements utilizing digital photographs.

Peripheral Nonperfusion and Tractional Retinal Detachment Associated with Congenital Optic Nerve Anomalies

Michael J. Shapiro, Clement C. Chow, Michael P. Blair, Lawrence M. Kaufman, *Ophthalmoscopy* March 2013;120:607-615

This is a retrospective observational case series of 15 patients with congenital optic nerve anomalies referred for pediatric retinal consultation. Sixteen eyes of the 9 patients with optic nerve hypoplasia and 8 eyes of 6 patients had congenital optic nerve anomalies, including optic nerve coloboma, morning glory disc deformity and peripapillary staphyloma, were included.

All patients underwent examination under anesthesia. Wide angle retinal photographs and fluorescein angiograms were reviewed. The severity of nonperfusion was graded. The presence of fiber vascular proliferation, vitreous hemorrhage, and traction retinal detachment were documented. The anatomic outcome was also recorded.

Conclusions: Congenital optic nerve anomalies may be associated with peripheral retinal nonperfusion and secondary complications of vascular proliferation, vitreous hemorrhage, and traction retinal detachment. In this select group of patients and nonperfusion associated with optic nerve hypoplasia seem to be more severe and associated more frequently with secondary complications. Peripheral retinal examination and eyes with optic nerve anomalies may identify nonperfusion or fibrovascular proliferation. The author suggests that laser treatment to the avascular retina may help prevent complications of proliferative retinopathy in the future.

Comments: This article strongly suggests the use of fluorescein angiograms to detail the peripheral area of the retinal nonperfusion or fibrovascular proliferation. These suggestions, if adopted by consensus with other investigation, may change the standard of care for patients with congenital anomalies of the optic nerve head.

Three-Year Follow-up after Unilateral Subretinal Delivery of Adeno-Associated Virus in Patients with Leber Congenital Amaurosis Type 2

Francesco Testa, Albert M. Maguire, Settimio Rossi, Eric A. Pierce, *Ophthalmology* June 2013;120:1283-1291

This is a clinical trial involving 5 patients with Leber congenital amaurosis and 2 patients with RPE65 gene mutations. The aim of the study was to show the clinical data of long-term (3-year) follow-up of 5 patients affected by Leber congenital amaurosis type 2 (LCA2) treated with a single unilateral injection of adeno-associated virus AAV2-hRPE65v2. This study included 5 LCA2 patients with RPE65 mutations.

Methods: Subjects were evaluated before and after surgery at designated follow-ups visits by complete ophthalmic examination. Each evaluation included best-corrected visual acuity, kinetic visual acuity, nystagmus testing, and pupillary light reflex.

Conclusions: The 3 year follow-up on 5-patient Italian cohort involved in the LCA2 gene therapy clinical trial showed a stability of improvement in visual and retinal function that had been achieved a few months after treatment. Longitudinal data analysis showed that the maximum improvement was achieved within 6 months after treatment, and the visual improvement was stable up to the last observed time point (3 years).

Comment: Photographs on page 1288, 1289, along with visual field assessment showed stability in all eyes and in some cases improvement in the Goldman visual field. This report describes a 3 year follow-up of 5 Italian subjects enrolled in the RPE65 gene therapy clinical trial performed at Children's Hospital of Philadelphia in conjunction with Second University of Naples.

A Phenotype-Genotype Correlation Study of X-Linked Retinoschisis

Ajoy Vincent, Anthony G. Robson, Magella M. Neveu, Genevieve A. Wright, *Ophthalmology* July 2013;120:1454-1464

This is a retrospective, comparative study of 57 patients with molecularly confirmed X-linked retinoschisis at Moorfields Eye Hospital in London, United Kingdom. The purpose of the study is to compare the clinical phenotype in detail with electroretinographic parameters and X-linked retinoschisis (XLRS). The clinical and electrophysiologic data associated with different types of mutation of the RS1 gene were used as main outcome measures. Pattern electroretinography (PERG) and full field electroretinography (ERG), incorporating international standard recordings, were performed in 44 cases. Thirteen cases were tested using a simplified ERG protocol. This autofluorescence imaging and optical coherence tomography were performed in most cases.

Conclusions: There is a profound phenotypic variability in patients with X-linked retinoschisis. Most patients have abnormal ERG with inner retinal dysfunction. Generalized cone system dysfunction is commonly associated with an abnormal "On-Response" and less commonly with an "Off-Response". Mutations in the RS1 gene consistently caused electronegative bright-flash electroretinogram responses.

Metastasis from Uveal Melanoma Associated with Congenital Ocular Melanocytosis A Matched Study

Arman Mashayekhi, Carol L. Shields, Jerry A. Shields, Neelema Sinha,
Ophthalmology July 2013;120:1465-1468

This is a matched retrospective study of 57 patients with uveal melanoma associated with ocular melanocytosis. The purpose of this study was to determine the rate of metastasis resulting from uveal melanoma associated with congenital ocular melanocytosis (COM) and to compare it with the rate of metastasis resulting from uveal melanoma not associated with congenital ocular melanocytosis. This study was performed at the Wills Eye Institute in Philadelphia.

Each patient in the melanocytosis group was matched with 2 patients with uveal melanoma not associated with ocular melanocytosis (nonmelanocytosis group) for age, gender, location of anterior tumor margin, location of tumor epicenter, tumor basal diameter, and tumor thickness were measured.

Conclusions: In this matched study, patients with uveal melanoma associated with congenital ocular melanocytosis were twice as likely to have systemic metastasis compared with patients with uveal melanoma not associated with congenital ocular melanocytosis.

Comments: This study reinforces the importance of taking careful photo images of both the sclera as well as the fundus in children affected with ocular melanocytosis. It also stresses the importance of following this patient throughout life.

Subclinical Macular Findings in Infants Screened for Retinopathy of Prematurity with Spectral-Domain Optical Coherence Tomography

Adam M. Dubis, C. Devika Subramaniam, Pooja Godara, Joseph Carroll,
Ophthalmology August 2013;120:1665-1671

This is a prospective, observational case series of 49 prematurely born neonates born in Milwaukee, Wisconsin. Forty-nine infants were imaged using a handheld spectral-domain OCT. Images were acquired in nonsedated infants in the neonatal intensive care unit. Some patients were followed and reimaged over the course of several weeks.

Main Outcome Measures: This included determination of foveal retinal lamination, image analysis, and clinical observation.

Conclusions: Data from this study suggested that there is persistence of the inner retinal layers in premature infants regardless of what stage of ROP was present. Subclinical cystic macular edema is seen in premature infants; however, cystic macular edema does not appear to be correlated with the stage of retinopathy of prematurity. The study shows that hand-held spectral-domain OCT imaging is a viable technique for evaluating subclinical macular findings in premature infants.

Varicella-Zoster Virus–Associated Multifocal Chorioretinitis in 2 Boys

Christina Meenken, Aniki Rothova, JAMA Ophthalmol. July 2013;131(7):969-970.

The authors report on 2 boys, one aged 17 years and the other, aged 14 years, with unilateral multifocal chorioretinitis that was proven to be of varicella zoster virus (VZV) origin by intraocular fluid analysis. VZV may cause severe posterior eye segment inflammation and represents a major cause of the clinical syndrome called acute retinal necrosis (ARN). Acute retinal necrosis is a sight-threatening condition and continues to have a poor visual outcome. Typically, visual acuity rapidly deteriorates, and the retinal inflammation may progress within several days to a full-thickness necrosis affecting the entire retinal periphery and often late retinal detachment.

Association of Ocular and Oculodermal Melanocytosis With the Rate of Uveal Melanoma Metastasis Analysis of 7872 Consecutive Eyes

Carol L. Shields, Swathi Kaliki, Michael Livesey, Brianna Walker, et.al. JAMA Ophthalmol. August 2013;131(8):993-1003.

The risk for metastases from uveal melanoma is greater in patients who have associated ocular melanocytosis. This could be ocular or oculodermal melanocytosis which is a congenital periorcular dermal pigmentary disorder. Uveal melanoma can develop in 1/400 patients and the risk for metastases is 1.6 times greater than those patients with uveal melanoma who did not have melanocytosis.

Retinal Vasoproliferative Tumors in 6 Patients With Neurofibromatosis Type 1

Jerry A. Shields, Marco Pellegrini, Swathi Kaliki, Arman Mashayekhi, et.al. JAMA Ophthalmol. 2014;132(2):190-196. February 2014
The authors present 6 patients with neurofibromatosis type 1 (NF-1) who had retinal vasoproliferative tumors (RVPT). The mean age at time of diagnosis was 12 and the mean visual acuity at presentation ranged from 6/7.5 to light perception. The RVPT was located between the equator and ora serrata in all patients. Associated features included subretinal fluid, subretinal exudation, epiretinal membrane, retinal hemorrhage, vitreous hemorrhage, retinal neovascularization, and cystoid macular edema. Treatment included cryotherapy, intravitreal injection of bevacizumab, plaque radiotherapy, and primary enucleation in 1 patient because of painful neovascular glaucoma. The authors emphasize periodic dilated funduscopic exams in NF-1 patients to allow for early identification and treatment of these tumors which can cause significant visual loss.

Inner Macular Hyperreflectivity Demonstrated by Optical Coherence Tomography in Niemann-Pick Disease

Danielle S. Rudich, Christine A. Curcio, Melissa Wasserstein, Scott E. Brodie, *JAMA Ophthalmol.* 2013;131(9):1244-1246. September 2013

Niemann-Pick disease is a lysosomal storage disease caused by mutations in the sphingomyelin phosphodiesterase 1 gene. Type A is characterized by severe visceral involvement and death usually by age 3. Type B is milder with hepatosplenomegaly, thrombocytopenia, interstitial lung disease, and dyslipidemia, with most patients having little or no neurologic involvement. Accumulation of lipid metabolites in the retinal ganglion cells produces a macular halo, with the common misnomer of “cherry red spot” applied. The center of the fovea, the “red spot,” is not abnormal, but the whitish halo around the fovea reflecting lipid accumulation is abnormal. Spectral domain optical coherence tomography (SD-OCT), with a resolution of 5-10 microns, allows for imaging retinal layers and to monitor disease progression. The authors describe the SD-OCT findings in 3 patients with Niemann-Pick disease type B.

Clinical characteristics and treatment of 22 eyes of morning glory syndrome associated with persistent hyperplastic primary vitreous

Ping Fei, Qi Zhang, Jing Li, Peiquan Zhao *British Journal of Ophthalmology* 2013;97:10 1262-1267 October 2013

This is a retrospective case series investigating clinical manifestations and treatment outcomes of morning glory syndrome (MGS) associated with persistent hyperplastic primary vitreous (PHPV). The records for 85 eyes of 74 patients diagnosed as MGS were reviewed retrospectively. 22 eyes of 19 patients diagnosed with MGS associated with PHPV were included in the study (25.88% of all MGS eyes). 78.95% of patients were diagnosed prior to 1 year of age. 86.36% of eyes had complications, including cataract (10 eyes), secondary glaucoma (8 eyes), corneal leucoma or edema (8 eyes), retinal detachment (8 eyes), strabismus (3 eyes), and nystagmus (2 eyes). Treatments varied depending the complications and severity of the complications. 8 patients underwent cranial MRI/MR angiography or CT examination. 3 of these patients were found to have abnormal MRI findings which included widened cerebral fissures of bilateral temporal lobes, abnormal dilated branch of middle cerebral artery in the left hemisphere and abnormal signal in the grey matter of frontal and occipital lobes. This retrospective review found the coexistence of PHPV in a significant percentage of patients with MGS, which the authors feel could suggest a common genetic link. The combination of MGS and PHPV manifested with a higher incidence and severity of complications when compared to either entity alone. The authors recommend close follow-up.

Wide-Field Fundus Autofluorescence Imaging of Retinitis Pigmentosa

Akio Oishi, Ken Ogino, Yukiko Makiyama, Satoko Nakagawa, *Ophthalmology* September 2013; 120:1827-1834

This is a cross-sectional case series involving 75 eyes of 75 patients with retinitis pigmentosa. Patients were examined with the Optos 200Tx imaging system. Patients also received wide-field fundus autofluorescence (FAF). This study was performed in Kyoto, Japan.

Main outcome measure: Predicting the visual size and duration of the disease of retinitis pigmentosa based on fundus autofluorescence patterns.

Conclusions: We can estimate the visual field in patients with retinitis pigmentosa using the objective measurements from wide-field fundus autofluorescence camera. The presence of patchy hypofluorescent lesions can be used as an indicator of the duration of retinitis pigmentosa.

Comments: Fundus autofluorescence imaging represents a recent advance in imaging technology and has enabled the status of the photoreceptor cells and retinal pigment epithelium to be evaluated. The usefulness of fundus autofluorescence imaging relies on changes in the FAF patterns resulting from abnormalities caused by retinal diseases.

Diffuse Choroidal Hemangioma Management with Plaque Radiotherapy in 5 Cases

Sruthi Arepalli, Carol L. Shields, Swathi Kaliki, Jacqueline Emrich, *Ophthalmology* November 2013; 120(11):2358-2359

This is a case series from the Ocular Oncology Service at Wills Eye Hospital and Thomas Jefferson University, Philadelphia, Pennsylvania. Choroidal hemangioma and benign vascular hamartoma classified as either circumscribed or diffuse. Diffuse choroidal hemangioma typically presents as an ill-defined choroidal mass with indistinct margins and a reddish hue labeled as the “tomato ketchup fundus.” The main concern with diffuse choroidal hemangioma is vision loss from induced hyperopia, amblyopia, secondary retinal detachment or macular edema.

Intervention: All patients were treated with plaque radiotherapy for treatment of the diffuse choroidal hemangioma.

Conclusion: Plaque radiotherapy for diffuse choroidal hemangioma with subretinal fluid is an affective modality, employing 4 days of radiotherapy with relatively rapid resolution of subretinal fluid and tumor. Plaque radiotherapy appears to be a safe and reliable option for the treatment of exudative diffuse choroidal hemangioma.

Retinal Structure and Function in Achromatopsia

Venki Sundaram, Caroline Wilde, Jonathan Aboshiha, Jill Cowing,
Ophthalmology January 2014; 121(1):234-245

This study comes from Moorfields Eye Hospital, London, UK, and the Department of Cell Biology, Medical college of Wisconsin, Milwaukee, Wisconsin. This is a cross-sectional study of 40 subjects with achromatopsia (ACHM). The purpose of this study is to characterize retinal structure and function in achromatopsia in preparation for clinical trials of gene therapy.

Methods: All subjects underwent spectral domain OCT (SD-OCT), microperimetry and molecular genetic testing.

Main outcome measures: Photoreceptor appearance on spectral domain OCT imaging, foveal and optic nerve layer thickness and the presence of foveal hypoplasia.

Conclusions: The lack of a clear association of disruption of retinal structure or function in achromatopsia with age suggests that the window of opportunity for intervention by gene therapy is wider in some individuals than previously indicated. The ability to directly assess cone photoreceptor preservation with SD-OCT and/or adaptive optics imaging is likely to prove invaluable in selecting subjects for future trials in measuring the impact of such trials.

High Prevalence of Peripheral Retinal Vascular Anomalies in Family Members of Patients with Familial Exudative Vitreoretinopathy

Amir H. Kashani, Daniel Learned, Eric Nudleman, Kimberly A. Drenser,
Ophthalmology January 2014; 121(1):262-268

This study comes from Associated Retinal Consultants PC, Royal Oak, Michigan, and Department of Ophthalmology, William Beaumont Hospital, Royal Oak, Michigan.

This is an uncontrolled and retrospective case series at a single tertiary referral vitreoretinal practice. A total of 148 eyes of 74 subjects were studied. The purpose of this study is to describe the prevalence and severity of familial exudative vitreoretinopathy in asymptomatic relatives of known symptomatic FEVR patients.

Main outcome measures: Clinical and angiographic findings.

Conclusions: Asymptomatic family members of FEVR patients frequently have early manifestations of stage 1 or 2 FEVR. Early-stage FEVR may progress to more advanced stages, which can result in vision loss. This study supports the concept of angiographic screening in addition to clinical examination in immediate relatives of patients with symptomatic FEVR.

Long-Term, Drug-Free Remission of Sympathetic Ophthalmia with High-Dose, Short-Term Chlorambucil Therapy

Sarju S. Patel, Emilio M. Dodds, Laura V. Echandi, Cristobal A. Couto, *Ophthalmology* February 2014; 121(2):596-602

This article comes from multiple centers including the University of Illinois, Chicago, Illinois, Weill Cornell College of Medicine, New York City, New York, Universidad of Buenos Aires, Buenos Aires, Argentina, and Northwestern University, Chicago, Illinois.

This is a retrospective case series of 16 patients with sympathetic ophthalmia treated with high-dose, short-term chlorambucil therapy between 1970 and 2010. The purpose of the retrospective case series is to evaluate the safety and effectiveness of short-term, high-dose chlorambucil therapy in achieving long-term, drug-free remission in treatment of sympathetic ophthalmia (SO).

Main outcome measures: Months of disease-free remission, prevalence rate of relapse and prevalence of serious treatment-related adverse events.

Conclusions: Short-term, high-dose chlorambucil therapy provides sustained periods of drug-free remission. With median follow-up of more than 8 years, there was a low rate of recurrence and minimal long-term serious health consequences or adverse events.

It is suggested by the authors that chlorambucil therapy may offer long-term, drug-free remission and is worth considering early in the decision making process for severe sight-threatening disease.

Spontaneous Vitreous Hemorrhage in Children Sudhalkar, J.

Chhablani, S. Jalali, A. Mathai, A. Pathengay. *Am J Ophthal* Dec. 2013; 156(6): 1267-1271.

This retrospective chart review looked at 124 eyes of 76 children who presented with a spontaneous vitreous hemorrhage and evaluated etiology and outcome over time. Mean age of the patients was 12.78 +/- 4.68 years. Forty-eight presented with bilateral vitreous hemorrhages. All patients identified with a cause had a local and/or systemic comorbidity. Mean follow up was 28 +/- 18.38 months. The most common complaint in children over 3 years was diminished vision; the most common complaint for children under 3 years was behavioural changes. Overall, 69 eyes required some surgical intervention. Nineteen eyes underwent surgery for RD. Two eyes had FEVR and 1 eye had retinoschisis. Other causes: hematologic disorders in 34 eyes, vasculitis in 41 eyes, ocular tumors in 8 eyes, FEVR in 13 eyes, RD in 13 eyes, DM in 4 eyes, unknown etiology in 8 eyes. Comprehensive evaluation is recommended in children presenting with vitreous hemorrhage.

Retinal Asymmetry in Children Measured with Optical Coherence Tomography.

I.Altemir, D. Oros, N. ELia, V. Polo, J. Larrosa, V. Pueyo. *Am J Ophthal* Dec. 2013; 156(6): 1238- 1242.

This prospective cross-sectional study evaluated 357 healthy children with the Cirrus OCT analyzing the RNFL, optic nerve head, and macula. 96% of children

were white; mean age was 9 years; refractive errors ranged from -3.00 to +4.50 diopters; strabismus was found in 11 children. Right and Left eye OCT parameters for RNFL differences were not statistically significant. However, interocular differences between the right and left eyes were statistically significant for nasal and temporal quadrants, with the right eyes showing a thicker RNFL than the left eyes. None of the macular or optic disc parameters were statically significant. There appeared to be moderate interocular correlation. These authors suggest that if the interocular difference in average RNFL and macular thickness is greater than 13 microns and 23 microns, respectively, pathology should be suspected.

Hand-held high-resolution spectral domain optical coherence tomography in retinoblastoma: clinical and morphologic

considerations. Rootman DB, Gonzalez E, Mallipatna A, Vandenhoven C, Hampton L, Dimaras H, Chan HS, Gallie BL, Heon E. Br J Ophthalmol. 2013 Jan;97(1):59-65.

The authors report on use of both handheld OCT and conventional upright OCT in following retinoblastomas in 16 patients. 22 lesions were imaged. Small lesions were imaged in five cases, all of which were localised to the middle retinal layers. Clinical uses for handheld OCT imaging identified included: diagnosis of new lesions, monitoring response to laser therapy and the identification of edge recurrences. While OCT does not replace indirect ophthalmoscopy, it is an important addition to the armamentarium and offers advantages for detecting very early lesions and recurrence at the edge of lesions.

Anomalous relation between axial length and retinal thickness in amblyopic children

Kok PHB, Kinkelder Rd, Braaksma-Besselink YC et al, J AAPOS December 2013;17:598-602

OCT has shown amblyopic eyes have thicker retina and/or nerve fiber layer. However the shorter axial length of many amblyopic eyes may be a confounding factor. This study analyzed pericentral retinal thickness, and its relationship to axial length in amblyopic and healthy children. Enrolled amblyopes had either strabismus, or anisometric amblyopia of at least 2 diopters of sphere and/or astigmatism. Thirty-six amblyopes (anisometropia (n=17), strabismus (n=11), combined (n=8)) and thirty healthy subjects were enrolled. Axial length for amblyopic eyes, was not found to be distributed normally. Mean axial lengths were: 22.00mm amblyopic eye, 22.18mm fellow eye, 23.28 mm healthy control right eye, 23.29 mm healthy control left eye. Mean pericentral retinal thickness was not significantly different between groups. There was a moderate linear correlation between retinal thickness and axial length in healthy subjects- shorter eyes had thicker retinas. However, this relationship was not found in the

amblyopic eye or the fellow eye of amblyopic patients. Therefore, unlike in healthy subjects, the relationship between axial length and retinal thickness was anomalous. This study was limited by the small number of patients, and the mixing of subjects with different types of amblyopia (subgroup analysis was not available because of small size groups).

Efficacy of Short-term Postoperative Perfluoro-n-octane Tamponade for Pediatric Complex Retinal Detachments

A. Imaizuaka, S. Kusaka, H. Noguchi, Y. Shimomura, S. Sawaguchimi. *Am J Ophthalmol* 2014; 157(2); 384-388.

This study looked at the efficacy of perfluoro-n-octane as a short term tamponade after vitrectomy in pediatric patients with complex RD and PVR. 10 eyes of 9 patients were reviewed. The PVR was caused by ROP, FEVR, and tractional RD. The medication was injected in 2 of the eyes during primary surgery and in 8 eyes at repeat surgery. The medication was removed after 4 months. These heavy liquids can cause mechanical retinal injuries but in these extremely difficult cases where reattachment is a problem, use of these liquids may be necessary.

Ultra-Widefield Imaging for the Management of Pediatric Retinal Diseases

Kang KB, Wessel MM, Tong J, D'Amico DJ, Chan RVP
J Pediatr Ophthalmol Strabismus 2013;50(5):282-288

Case series describing the utility of using ultra-widefield digital fundus photography and fluorescein angiography (UWFA) in the pediatric population to evaluate peripheral retinal pathology and to assist in the management and treatment of Coats' disease and FEVR. The Optos Optomap Panoramic 200A imaging system (Optos, PLC, Dunfermline, Scotland) was used to capture up to 200 degrees of high-resolution image. The authors conclude that ultrawidefield photography and UWFA can be successfully used in the pediatric population to evaluate peripheral retinal pathology and directing laser photocoagulation in treatment. They demonstrate the feasibility of using this modality in physician offices without the use of anesthesia in the cooperative patient.

Combination Treatment of Pediatric Coats' Disease: A Bicenter Study in Taiwan

Lin CJ, Chen SN, Hwang JF, Yang CM
J Pediatr Ophthalmol Strabismus 2013;50(6):356-362

This was a retrospective, non-comparative, consecutive interventional study of different combination treatment modalities in pediatric Coats' disease and their clinical outcomes in two Taiwan hospitals. The main treatment modalities included argon laser photocoagulation, micropulse laser and cryotherapy. In cases of significant subretinal fluid, adjunctive intravitreal triamcinolone, bevacizumab or ranibizumab were given. In this review laser photocoagulation combined with intravitreal anti-VEGF was the better choice in obliterating

telangiectatic vessels and reducing subretinal exudates. Cryotherapy with intravitreal bevacizumab for exudative retinal detachment may carry the risk of vitreoretinal traction and tractional retinal detachment. Adjunctive intravitreal anti-VEGF may act as useful adjuncts to improve anatomic and functional outcome.

19. RETINOBLASTOMA

Clinical Profile, Management, and Outcome of Retinoblastoma in Singapore

Fiona Pin Miao Lim, Shui Yen Soh, Jayant Venkatramani Iyer, Ah Moy Tan, et al J Pediatr Ophthalmol Strabismus 2013; 50:106-112 (March/April)
A review of the various clinical manifestations of retinoblastoma in Singapore. The article reviews 51 patients diagnosed with retinoblastoma collecting data such as laterality, genetics, presentations, disease severity, treatment and prognosis. The study found a comparable 5-year survival rate to international data but did find that the severity of disease was worse which made globe preservation rate lower than more developed countries. Better education to the public as well as healthcare professionals may help to improve the rate of globe preservation.

Differentiation in Retinoblastoma and Histopathological Risk Factors in Mexico

Ricardo Gómez-Martínez, María Elena Rosales-Gradilla, Noemí Silva-Padilla,, Adrián Corona-Macías, J Pediatr Ophthalmol Strabismus 2013; 50:174-177 (March/April)

This study describes histopathological risk factors (massive choroidal infiltration, postlaminar optic nerve invasion, tumor in optic nerve cut, scleral invasion, and involvement of orbital soft tissues) and differentiation of retinoblastoma using enucleated eyes. The study found that advanced age is associated with moderately differentiated tumors as well as increases the risk of having a tumor with histopathological risk factors.

Study On Clinical Therapeutic Effect Including Symptoms, Eye Preservation Rate, And Follow-Up Of 684 Children With Retinoblastoma

Dongsheng Huang, Yi Zhang, Weiling Zhang, Yizhou Wang
Eur J Ophthalmol July Aug 2013; 23(4): 532 – 538

A retrospective analysis was made of 684 children (885 eyes) with advanced retinoblastoma diagnosed in Beijing, China. The average age at first diagnosis was 2.2 ± 1.7 years with overall median age 1.91 years. Leucocoria was the most common sign at the initial diagnosis. Three percent had positive family history. 551 cases (80.57%, 723 eyes) were A-E stage and 81.47% (589/723) were D-E stages of retinoblastoma; extraocular stage was present in 101 cases (120 eyes, 14.76%);

metastatic stage was present in 32 cases (44 eyes, 4.67%). Pathology diagnosis was performed in 494 cases of unilateral or bilateral enucleation; most cases were grade II (260), 10% (49) were grade IV. Total survival rate was 95.13%. Key factors of clinical treatment and long survival rate were diagnosis and treatment at the early stage with multidisciplinary methods.

Sporadic unilateral retinoblastoma or first sign of bilateral

disease? Petra Temming, Anja Viehmann, Eva Biewald, Dietmar Lohmann. *Br J Ophthalmol* April 2013; 97: 475-480.

This study looked at the clinical and genetic characteristics of children with sporadic unilateral retinoblastoma to see if factors could be identified for the development of metachronous bilateral disease. About 4% of children with initial monocular retinoblastoma will develop a new tumor in the other eye after treatment. Retrospectively, 480 records were reviewed. No child with a positive family history or treatment at another facility was included. The most decisive factor indicating high risk of second eye involvement was the presence of the oncogenic RB1 mutation in DNA of the blood. Early age at diagnosis was also considered high risk. In total, 9 (22.5%) of the 40 children with positive RB1 mutation developed bilateral retinoblastoma. None of the 155 children without a mutation in the blood developed bilateral disease.

Retinoblastoma presenting with orbital cellulitis

Walinjkar J, Krishnakumar S, Gopal L, et al *J AAPOS* June 2013 17:3;282-286
In developing nations, an orbital cellulitis-like presentation of retinoblastoma is more common. Over a three-year period, retinoblastoma-associated cellulitis was seen in 14/260 (5.39%) patients in this article out of India. All had large intraocular tumors and showed endophytic growth. The authors excluded 4 patients for having received neoadjuvant chemotherapy, and another patient was excluded because the cellulitis was not the initial presentation sign. All of the remaining patients were enucleated, but 5 received pre-enucleation systemic steroids. This produced a marked reduction in inflammation. The reduced inflammation facilitated the enucleation procedure, by reducing vascularity and soft-tissue edema. No direct comparison was performed with those patients who did not receive systemic steroids.

Ophthalmic Artery Chemosurgery for Retinoblastoma Prevents New Intraocular Tumors

David H. Abramson, Jasmine H. Francis, Ira J. Dunkel, Y. Pierre Gobin, *Ophthalmology* March 2013;120:560-565
This is a single-center retrospective review of all genetic retinoblastoma cases managed at Memorial Sloan-Kettering Cancer Center/Weil-Cornell Medical School since May 2006.

This study evaluates 81 patients (80 with bilateral disease and 1 with unilateral disease) with genetic retinoblastoma. There were a total of 116 eyes treated with ophthalmic artery chemosurgery (OAC) since May 2006.

Results: 41 eyes were treated primarily with ophthalmic artery chemosurgery and 75 eyes were treated with ophthalmic artery chemosurgery after prior treatment with systemic chemotherapy, external beam radiation, or both.

Conclusions: The eyes receiving ophthalmic artery chemosurgery demonstrated fewer, new intraocular retinoblastomas after radiation or systemic chemotherapy than has been reported in the literature. This suggests that ophthalmoscopically the undetectable tumors are present at the initial diagnosis are eliminated as a result of ophthalmic artery chemosurgery.

High-Risk Retinoblastoma based on International Classification of Retinoblastoma: Analysis of 519 Enucleated Eyes

Swathi Kaliki, Carol L. Shields, Jerry Shields, Ralph C. Eagle, Jr.,

Ophthalmology May 2013;120:997-1003

This is a retrospective study of 519 patients who underwent primary enucleation for retinoblastoma. The purpose of the study is to determine the correlation between the International Classification of Retinoblastoma (ICRB) and histopathologic high-risk retinoblastoma.

Conclusions: On the basis of the International Classification of Retinoblastoma, 17% of group D and 24% of group E eyes are at increased risk for metastatic disease. In this study, 8% of patients developed metastasis. There was no metastasis in any patient classified with a non-high-risk retinoblastoma.

Comments: Group D and group E eyes have the most severe pathology and therefore are at an increased risk for metastatic disease. There are excellent pictures on page 999 and also on the cover of May 2013, volume 120, number 5.

Blue Toe Syndrome as a Complication of Intra-arterial Chemotherapy for Retinoblastoma

Ahmet Sarici, Osman Kizilkilic, Tiraje Celkan, Safa Gode, *JAMA Ophthalmol.* June 2013;131(6):801-802.

Intraarterial chemotherapy has become more popular to treat advanced retinoblastoma. However, severe ocular vascular adverse effects, including ophthalmic artery stenosis and retinal arteriolar embolization have been reported. The authors report a case of extraocular vascular occlusion in a 7 month old infant with retinoblastoma who was treated with intraarterial melphalan. Blue toe syndrome is defined as the sudden onset of acute pain and cyanosis in one or more toes with evidence of a proximal source of emboli, primarily in the femoral or popliteal arteries. The patient was given both oral aspirin and parenteral low-molecular-weight heparin. After 1 week, the blue color and tenderness disappeared.

Superselective Intraocular Artery Chemotherapy in a Nonhuman Primate Model Histopathologic Findings

Brian C. Tse, Jena J. Steinle, Dianna Johnson, Barrett G. Haik, et.al. JAMA Ophthalmol. July 2013;131(7):903-911.

Superselective intraarterial chemotherapy (SSIAC) is a treatment for certain patients with retinoblastoma. No preclinical models have been studied to assess variables of flow and drug concentration in an attempt to mitigate ocular and orbital vascular toxicity. The authors studied 6 Macaque monkeys who underwent SSIAC with melphalan or carboplatin. Histopathology of the eye and orbit revealed widespread vascular damage. All contralateral eyes, which were not treated, were normal.

Retinal Vascular Precipitates During Administration of Melphalan Into the Ophthalmic Artery

Rosanne Superstein, David Lederer, Josee Dubois, Patrick Hamel, et.al. JAMA Ophthalmol. July 2013;131(7):963-965.

The authors describe real-time fundusoscopic findings during superselective intraarterial chemotherapy with melphalan in a 5 month old baby with bilateral retinoblastoma. Vaso-occlusive disease has been described a potentially sight-threatening complication. The authors hypothesize that intraprocedural vaso-occlusive findings are the cause of vaso-occlusive disease reported by others as late findings. Real-time observation combined with titration of chemotherapy administration may prevent some of these late vaso-occlusive complications. Once intraarterial retinal precipitates or impaired retinal blood flow was detected, the infusion was aborted and findings normalized with time. Electroretinography and examination of retinal and choroidal blood flow performed two months after the procedure were normal and the tumors had regressed.

Comparison of Staging Systems for Extraocular Retinoblastoma Analysis of 533 Patients

Guillermo L. Chantada, Claudia Sampor, Andrea Bosaleh, Verónica Solernou, et.al. JAMA Ophthalmol. 2013;131(9):1127-1134. September 2013

Extraocular retinoblastoma on presentation occurs in about 5% of patients in the developed world, but can represent up to 50% of cases in developing nations. The authors acknowledge that there is paucity of studies which validate staging systems for extraocular retinoblastoma. 533 patients with retinoblastoma were reviewed, including pathology slides, and reclassified according to the modified St Jude Children's Research Hospital staging system, Grabowski-Abramson staging system, International Retinoblastoma Staging System (IRSS), and American Joint Committee on Cancer TNM staging system. The main outcome was disease-free survival, considering extraocular relapse only as an event. The authors conclude that only the IRSS and the St Jude system allowed for grouping of patients with increasing risk of extraocular relapse. For lower stages, only the IRSS considers all unequivocal pathological prognostic factors. For higher stages, all systems had redundant information, resulting in an excess of substages.

Evaluating the risk of extraocular tumour spread following intravitreal injection therapy for retinoblastoma: a systematic review

Stephen J Smith, Brian D Smith *British Journal of Ophthalmology* 2013;97:10 1231-1236 October 2013

This is a review article evaluating the risk of extraocular tumor spread in patients receiving therapeutic intravitreal injections for retinoblastoma. PUBMED, SCOPUS, Science Citation Index, and Conference Proceedings Citation Index-Science electronic databases were searched to identify all reports of intravitreal injection therapy (IviT) for retinoblastoma in humans. 14 studies were included in this review. 1304 intravitreal injections were given in 315 eyes of 304 patients. There was one report of extraocular tumor spread and one patient with metastatic disease where the intravitreal treatment could not be excluded as a contributor. The mean follow-up was 72.1 months and over this time the proportion of subjects with extraocular tumor spread was 0.007. In a subset of 61 patients that received IviT with safety enhancing injection techniques there were no reports of extraocular tumor spread. The authors conclude that local and systemic tumor spread following intravitreal injections in cases of retinoblastoma is rare. There is a potential that the risk is reduced by the use of safety enhancing injection techniques. They suggest that the risk of tumor spread should not preclude the use of intravitreal injections for carefully selected patients.

Management and Outcome of Retinoblastoma with Vitreous Seeds

Fairooz P. Manjandavida, Santosh G. Honavar, Vijay Anand P. Reddy, Rohit Khanna, *Ophthalmology* February 2014; 121(2):517-524

This article comes from L.V. Prasad Eye Institute, Hyderabad, India.

This is a retrospective, interventional case series designed to report the treatment and response of retinoblastoma with vitreous seeds to high dose chemotherapy coupled with periocular carboplatin.

Participants: Consecutive patients with retinoblastoma with vitreous seeds managed over 10 years at a comprehensive ocular oncology center and followed up for at least 12 months after the completion of treatment.

Intervention: High-dose chemotherapy with a combination of vincristine, etoposide and Carboplatin in patients with focal vitreous seeds. Additional treatment was also performed which included periocular carboplatin in patients with diffuse vitreous seeds.

Main outcome measures: Tumor regression, vitreous seed regression and eye salvage.

Conclusions: Intensive management with primary high-dose chemotherapy and concurrent periocular Carboplatin and external beam radiotherapy selectively in chemotherapy failures provides gratifying outcome in retinoblastoma with vitreous seeds.

Retinoblastoma. Villegas VM, Hess DJ, Wildner A, Gold AS, Murray TG. *Curr Opin Ophthalmol.* 2013 Nov;24(6):581-8.

Recent publications suggest new applications of intraocular imaging, which include fundus autofluorescence and optical coherence tomography (OCT), may help in the diagnosis and management of retinoblastoma. Fundus autofluorescence reveals hyperautofluorescence of calcium within the tumor. Optical coherence tomography (OCT) may be more sensitive than a fundus examination in the detection of macular disease associated with retinoblastoma.

The International classification of retinoblastoma categorizes tumors by size and intraocular seeding (Groups A-E). Treatment is based the tumor's classification, laterality, location, prior treatment and family history. Small tumors may be treated with local ablative therapy whereas intravenous chemotherapy may be used in advanced tumors. Bilateral or hereditary cases routinely undergo chemoreduction in order to prevent trilateral retinoblastoma. Recent studies have evaluated subconjunctival carboplatin in Group C and D eyes but results were unsatisfactory. Multiple institutions have reported small cases series of successful globe sparing chemoreduction with ophthalmic artery infusion of melphalan in Reese-Ellsworth Group 5 eyes. Intravitreal melphalan has recently been used for recurrent vitreous seeds after previous intra-arterial chemotherapy or systemic chemoreduction. Further studies are necessary to evaluate the safety of intra-arterial and intravitreal chemotherapy over time.

20. ORBIT

Improving ophthalmic outcomes in children with unilateral coronal synostosis by treatment with endoscopic strip craniectomy and helmet therapy rather than fronto-orbital advancement MacKinnon S, Proctor MR, Rogers GF, et al *J AAPOS* June 2013 17;3:259-265

This study compares long-term ophthalmic outcomes of two different surgical techniques for the treatment of children with unilateral coronal synostosis (UCS). A 7-year retrospective record review was performed of consecutive UCS patients, who had undergone endoscopic strip craniectomy (ESC), or fronto-orbital advancement (FOA). Both groups had a mean follow-up of over 21 months. Aniso-stigmatism

mean was equivalent in the two groups but the FOA group had a greater standard deviation. FOA patients were more likely to have torticollis, amblyopia, more severe V-pattern and overelevation in adduction, and undergo surgical correction. Parents of children who presented before 4 months of age were given the option of either procedure. Those presenting after 4 months of age underwent FOA because the effectiveness of ESC after 4 months of age is questionable. Twenty-two patients underwent FOA and 21 underwent ESC and helmet therapy. The mean age at first visit was significantly older in the FOA group (9.3 months vs 4.0 months). The authors correctly identify the fact that the disparate timing of surgical intervention in these two groups may have been a significant factor. In the FOA group, strabismus was more likely to have already been present. FOA is not generally recommended as a surgical procedure at a very young age because of greater operative morbidity and increased likelihood of recurrence. Also UCS may have produced greater orbital symmetry in the FOA group because it had more time to progress. FOA also separates the trochlea from the orbital wall, which could affect pattern strabismus as well. This study was retrospective and the two treatment groups were not randomized which limits comparison. The later intervention, rather than the surgical procedure, could explain the greater ocular morbidity seen in patients who underwent FOA. Early determination of the presence of UCS, as opposed to simple positional plagiocephaly allows earlier diagnosis and potential treatment. This alone, may improve ophthalmic outcomes.

A Quantitative Method for Assessing the Degree of Axial Proptosis in Relation to Orbital Tissue Involvement in Graves' Orbitopathy

Irene Campi, Guia M. Vannucchi, Andrea M. Minetti, Mario Salvi, *Ophthalmology* May 2013;120:1092-1098

This is a retrospective case study that included 50 patients and 29 control subjects who underwent orbital computed tomography (CT). The purpose of the study was to define a method of quantifying axial proptosis in patients with Graves' orbitopathy (GO) and to validate a score that correlates with the orbital involvement and helps determine the degree of proptosis correction for elective orbital decompression.

The main outcome measures included diagrammatic triangulation of orbital CT. This is best explained on page 1094 of the article.

Conclusions: By measuring the ratio of intraorbital dimensions, the authors were able to quantify the degree of axial proptosis in patients with Graves' orbitopathy. Significant correlation of these measurements with some orbital parameters confirms that this parameter also may be used to measure orbital involvement (GO).

Comments: This is a technical and geometric construction to be used as an alternative to clinical exophthalmometer. This also allows you to look carefully at the size and structure of the extraocular muscles.

Pediatric Anophthalmic Sockets and Orbital Implants Outcomes with Polymer-Coated Implants

Maria Kirzhner, Yevgeniy Shildkrot, Barrett G. Haik, Ibrahim Qaddoumi,
Ophthalmology June 2013; 120:1300-1304

This is a retrospective, interventional, cohort study designed to compare wrapped and polymer-coated hydroxyapatite implants in children undergoing primary enucleation with no adjuvant therapies. Outcome measures including implant exposure, extrusion and migration, socket contracture, and formation of pyogenic granuloma.

Conclusions: The use of polymer-coated hydroxyapatite implants is associated with favorable outcomes in the pediatric population. Long-term implant retention is possible in most children.

Prenatal Presentation of Fronto-orbital Congenital Infantile Fibrosarcoma: A Clinicopathologic Report

Hughie H. Tsang, Peter J. Dolman, Douglas J. Courtemanche, Shahrad Rod Rassekh, et.al. *JAMA Ophthalmol.* July 2013;131(7):965-967.

The authors present a patient who was diagnosed prenatally with congenital infantile fibrosarcoma (CIFS), a mesenchymal spindle tumor which typically occurs in the first year of life. Forty percent of cases are diagnosed at birth or in utero, mainly affecting the extremities. The author's patient presented with the tumor involving the orbit and frontal bone. The tumor was excised with vision sparing surgery. The local recurrence rate is 40% to 50%. The differential diagnosis of a mass in this location include teratoma, rhabdomyosarcoma, neuroblastoma, and granulocytic sarcoma, a manifestation of leukemia.

Synostotic anterior plagiocephaly: a cause of familial congenital superior oblique muscle palsy

Jyoti Matalia, Nirupama Kasturi, Michael Brodsky, *Am Orthopt J* 2013;63:80-84

This report of 2 cases describes 2 sisters aged 6 and 2 years presenting with a congenital torticollis and findings consistent with unilateral superior oblique palsy. External examination also revealed unilateral forehead depression and CT scan showed unilateral coronal synostosis. Both were diagnosed with simulated superior oblique palsy associated with ipsilateral coronal synostosis. Both children underwent unilateral inferior oblique weakening procedures ipsilateral to the coronal synostosis and had improvement in ocular alignment, motility and head position. The authors note that unicoronal craniosynostosis may be difficult to differentiate from congenital superior oblique palsy. Careful examination to look for head asymmetry is necessary in patients presenting with signs of congenital superior oblique palsy.

21. OCULOPLASTICS

Amblyopia in Childhood Eyelid Ptosis Gregory J. Griepentrog, Nancy Diehl, Brian Mohny. Am J Ophthal June 2013;155(6); pg. 1125-1128.

This retrospective study evaluated the prevalence of amblyopia among children with ptosis over a 40 year period. Sixteen (14.9%) of the 107 patients were diagnosed with amblyopia. All cases of amblyopia occurred in patients with unilateral ptosis with the exception of one. Twelve (14.8%) of the 81 patients with simple congenital ptosis were diagnosed with amblyopia of which 7 (8.6%) cases were the result of occlusion of the visual axis from the ptotic lid. In conclusion, amblyopia affects 1 in 7 patients diagnosed with childhood ptosis.

Intraoperative Prognostic Factors For Probing Outcome In Children With Congenital Nasolacrimal Duct Obstruction Dima Andalib, Reza Nabei Eur J Ophthalmol May June 2013; 23(3): 329 – 332

The authors evaluated the intraoperative prognostic factors for probing outcome in children with congenital nasolacrimal duct obstruction (CNLDO). Prospectively, 69 eyes of 60 children aged 12 to 24 months underwent probing and irrigation by a single oculoplastic surgeon. The surgeon classified the obstruction (simple or complex) and the fluency of irrigation after probing (easy or difficult). There was a significant difference in success rate of probing in eyes with simple obstruction (87.8%) compared with complex obstruction (65%) ($p=0.02$). Also, there was a significant difference in success rate of probing in eyes with easy irrigation (100%) compared with difficult irrigation (53.6%) ($p<0.001$). Probing was more successful in eyes with simple obstruction or easy irrigation in children aged 12 to 24 months. The fluency of irrigation as an objective finding was a reliable intraoperative prognostic factor for probing success.

Clinical And Demographic Characteristics Of Ptosis In Children: A National Tertiary Hospital Study Rania El Essawy, Mohamed A. El sada Eur J Ophthalmol May June 2013; 23(3): 356 – 360

A retrospective review of 408 eyes in 336 children with blepharoptosis was conducted in Cairo, Egypt. The mean age at presentation was 3.2 years. The ptosis was unilateral in 65% of the cases, 74% of which involved the left eye. A positive family history was elicited in 19% of the cases. The commonest type was congenital (69%) followed by blepharophimosis syndrome (17%). Frontalis suspension was the most common surgery (58%) followed by anterior approach levator muscle resection (29%) and Whitnall sling procedure (13%). The mean number of operations performed was 1.5 (range 1-4). Associated strabismus, refractive errors, and amblyopia should be considered for proper management of these patients.

Anisometropia and amblyopia in nasolacrimal duct obstruction

Kipp MA, Kipp MA and Struthers W J AAPOS June 2013 17;3:235-238

This paper was a 10-year retrospective review of children age 0-6 years with a diagnosis of nasolacrimal duct obstruction (NLDO). 887/1218 (72.8%) of identified cases were unilateral. Almost 300 patients were excluded for unsatisfactory clinical data. The rate of anisometropia was more than double (7.6% versus 3.6%) when comparing the unilateral NLDO cases with the bilateral cases. This difference was statistically significant. The greater hyperopia was found on the side with the NLDO in a statistically significant percentage of the cases (85%). Also the NLDO cohort as a whole showed a greater rate of anisometropia than the general pediatric population.

This study supports complete eye examinations, including cycloplegic refraction for all pediatric patients who present with a NLDO. These children have a higher risk of anisometropia and amblyopia. This does not appear to be a coincident finding alone; rather the NLDO appears to contribute to anisometropia.

Positional Change of Lower Eyelid After Surgical Correction of Congenital Ptosis in the Korean Population

Chang Yeom Kim, Su Yan Zhao, Cheng Zhe Wu, Jin Sook Yoon, et.al. JAMA Ophthalmol. April 2013;131(4):540-542.

The authors have found that some patients with congenital ptosis have preoperative lower scleral show that is diminished after ptosis surgery. This quantitative study investigates the positional change in the lower eyelid after surgery to correct congenital ptosis. Medical records and clinical photographs of 55 Korean patients with congenital ptosis who underwent corrective surgery were reviewed. Lower scleral show was found in 7 ptotic eyes (8.9%) preoperatively and disappeared in all but 1 eye postoperatively. This study shows lower eyelid elevation after surgical correction of congenital ptosis, especially after frontalis suspension or in bilateral ptosis. Surgeons should inform patients that lower eyelids can displace upward after ptosis surgery and that preoperative lower scleral show can be diminished postoperatively.

Failure of Systemic Propranolol Therapy for Choroidal Hemangioma of Sturge-Weber Syndrome: A Report of 2 Cases

Hatem Krema, Yacoub A. Yousef, Priya Durairaj, Ronaldo Santiago, JAMA Ophthalmol. May 2013;131(5) 681-683.

Propranolol was incidentally discovered to induce accelerated involution of infantile cutaneous hemangioma. Since that observation, propranolol has successfully been used in the treatment of cutaneous, orbital and ocular hemangioma. The authors report the outcome of systemic propranolol in 2 patients with choroidal hemangioma and Sturge Weber syndrome. The first patient is a 14 year old girl with nevus flammeus of the left side of the face. She has 20/20 vision OD and HM vision OS. Ultrasonography OS revealed a diffuse choroidal mass, of medium to high internal reflectivity and thickness of 6.3mm causing an exudative retinal detachment. The

second patient, a 22 year old man, had bilateral nevus flammeus and choroidal hemangioma with NLP vision OD and 20/300 vision OS. Ultrasound demonstrated a diffuse choroidal hemangioma OS with 2.9 mm thickness. Both patients were treated for 6 months with oral propranolol at a dose of 2 mg/kg/d. No change in the facial or choroidal hemangiomas was noted after 6 months of treatment. The authors postulate that failure of their patients to respond to propranolol may reflect the fact that choroidal hemangiomas have both cavernous and capillary components, which may affect treatment response.

Sildenafil for Pediatric Orbital Lymphangioma

Nandini G. Gandhi, MD; Lily Koo Lin, MD; Mary O'Hara, MD
JAMA Ophthalmol. 2013;131(9):1228-1230. September 2013

Orbital lymphangiomas can be difficult to treat and enlargement of these hamartomatous lymphovascular lesions can cause disfigurement and visual compromise. The authors present the clinical course of 2 children with orbital lymphangiomas who dramatically responded to sildenafil after failing other treatments. Conventional treatment includes drainage with injection of sclerosing agents, systemic steroids and surgical debulking. These unencapsulated lesions may spontaneously bleed and can increase in size with infection. Sildenafil is a phosphodiesterase inhibitor, and causes vasodilation by decreasing the contractility of vascular smooth muscle. Because the cystic dilation of lymphangiomas is thought to result from contraction of the muscular lining of the vascular channels, one proposed mechanism of action of sildenafil is smooth muscle relaxation and subsequent collapse of the cystic spaces

Deep Periocular Infantile Capillary Hemangiomas Responding to Topical Application of Timolol Maleate, 0.5%, Drops

Kanmin Xue, MBBChir, Göran Darius Hildebrand, JAMA Ophthalmol
2013;131(9):1246-1248. September 2013

The authors note that the general paradigm with regard to beta blocker treatment of capillary hemangiomas is that topical timolol is a good option for superficial infantile hemangiomas, while systemic propranolol remains the treatment of choice for deep infantile hemangiomas. The authors challenge this paradigm with a description of 2 infants with deep periocular infantile hemangioma who responded with topical timolol maleate, 0.5%, drops. The lesions had sustained near-complete involution.

Randomized Trial on Silicone Intubation in Endoscopic Mechanical Dacryocystorhinostomy (SEND) for Primary Nasolacrimal Duct Obstruction

Kelvin K.L. Chong, Frank H.P. Lai, Mary Ho, Abbie Luk, *Ophthalmology* October 2013; 120(10):2139-2145

This study was done at the Department of Ophthalmology and Visual Sciences, Prince of Wales Hospital, Hong Kong, China, and Department of Ophthalmology and Visual Science, The Chinese University of Hong Kong, China.

This is a randomized clinical trial of 120 consecutive adults (103 females) with a presenting average age of 64 years (range, 39-92 years). These patients underwent endoscopic mechanical dacryocystorhinostomy (EEM-DCR) for primary acquired nasolacrimal duct obstruction (PANDO) from November 2005 to May 2009 in a lacrimal referral center (Hong Kong, China).

Results: A total of 118 of the 120 randomized cases completed 12 months of follow-up. Two patients died of unrelated medical illnesses. At 12 months postoperatively there was no statistical difference in the success rate between patients with and without intubation. There was no difference in the incidence or the time to develop granulation tissue between the 2 groups. There was no significant difference between successful and failed cases in terms of age, laterality, mode of anesthesia, surgeon, use of a stent or presence of granulation tissue postoperatively.

Conclusions: The current study found no difference between whether intubation was used or not used in endoscopic mechanical dacryocystorhinostomy for primary acquired nasolacrimal duct obstruction at the 12 month follow-up.

Surgical Debulking for Idiopathic Dacryoadenitis

A Diagnosis and a Cure

Ilse Mombaerts, J. Douglas Cameron, Waruttaporn Chanlalit, James A. Garrity, *Ophthalmology* February 2014; 121(2):603-60

This article comes from the Department of Ophthalmology in Leuven, Belgium, Minneapolis, Minnesota, Rochester, Minnesota, and Bangkok, Thailand.

This is a retrospective case series from 2 tertiary referral centers involving 46 patients who had idiopathic inflammatory tumor of the lacrimal gland, also called idiopathic dacryoadenitis. This condition was treated with high-dose, long-term systemic corticosteroids with limited success and high recurrence rate.

This study describes the outcome of patients with idiopathic dacryoadenitis who were managed with surgical debulking.

Participants: Forty-six patients

Methods: Review of the clinical records, radiologic scans, and histopathologic specimens.

Conclusions: Debulking biopsy procedures for idiopathic dacryoadenitis in addition to being diagnostic may be therapeutic and should be considered prior to instituting long-term systemic corticosteroids or other immunomodulatory medications.

Hemangioma treated with propranolol: do the rewards outweigh the risks?

Kathryn M. Haider, Daniel E. Neely, David A. Plager, *Am Orthopt J* 2013;63:2-5

This article reviews the evolution of capillary hemangioma treatment since the discovery of propranolol's treatment effect reported in 2008. The authors discuss their shift in practice from initiating propranolol during hospitalization to an entirely outpatient protocol. Their patients with normal baseline vitals and EKG are started on outpatient treatment with propranolol 0.5 mg/kg/day divided 3

times daily. The dose is increased to 2.0 mg/kg/day divided 3 times daily. Parents are counseled on symptoms of hypotension and hypoglycemia and followed closely by the ophthalmologist and pediatrician. The authors highlight 2 small cases series describing a total of 5 patients on propranolol for hemangioma that developed hypotension or hypoglycemia. The authors conclude that propranolol has replaced systemic steroids but that other options such as observation, topical or injected intralesional steroids and resection continue to have a role in hemangioma management.

Infantile hemangioma treated with surgery or steroids

Louise A. Mawn ,Am Orthopt J 2013;63:6-13

This paper includes a report of 12 cases of periocular hemangioma treated surgical as well as a literature review on propranolol treatment for hemangioma. Nine of the 12 patients had surgery by 6 months of age. Two surgical patients had previously failed propranolol and amblyopia. One patient required patching to reverse the amblyopia. The surgical results were reported as good but metrics were not well defined. The literature review portion of this paper summarizes 7 cases series of propranolol treatment of more than 20 patients. The author highlights that many patients had only partial response to propranolol and that some clinicians have concerns about propranolol's ability to block beta-noradrenergic receptors active in learning. The author concludes that compared with propranolol, surgery produces a more immediate improvement in the mechanical ptosis associated with some hemangiomas and therefore hastens treatment for amblyopia and astigmatism.

Prevalence of amblyopia in children undergoing nasolacrimal duct irrigation and probing

Ozlen Rodop Ozgur, Isil Bahar Sayman, Yesim Oral, Berkay Akmaz
Indian J Ophthalmol 2013;61:698-700.

The medical records of patients who had undergone NLD irrigation and probing for Congenital NLDO at an age of 3 years or younger were reviewed, and 51 of the patients were recalled between October 1 and December 31, 2011 for a detailed ophthalmic examination to determinate amblyopia or amblyopia risk factors. Amblyopia was accepted as difference in visual acuity of two or more Snellen lines between the two eyes or visual acuity of 20/30 or worse in either eye.

Results: The median age of the 51 (70 eyes) patients to whom NLD irrigation and probing were attempted for CNLDO was 23 months. All patients were reviewed for best-corrected visual acuity, refractive errors, and strabismus at a median age of 70.5 months (range 31 -95 months). Amblyopia or amblyopia risk factors were identified in 14 patients (27.5%). One child (7.15%) had only strabismus, six children (42.8%) had only amblyogenic refractive errors, two (14.3%) had a combination of two, one child (7.15%) had a family history for amblyopia, but four children (28.6%) had no amblyopia risk factors but had amblyopia.

Conclusion: Amblyogenic risk factors are higher in patients with CNLDO and patients undergoing NLD irrigation and probing in comparison to the normal population. Therefore, the authors recommend these children to routinely undergo cycloplegic refractions and full ophthalmic examinations.

22. INFECTIONS

Trends in ophthalmic manifestations of methicillin-resistant Staphylococcus aureus (MRSA) in a northern California pediatric population

Amato M, Pershing S, Walvick M and Tanaka S J AAPOS June 2013 17;3:243-247
Over an 8-year period, all pediatric cases of culture-positive ophthalmic MRSA were identified in a retrospective cross-sectional review of the largest managed-care healthcare system in Northern California. Over half (58%) of the 137 pediatric cases were community acquired. There was a trend of more new cases towards the end of the study period. The most common presentations were conjunctivitis (40%), styel/chalazion (25%), orbital cellulitis/abscess (19%), dacryocystitis (11%) and brow abscess (3%). Risk of ocular infection increased with male sex, neonates, and multiple infection sites on the body. There was high resistance to bacitracin and ofloxacin. Oral Trimethoprim.sulfamethoxazole showed low resistance, and was the predominant form of therapy, along with topical gentamicin. Resistance to antibiotics increased during the study period. Topical therapy was effective in 29%, oral antibiotics were effective in 47%. IV therapy was required in 12% and 19% required incision/drainage. There were no cases of permanent visual impairment. Unlike prior studies, diabetes was not found to be associated with an increased risk of MRSA infection. The authors recommend early recognition, proper antibiotic selection, and obtaining cultures & sensitivities when resistant or severe ocular infections are present.

Our Weak Defense Against the Gonococcus

James G. Ravin, JAMA Ophthalmol. 2013;131(12):1505-1506. December 2013
This opinion piece provides a brief review of Neisseria gonococcal eye infections throughout history. Neisseria gonococcus can penetrate intact corneal epithelium leading to perforation, so timely diagnosis is crucial. Neisseria gonorrhoea is second only to Chlamydia in reportable infectious diseases in the United States, with an incidence of 600,000 cases a year. It causes 1% of neonatal conjunctivitis in developed countries with a much higher percentage in developing countries. In the 1980's resistance to penicillins developed and in 2007 resistance to fluoroquinolones occurred. The treatment of choice is a 3rd generation cephalosporin, such as ceftriaxone. Newborn prophylaxis includes a single application of erythromycin 0.5% ointment. Povidone iodine solution is noted as an alternative, but is not yet standard of care to prevent ophthalmia neonatorum.

23. PEDIATRICS/INFANTILE DISEASE

Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism

Warren Jones and Ami Klin *Nature* November 6, 2013 [epub ahead of print]

This prospective longitudinal observational study evaluated eye fixation from birth to 36 months in 59 subjects at high risk for autism based on family history and in 51 at low risk for based on negative family history. Eye fixation was assessed in all subjects while viewing a video recording of a caregiver looking directly into the camera attempting to visually engage the subjects at months 2, 3, 4, 5, 6, 9, 12, 15, 18 and 24. Of the high-risk infants, 12 (20.3%) were found to have autism at age 36 months. One child from the low-risk cohort was also diagnosed with autism. When compared to those without autism, the subjects with autism demonstrated a statistically significant decline in eye fixation ($p=0.100$) between month 2 to 9. While these data may provide interesting insights and stimulate future research, no validated clinical test was presented or recommended for use by developmental pediatric specialists or ophthalmologists in order to facilitate making the diagnosis of autism in infancy.

Waardenburg Syndrome: Iris and Choroidal Hypopigmentation Findings on Anterior and Posterior Segment Imaging

Carol L. Shields, Stephanie J. Nickerson, Saad Al-Dahmash, Jerry A. Shields, *JAMA Ophthalmol.* 2013;131(9):1167-1173. September 2013

Waardenburg delineated the 6 chief characteristics of Waardenburg syndrome, including telecanthus, a broad nasal root, synophrys of the eyebrows, a white forelock (termed piebaldism), heterochromia iridis, and deaf-mutism. The authors highlight choroidal hypopigmentation as another characteristic of this syndrome. 7 patients with Waardenburg syndrome were studied. Using wide-angle montage fundus photography, AS-OCT, posterior segment OCT, and autofluorescence, the broad spectrum of pigmentary anomalies of the iris and choroid are described. Vision in these patients remained good.

Microphthalmia, Anophthalmia, and Coloboma and Associated Ocular and Systemic Features Understanding the Spectrum

Simon E. Skalicky, Andrew J. R. White, John R. Grigg, Frank Martin, et.al. *JAMA Ophthalmol.* 2013;131(12):1517-1524. December 2013

The authors categorize the clinical features of 141 children with microphthalmia, anophthalmia and coloboma. Microphthalmia was defined as an abnormally small eye or cornea (microcornea) (axial length <16 mm at birth and <19 mm at 12 months of age; and corneal diameter <10 mm at birth). Anophthalmia was defined as no evidence of a globe or ocular tissue in the orbit on clinical examination since birth. Coloboma was defined as a predominantly inferior deficiency of iris, chorioretinal, or optic disc tissue. Associated ocular and

systemic conditions were noted. The patients were then stratified into those with optic fissure closure defects (OFCD) and those without (NOFCD). The authors conclude that such classification can better help with genotype phenotype correlations in this heterogeneous group of patients.

Electronic Health Record Systems in Ophthalmology Impact on Clinical Documentation

David S. Sanders, Daniel J. Lattin, Sarah Read-Brown, Daniel C. Tu,
Ophthalmology September 2013; 120:745-1755

This comparative case series was performed at the Casey Eye Institute, Oregon Health and Science University, Portland, Oregon. One hundred fifty consecutive pairs of matched paper and electronic health record notes documented by 3 attending ophthalmologist providers. The main outcome measures including documentation score and paired comparison of qualitative differences in paper versus EHR.

Conclusions: There were quantitative and qualitative differences in the nature of paper versus EHR documentation of ophthalmic findings in this study. The EHR notes included more complete documentation of examination elements using structured textual descriptions and interpretations. Paper notes used graphical representations of findings.

Comments: The article did not particularly give a strong presentation for either method of record keeping. It did emphasize the importance of well placed pictures in the EHR versus drawings in the paper record.

24.SYSTEMIC/UVEITIS

Analysis of a Novel Protocol of Pulsed Intravenous Cyclophosphamide for Recalcitrant or Severe Ocular Inflammatory Disease

Ana M. Suelves, Cheryl A. Arcinue, Jesus Maria Gonzalez-Martin, Jonathan N. Kruh, *Ophthalmology* June 2013;120:1201-1209

This is a retrospective, interventional, noncomparative cohort study involving 110 eyes of 65 patients. The purpose of the study was to analyze the success rate of pulsed intravenous cyclophosphamide for noninfectious ocular inflammatory disease and to identify risk factors for failure of therapy. The study occurred in Cambridge, Massachusetts.

Conclusions: Pulsed intravenous cyclophosphamide, when applied according to protocol used by the researchers, results in an extremely high rate of sustained complete remission in patients with recalcitrant and fulminant, vision-threatening ocular inflammatory disease.

The authors describe an excellent safety profile in appropriately trained physicians. This also allows tapering and discontinuing corticosteroids in most patients. Early initiation of therapy may decrease the risk of relapses.

Ocular Manifestations of Xeroderma Pigmentosum Long-Term Follow-up Highlights the Role of DNA Repair in Protection from Sun Damage

Brian P. Brooks, Amy H. Thompson, Rachel J. Bishop, Kenneth H. Kraemer, *Ophthalmology* July 2013;120:1324-1336

This is a retrospective, observational, case series from the clinical center at the National Institute of Health, USA. The study involved 87 participants age 1 to 63 years of age from 1964 to 2011. Eighty-three patients had XP, 3 patients had XP/Cockayne syndrome complex, and 1 patient had XP/trichothiodystrophy complex.

All patients had appropriate ophthalmic examinations consistent with age and developmental stage. Ninety-one percent had at least 1 ocular abnormality. The most common abnormalities were conjunctivitis 51%, corneal neovascularization 44%, dry eye 38%, corneal scarring 26%, ectropion 25%, blepharitis 23%, conjunctival melanosis 20%, and cataracts 14%. Thirteen percent of patients had some degree of visual axis impingement. Five percent of patients had no light perception in one or both eyes. OCULAR SURFACE CANCER OR A HISTORY OF OCULAR SURFACE CANCER WAS PRESENT IN 10% OF PATIENTS. Patients with acute sun burning phenotype were less likely to develop conjunctival melanosis and ectropion but more likely to develop neoplastic ocular surface lesions than nonburning patients. Some patients showed signs of limbal stem cell deficiency.

Conclusions: This longitudinal study reported the ocular status of the largest group of patients systematically examined at 1 facility over an extended period of time. There was a high incidence of structural lid deformities, neoplasms of the ocular surface and eyelids, and inflammatory ocular surface disease. Corneal abnormalities were present in this population.

Burning and nonburning patients with XP exhibit different rates of important ophthalmologic findings including neoplasia. Ophthalmologic characteristics can help refine diagnoses in the case of XP complex phenotypes. DNA repair plays a major role in protection of the eye from sunlight-induced damage.

Comments: This is a must read landmark article for all ophthalmologists. Please see the impressive photographs on pages 1328 and 1329.

Tubulointerstitial Nephritis and Uveitis Syndrome in Children: A Prospective Multicenter Study

Ville Saarel, Matti Nuutinen, Marja Ala-Houhala, Pekka Arikoski, *Ophthalmology* July 2013;120:1476-1481

Tubulointerstitial Nephritis (TIN) is an inflammatory disease of the kidneys. It may be triggered by infectious diseases and numerous medications including non-steroidal anti-inflammatory drugs and antibiotics. However, in these children the cause remains unknown in the majority of cases. The condition may be accompanied by uveitis in which case it is referred to as tubulointerstitial nephritis and uveitis (TINU syndrome). Uveitis is typically anterior and bilateral.

This is a prospective, observational, multicenter, partly placebo-controlled treatment trial performed in Finland. Nineteen children with biopsy proven tubulointerstitial nephritis were evaluated. Clinical features and outcome of uveitis were the main outcome measures.

Conclusions: There is no statistically significant difference in the occurrence of uveitis in patients with tubulointerstitial nephritis in the prednisone and nontreatment groups. In this study the occurrence of uveitis associated with tubulointerstitial nephritis was considered higher than previously reported. UVEITIS RELATED TO TUBULOINTERSTITIAL NEPHRITIS MAY DEVELOP LATE AND IS OFTEN ASYMPTOMATIC . **The ophthalmologic follow-up of all patients with tubulointerstitial nephritis is warranted for at least 12 months starting with 3-month intervals.**

Prevalence of Oculo-auriculo-vertebral Spectrum in

Dermolipoma Jwu Jin Khong, Thomas G. Hardy, Alan A. McNab,
Ophthalmology August 2013;120:1529-1532

This is a retrospective case series involving patients with primary presentation of ocular dermolipoma. The purpose of the study is to describe the observed frequency of oculo-auriculo-vertebral spectrum (OAVS) in patients with dermolipoma.

Conclusions: Dermolipoma is an independent ocular association of oculo-auriculo-vertebral spectrum (OAVS) that is more commonly observed than previously reported. It is an ocular feature in both the milder and more complex forms of the spectrum.

Comments: Oculo-auriculo-vertebral spectrum (OAVS) is a term first applied by Cohen to describe a phenotypically heterogenous disorder owing to developmental abnormality of the first and second branchial arches. This rare and complex condition is also known as hemifacial microsomia or Goldenhar's syndrome. The diagnosis is based on the presence of combination of features, including microtia, mandibular hypoplasia, anomalies of the cervical spine, and epibulbar dermoid or ocular dermolipoma, also known as lipodermoids.

Ocular Complications in Children Within 1 Year After Hematopoietic Stem Cell Transplantation

Viera Kalinina Ayuso, Ymkje Hettinga, Patricia van der Does; Jaap J. Boelens, et.al. *JAMA Ophthalmol.* April 2013;131(4):470-475.

The authors stress the importance of understanding the risk of ocular involvement after hematopoietic stem cell transplantation (HSCT) in the pediatric population because young and severely ill children are unaware of their ocular problems. Forty nine consecutive patients underwent ophthalmologic examination before HSCT, during HSCT, and 3, 6, and 12 months after HSCT. Thirteen (27%) developed an ocular complication during HSCT. These complications included dry eye syndrome in 7 (14%), subretinal hemorrhage in 6 (12%), optic disc edema in 3 (6%), chorioretinal lesions in 2 (4%), vitritis in 1 (2%), and increased intraocular pressure in 1 (2%). Median time to the development of dry eye syndrome was 5 months after HSCT, whereas all other

ocular complications were detected within the first 3 months. Children with malignant

disease had a higher risk of the development of ocular complications compared with children with nonmalignant disease.

Interval Spectral-Domain Optical Coherence Tomography and Electrophysiology Findings in Neonatal Adrenoleukodystrophy

Robert J. Courtney, Mark E. Pennesi, JAMA Ophthalmol June. 2013;131(6): 807-810.

The authors present the ocular findings in a 20 month old toddler with neonatal adrenoleukodystrophy(NALD), confirmed by elevated serum very long-chain fatty acid and phytanic acid levels and cultured skin fibroblast analysis. Vision was noted as fix and follow with each eye. Examination revealed an absent foveal light reflex, and there was chorioretinal atrophy with pigmentary changes in a leopard-spot pattern throughout the midperiphery. Spectral domain OCT through the fovea revealed outer retinal atrophy with loss of the external limiting membrane and the inner-segment ellipsoid line; additionally, hyperreflective opacities were suspended in the vitreous. A linear scan through an area of pigmentary change in the midperiphery showed severe atrophy of outer retinal structures and pigment epithelium atrophy with nodules of hyperreflective material on top of the Bruch membrane. The ERG demonstrated severe loss of both rod- and cone-driven responses.

Distinct Ocular Expression in Infants and Children With Down Syndrome in Cairo, Egypt :Myopia and Heart Disease

Hanan H. Afifi, Amira A. Abdel Azeem, Hala T. El-Bassyouni, Moataz E. Gheith, , et.al. JAMA Ophthalmol. August 2013;131(8):1057-1066.

The authors believe there is a distinct Down syndrome phenotype in Cairo, a historically isolated area. The study compares Down syndrome patients in Cairo with Down syndrome patients in other geographic areas. In this population of patients with Down syndrome, 90 infants and children with Down syndrome were examined and followed over a 3 year period. At initial exam 58% had ocular finding with significant refractive error being most common (41%). Nasolacrimal duct obstruction, blepharoconjunctivitis, or conjunctivitis was found in 18 (20%), strabismus in 13 (14%), cataract in 5 (6%), nystagmus in 3 (3%), and optic nerve dysplasia in 2 (2%). Brushfield spots were not found. 40% had cardiac anomalies. An association with myopia was established.

Congenital Cystic Eye In Utero: Novel Prenatal Magnetic Resonance Imaging Findings

James R. Singer, Patrick J. Droste, Adam S. Hassan, JAMA Ophthalmol. August 2013;131(8):1092-1095.

Congenital cystic eye is a rare orbital malformation due to failure of optic vesicle invagination during embryogenesis The malformation consists of anophthalmic orbit containing a fluid-filled cyst and, frequently, rudimentary ocular structures. Associated nonocular malformations include intracranial anomalies and

systemic malformations. The authors present a case of congenital cystic eye identified prenatally on ultrasound. After birth, MRI of the brain revealed absence of the corpus callosum and septum pellucidum, in addition to frontal lobe dysplasia, colpocephaly and contralateral dacryoceles. Repeated aspiration is often insufficient and their patient ultimately required surgical excision with silicone implant. The authors suggest that congenital cystic eye in association with midline intracranial defects may represent a novel presentation in the septo-optic dysplasia sequence.

Use of a Comprehensive Polymerase Chain Reaction System for Diagnosis of Ocular Infectious Diseases

Sunao Sugita, Manabu Ogawa, Norio Shimizu, Tomohiro Morio, *Ophthalmology* September 2013; 120:1761-1768

This is a prospective clinical trial of 500 patients with infectious uveitis and endophthalmitis examined at Tokyo Medical and Dental University and other institutions in Japan. Genomic DNA of bacteria, fungi, parasites, and viruses in collected intraocular samples were examined by comprehensive polymerase chain reaction technique (PCR).

Conclusions: Use of our comprehensive PCR assay to examine ocular samples in patients with endophthalmitis and uveitis seems to be clinically useful for detecting infectious antigen DNA. The authors felt that PCR method is a reliable tool for both diagnosing ocular disorders and further screening of patients for intraocular infections.

Evidence-Based Ophthalmology

Richard Wormald, Kay Dickersin, *Ophthalmology* December 2013; 120(12):2361-2363

This is an editorial that talks about evidence-based ophthalmology. It is written by authors from the United Kingdom and the United States of the Cochrane Eyes and Vision Group. This editorial is really mandatory reading for anybody who is interested in research. The editorial gives a summary of how the Cochrane Collaboration Group. This group was started in 1979 and how it evolved into its current level of the Cochrane Eyes and Vision Group.

The things that we have learned through the Cochrane Eyes and Vision Group's systematic reviews:

- 1) Patching is wrong for corneal abrasions.
- 2) Screening the elderly for sight loss does not reduce the prevalence of vision impairment, at least in the existing models.
- 3) Vitamin supplements for the prevention of cataract make no difference.
- 4) Vitamin E and betacarotene do not prevent age-related macular degeneration.
- 5) Non-steroidal anti-inflammatory agents probably are effective in treating macular edema after cataract surgery.
- 6) Antimetabolites decrease the risk of failure of trabeculectomy.
- 7) Acyclovir is marginally better than trifluorothymidine at accelerating the healing of a herpetic dendritic ulcer.

Meibomian Gland Dysfunction and Hypercholesterolemia

Antonio Pinna, Francesco Blasetti, Angelo Zinellu, Ciriaco Carru, *Ophthalmology* December 2013; 120(12):2385-2389

This is an observational, case-control pilot study. There were 60 symptomatic patients with meibomian gland dysfunction with no history of hypercholesterolemia and 63 controls without meibomian gland dysfunction and no history of hypercholesterolemia between January 2011 and June 2012.

Objective: To investigate a possible correlation between meibomian gland dysfunction and hypercholesterolemia in young and middle-aged patients.

Conclusions: The results suggest that young and middle-aged patients with meibomian gland dysfunction with no history of hypercholesterolemia may have higher blood cholesterol levels than controls of similar age without meibomian gland dysfunction. Meibomian gland dysfunction may become a marker of previously unknown hypercholesterolemia and ophthalmologists may increase their role in the early detection of important risk factor for cardiovascular disease.

The Future of Uveitis Treatment

Phoebe Lin, Eric B Suhler, James T Rosenbaum, *Ophthalmology* January 2014; 121(1):365-376

Uveitis is a heterogeneous collection of diseases with polygenic and environmental influences. This heterogeneity presents challenges in trial design and selection of end points. Despite the multitude of causes, therapeutics targeting common inflammatory pathways is effective in treating diverse forms of uveitis. These treatments include corticosteroids and immunomodulatory agents. Both of these agents are often effective but can have untoward side effects limiting their utility.

New technology has resulted in novel approaches of delivering a therapeutic substance include, but are not limited to, the use of small interfering RNA, viral and nonviral gene therapy, and microparticle or viscous gel sustained-release drug-delivery platforms. The goal is for pathogenesis of uveitis, barriers to new drug development, targeting inflammatory cytokines, emerging therapies for uveitis, targeting T-cell activation, molecular inhibitors and enhancing inflammatory pathways.

Reviewers Comment: This is a very comprehensive survey on the future of uveitis treatment. This is recommended reading for all ophthalmologists.

Isolated abducens nerve palsy with hyperhomocysteinemia: Association and outcomes

Virender Sachdeva, Vaibhev Mittal, Avinash Pathengay, Ramesh Kekunnaya, Amit Gupta, Bhoompally V Rao *Indian J Ophthalmol* 2013;61:598-600.

This short series of 4 cases shows an association between hyperhomocysteinemia and isolated sixth palsy. Homocysteine levels could be checked in all cases if the work up negative for the isolated sixth nerve. All these cases resolved in few weeks.

Adalimumab therapy for refractory childhood uveitis

Bravo-Ljubetic L, Peralta-Calvo J, Noval S, et al

J AAPOS October 2013;17:456-459

Adalimumab (Humira), infliximab (Remicade), and etanercept (Enbrel) are all anti-TNF drugs used to treat uveitis in children. This paper examined the results of adalimumab therapy in children with refractory noninfectious uveitis. The uveitis was either idiopathic or JIA-associated. Adalimumab was administered by subcutaneous injection. Treatment and follow-up ranged between 15 and 58 months. Fifteen children (12 of whom were girls) were enrolled. Mean age was 10 years. Ten patients had JIA-associated uveitis, 4 had idiopathic uveitis and 1 had juvenile systemic granulomatosis (Blau syndrome). Of the 14 patients who had ocular inflammation at the onset of therapy, 12 (85.7%) showed improvement. Mean time to control inflammation was 6 weeks. In children with recurrence of uveitis, adalimumab was effective in 9/15 (60%), and mildly effective in 2/15 (13%). Therapy was discontinued in 3 patients because of lack of response and in 1 patient because of a satisfactory clinical course without relapse 17 months after treatment. Only minor side effects were observed. This was a small study but it appears that adalimumab is an effective treatment and should be considered as a first biological agent in the treatment of refractory noninfectious uveitis in children.

Risk factors associated with the relapse of uveitis in patients with juvenile idiopathic arthritis: a preliminary report

Saboo US, Metzinger JL, Radwan A, et al, J AAPOS October 2013;17:460-464

After the withdrawal of immunomodulatory therapy (IMT) for uveitis treatment, it is unclear what the risk factors for relapse are. This paper examines the risk factors associated with relapse after the patient has been in remission off of all IMT therapy and corticosteroid therapy for at least one year. IMT treatment had been continued for approximately 2 years once remission was achieved. This was a retrospective review of all JIA-associated chronic or recurrent uveitis patients with onset of disease in childhood. Relapse was defined as $\geq 1+$ cell in the anterior chamber or $\geq 1+$ vitreous haze. Eleven patients were excluded because of loss to follow-up and thirty patients were included. 13/30 relapsed (43.3%). When comparing those that relapsed with those that did not, there was no significant difference in sex, age at diagnosis of uveitis, age at diagnosis of arthritis, family history of JIA, type of arthritis, or ANA positivity. The patients who remained in remission received IMT drugs at an earlier age (7 yrs vs 13 yrs) and had a shorter interval between onset of uveitis and initiation of IMT therapy (12 months vs 72 months). The remission group was treated for a longer period of time (2 years more on average), than the relapse group. The remission group also had a slightly longer median duration of activity of the uveitis before IMT withdrawal (24 months vs 18 months). Nausea and fatigue were the most common side effects, and a number of patients developed leucopenia. It is important to note that patients who relapsed within 1 year of treatment withdrawal

were excluded because they did not meet the definition of durable remission. These results suggest we should continue to keep patients on IMT therapy for 2-years after inactivity of the uveitis is obtained. Also IMT therapy should be considered earlier in the course of the disease if lesser therapies prove ineffectual. This was a retrospective study with a small sample size at a tertiary referral center.

Indications for and Outcomes of Deep Anterior Lamellar Keratoplasty in Mucopolysaccharidoses

Silva Ricardo JR, Medhi J, Pineda R, J Pediatr Ophthalmol Strabismus 2013;50(6):376-381

The authors aim to describe the outcome of deep anterior lamellar keratoplasty (DALK) for visually significant corneal clouding in patients with mucopolysaccharidoses (MPS). Corneal clouding commonly causes visual disability in Hurler, Hurler-Scheie, Morquio and Marote-aux-Lamy syndromes. All layers of the cornea are affected. The authors present four eyes of two patients with Hurler syndrome who underwent DALK as well as 7 others from the literature. Visual acuity improved in all eyes and there was no recurrence of clouding in the corneal grafts. They conclude that DALK should be considered preferable to PKP in cases of Hurler disease although the effects of the disease on endothelium is controversial. Improvement in vision can be achieved with stable clear grafts, although other ocular manifestations may limit vision.