What’s New and Important in Pediatric Ophthalmology and Strabismus for 2015
The Complete and Unabridged handout

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Presented by the
AAPOS Professional Education Committee

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1. AMBLYOPIA

Atropine vs Patching for Treatment of Moderate Amblyopia Follow-up at 15 Years of Age of a Randomized Clinical Trial

Long term data on durability of treatment effect is provided in this study of 147 moderate amblyopes who were younger than age 7 when randomized to treatment with atropine or patching. Outcome measure is visual acuity using ETDRS chart of amblyopic and fellow eye in children originally enrolled in the study who are now 15 years old. Original treatment cohort was 419 children with moderate amblyopia (20/40 – 20/100) who were randomized to treatment consisting of 6 hours a day of patching or Atropine 1% once daily for 6 months. At age 15, mean acuity in amblyopic eye was 20/25 (0.14 logMAR) Mean interocular acuity difference (IOD) was 2.1 lines (0.21 logMAR). Better visual acuity occurred in patients whose treatment began less than age 5 (p<0.001). Visual acuity at age 15 years did not significantly differ with initial treatment with patching or Atropine.

Binocular Training Reduces Amblyopic Visual Acuity Impairment

It has been hypothesized that amblyopia is a result of damage to the binocular system and hence, a binocular treatment is necessary to ameliorate both monocular and binocular visual deficits. This non-randomized clinical trial assessed the efficacy of binocular training for improvement of the visual acuity in children and adults with amblyopia. Twenty-two amblyopic subjects ranging in age from 5 to 73 (mean: 36.2) years for whom patching and/or surgical treatments did not correct their visual impairment completed an average of 14.5 sessions of binocular training over a period of 4 to 6 weeks. Random dot kinematograms were presented dichoptically to the two eyes and the participants’ task was to identify the direction of motion of the targets. Mean visual acuity improvement was 0.34 LogMAR and was shown to persist 6 months following the cessation of binocular training. Visual acuity increased significantly as a function of the number of sessions completed; in contrast, age and severity of amblyopia did not predict the improvement in acuity. Weaknesses of the study include the wide range of severity of amblyopia and age of subjects, combination of strabismic and anisometropic amblyopia, and small number of patients.
An educational intervention to improve adherence to high-dosage patching regimen for amblyopia: a randomised controlled trial.

This study tried to evaluate the adherence of patching therapy. It is felt that adherence to therapy is the major issue in amblyopia treatment. This was an unmasked controlled clinical trial on whether intense educational intervention improved therapy.
62 newly diagnosed children with amblyopia were included. They were randomly assigned into the two treatment arms. Both were given 10 hours/day, 6 day/week for a 12 week period. The educational group received a booklet, video, cartoon story book, and dedicated session with educated personnel. The success rate for the intervention group was 80.6% and the control group was only 45.2%. The actual visual outcome though was not significantly better. The actual vision was not disclosed in the study and only a percentage of improvement was shown in a graph. One can not determine the actual vision change in this study. Their primary outcome measure was compliance with therapy.


This study was a retrospective study looking at the affects of oblique astigmatism on refractive amblyopia in children 3-7 years of age. 72 patients with oblique astigmatism and 82 children with orthogonal astigmatism were chosen. The oblique group showed worse vision initially, slower improvement in vision, and higher prevalence of parental oblique astigmatism. The average cylinder was 2.43 in the oblique group and was 2.93 in the orthogonal group. These children still improved with treatment although at a slower rate.


This is a case report of an adult patient who regained sight in an amblyopic eye after the decline of vision in the dominant eye caused by glaucoma. The patient was a 41-year-old patient with Axenfeld–Rieger syndrome and a mutation in the FOX C1 gene. At 6 years old, she was diagnosed with anisometric amblyopia in the left eye. She was treated with refractive correction and a part-time patching of her dominant right eye. She was subsequently lost to follow up and, at 15 years of age, re-presented with advanced Axenfeld–Rieger glaucoma. She was treated medically and surgically to control her intraocular pressure in the right eye; however, despite treatments, her vision eventually declined to light perception only. Since then, the patient’s vision in the amblyopic left eye gradually improved without any attempts at treatment. Since 2010, the patient’s
vision in the amblyopic left eye experienced drastic improvements from 20/150 to 20/60.


This is a multi-center, cross-sectional study funded by the National Institutes of Health. This study was designed to evaluate risk factors for unilateral amblyopia and for bilateral amblyopia in the Vision In Preschoolers Study (VIP study). Participants: 3,869 Head Start Preschoolers 3 to 5 years of age were evaluated. These children were from 5 clinical centers representing children of various vision disorders in geographically distinct parts of the United States. Main Outcome Measures: Risk of amblyopia was summarized by the odds ratio and their 95% degree of confidence intervals estimated from logistic regression models. Conclusions: Strabismus and significant refractive errors were risk factors for unilateral amblyopia. Bilateral astigmatism and bilateral farsightedness were risk factors for bilateral amblyopia. Despite differences in selection of the study population these results validated the findings of the Multi-Ethnic Pediatric Eye Disease Study (MEPED study) and the Baltimore Pediatric Eye Disease Study (BPED study).


The purpose of this study was to examine the effects of impaired spatiotemporal vision on reaching movements in 16 participants with strabismic amblyopia and to compare their performance to 14 with strabismus only without amblyopia and to 16 visually normal participants. Participants executed degree to the left reach-to-touch movements toward targets presented randomly 5degree or 10or right of central fixation in three viewing conditions: both eyes, monocular amblyopic eye (nondominant eye for participants without amblyopia), and monocular fellow eye (dominant eye for participants without amblyopia). Both groups with abnormal binocular vision (strabismic amblyopia and strabismus only) had reach latency, accuracy, and precision comparable to visually normal participants when viewing with both eyes and fellow (dominant) eye. Latencies were significantly delayed by more than 30 ms in all participants with reduced binocularity during amblyopic eye or nondominant eye viewing compared with controls (P < 0.0001). Subjects with strabismic amblyopia and those with strabismus only attain relatively normal reach accuracy and precision. However, they use a different reach strategy that involves changing the motor plan.
Effects of strabismic amblyopia and strabismus without amblyopia on visuomotor behavior: III. Temporal eye-hand coordination during reaching.
The purpose of this study was to examine the effects of strabismic amblyopia and strabismus only, without amblyopia, on the temporal patterns of eye-hand coordination during both the planning and execution stages of visually-guided reaching in adult subjects (16 with strabismic amblyopia, 14 with strabismus only, and 16 visually normal) executed reach-to-touch movements toward targets presented randomly 5degree or 10degree to the left or right of central fixation. Temporal coordination between eye and hand movements was examined during reach planning (interval between the initiation of saccade and reaching, i.e., saccade-to-reach planning interval) and reach execution (interval between the initiation of saccade and reach peak velocity [PV], i.e., saccade-to-reach PV interval).
The temporal patterns of eye-hand coordination prior to reach initiation were comparable among participants with strabismic amblyopia, strabismus only, and visually normal adults. However, the reach acceleration phase of participants with strabismic amblyopia and those with strabismus only were longer following target fixation (saccade-to-reach PV interval) than that of visually normal participants (P < 0.05). The amplitude and peak velocity of these saccades were significantly greater during amblyopic eye viewing in participants with amblyopia who also had negative stereopsis.
Adults with strabismic amblyopia and strabismus only showed an altered pattern of temporal eye-hand coordination during the reach acceleration phase, which might affect their ability to modify reach trajectory using early online control. Secondary reach-related saccades may provide a compensatory mechanism with which to facilitate the late online control process in order to ensure relatively good reaching performance during binocular and fellow eye viewing.

The authors demonstrate the efficacy of using an Ipad platform technology to treat children with anisometropic and strabismic amblyopia. Children wear anaglyphic glasses and play binocular games for just 4 hours per week, in this well controlled study. Vision improved and was sustained for 3 months after cessation of therapy. Patching did not add any benefit. This pilot study involving 75 children demonstrates that new technology may finally bring amblyopia therapy into the 21st century.
Eye (2014) 28, 1310–1314

The authors implanted phakic IOLs and performed scleral reinforcement procedures on 11 eyes of eight children who were highly myopic and amblyopic. The authors state the procedure was safe and effective. Axial length was stable over 3 years. However, best corrected visual acuity did not improve, there was minimal change in the amblyopia and no improvement in the few children who had any stereopsis preoperatively. This is a New modality, but not yet proven to be important.


This study assessed the ability of SD-OCT measured peripapillary retinal nerve fiber layer (RNFL) thickness to detect optic neuropathy compared to fundus examination in patients with craniosynostosis. They compared indication of optic neuropathy by RNFL thickness and fundus exam with evidence of altered visual function (acuity and field), and investigated the correlation of fundus examination abnormalities with historical evidence of elevated ICP. There was a moderate correlation between logMAR acuity and optic neuropathy on fundus exam (very low sensitivity but excellent specificity). SD-OCT was more sensitive at detecting optic neuropathy (88%) versus optic atrophy (60%). SD-OCT was a significant predictor of papilledema. Abnormal visual fields along with optic neuropathy on fundus examination guaranteed predicted SD-OCT abnormalities. Peripapillary RNFL thickness measured by SD-OCT confirmed fundus examination findings of optic neuropathy with a sensitivity of 77% and specificity of 83%. RNFL thickness measurements were more sensitive at detecting optic neuropathy than visual field testing. Axial length was not measured. Peripapillary total RNFL thickness or volume were not obtained. Elevated ICP was based on historical data.


The authors investigate the correlation between false positive results on standardized binocular fixation preference testing and ocular dominance, hand dominance and patching history. They also assessed the overall predictive value of the binocular fixation preference test for strabismic amblyopia. This was a prospective cohort study over a 12-month period. Fixation was graded according to Zipf’s criteria. 114 subjects were enrolled and 34% had false positives or pseudoamblyopia. In those students there was a strong correlation between eye fixation preference and ipsilateral ocular dominance, but not ipsilateral hand dominance. True positives also showed a strong correlation between eye preference and ocular dominance but not hand dominance. Overall sensitivity
was high 97.1%, but specificity was low (51.3%). Overall positive predictive value of the binocular fixation preference test for strabismic amblyopia was poor but the negative predictive value was high. So the authors found lack of fixation preference was a good sign of the absence of amblyopia, but its presence was not a strong indicator of the presence of amblyopia. In pseudoamblyopia cases, ocular dominance was a major factor for fixation preference. In true amblyopia cases, there was a strong correlation between ocular dominance and the fixing eye. The same examiner performed both ocular dominance testing and binocular fixation preference testing and was not masked. Only strabismic patients were enrolled, and no effort was made to categorize the type of strabismus.

Visual Cycle Suppression via Patching in Central Serous Chorioretinopathy
James B. Earl, Cecilia S. Lee, Victoria Yom, Gregory P. VanStavern, Ophthalmology December 2014; 121(12):2502-2504

This study comes from Washington University School of Medicine, Department of Ophthalmology and Visual Sciences, St. Louis, Missouri and Moorfields Eye Hospital, London, United Kingdom. This is a prospective, single-arm clinical trial involving 8 treatment-naïve participants with Neurosensory retinal detachments. The patient was patched for 24 hours. Multifocal ERGs and OCTs were performed after 1 full day of patching. This study provides evidence that in some cases short-term suppression of the visual cycle via patching results in improved visual function as assessed by multifocal ERG in patients with central serous choroidopathy. The lack of resolution or improvement of subretinal fluid as determined by OCT evaluation indicates that the improvement seen in multifocal ERG is not owing to anatomic changes, but may be due to functional improvement owing to “visual cycle suppression.” The authors stress that this is a novel approach and requires further investigation.

The Effect of Amblyopia on Visual-Auditory Speech Perception
Why Mothers May Say “Look At Me When I’m Talking To You”

This is a retrospective observational study to determine if ambylopes have visual auditory processing difficulties. The McGurk phenomenon demonstrates that how you interpret what you hear is influenced by what you see. An examiner will say “ba,ba,ba” which the test subject will hear as “ba,ba,ba”, but if the examiner changes his mouth expressions while saying “ba,ba,ba” the test subject will hear “fa,fa,fa.” The McGurk effect is an example of visual auditory integration. Thirty three children older than age 3 with no hearing or neurologic problems were examined. Twenty four of the children had amblyopia and nine children did not have amblyopia and served as controls. An audio track played the sound “pa” and a video track showed a person verbalizing “ka.” The integrated sound was “ta.” The McGurk effect, that is, the fused sound “ta,” was perceived by 11 of the 24 children with amblyopia (45.8%) and all 9 controls (100%). The McGurk effect was perceived by 100% of children with amblyopia that was
resolved by 5 years of age and by 100% of participants whose onset at amblyopia developed at or after 5 years of age. However, only 18.8% of participants with amblyopia that was unresolved by 5 years of age (n = 16) perceived the McGurk effect. The authors conclude that children with amblyopia have impaired visual auditory speech recognition and the timing of onset and resolution of amblyopia affects this process of integration.

**Risk of Musculoskeletal Injuries, Fractures, and Falls in Medicare Beneficiaries With Disorders of Binocular Vision**

This is a retrospective study which looked at a random 5% sample of Medicare Part B beneficiaries from 2002-2011. Outcome measures studied included the ten-year prevalence of musculoskeletal injury, fracture, or fall in individuals with and without disorders of binocular vision. Analyses were adjusted for age, sex, race/ethnicity, region of residence, systemic and ocular comorbidities, and duration of follow-up. There were 2,196,881 Medicare beneficiaries identified. Of these, 99,525 (4.5%) had at least 1 reported disorder of binocular vision (strabismus, 2.3%; diplopia, 2.2%; amblyopia, 0.9%; and nystagmus, 0.2%). During the 10-year study period, there were 1,272,948 (57.9%) patients with documented musculoskeletal injury, fracture, or fall. The unadjusted odds ratio (OR) for the association between disorders of binocular vision and any of the 3 injury types was 2.23 (95%CI, 2.20-2.27; P < .001). The adjusted OR was 1.27 (95% CI, 1.25-1.29; P < .001). The authors conclude that Medicare beneficiaries with a disorder of binocular vision have significantly higher odds of sustaining a musculoskeletal injury, fracture, or fall.

### 2. VISION SCREENING

**Accuracy of Noncycloplegic Retinoscopy, Retinomax Autorefractor, and SureSight Vision Screener for Detecting Significant Refractive Errors.**

**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.

**Beyond Screening for Risk Factors Objective Detection of Strabismus and Amblyopia**


The authors identify a limitation of commercially available vision screening devices. These devices identify refractive risk factors for amblyopia, not amblyopia or strabismus itself. This study examined the Pediatric Vision Scanner (PVS), a device which relies on retinal birefringence to detect amblyopia, with the SureSight autorefractor.

Primary outcome was sensitivity and specificity of identifying amblyopia and strabismus in a cohort of children age 2-6 years old. Secondary outcomes included positive and negative likelihood ratios of identifying amblyopia and strabismus. A masked complete pediatric ophthalmology exam was the gold standard. Of 300 patients, 188 had strabismus only, amblyopia only, or both and 112 had neither strabismus nor amblyopia. The sensitivity of the PVS to detect strabismus and amblyopia was higher than the SureSight (0.97 vs. 0.74). Specificity was also significantly higher for the PVS than the SureSight (0.87 vs. 0.62). The SureSight autorefractor had 8.8 x as many false negatives and 3.1 times as many false positives as the PVS. The PVS was easy to use with only one child not being able to be screened, compared with 17 children not completing a successful screening with the SureSight. A limitation of the study is that examiners, during the gold standard complete exam, used fixation preference as a surrogate for amblyopia in children too young to cooperate for visual acuity testing. Also, the setting for the study was “enriched” and not the primary care setting, which is the environment a pediatric vision screening device would be most useful.
Screening, Confirming, and Treating Amblyopia
Based on Binocularity

Jonathan Holmes’ invited commentary highlights the difficulty of definitively identifying amblyopia on the basis of visual acuity alone. Obstacles include test re-test reliability and age. The Pediatric Vision Screener (PVS) may have more uses than just as an objective detector of amblyopia and strabismus. The PVS is useful as a measure of binocular impairment. Dr. Holmes suggests that the PVS may be useful in the pediatric ophthalmologist’s office to further define the nature of the child’s visual deficit and provide another measure of following a child’s response to treatment. Objective binocular identification of amblyopia by the PVS can one day be paired with binocular amblyopia treatment as demonstrated by Hess and colleagues.

Comparison of SureSight autorefractor and plusoptiX A09 photoscreener for vision screening in rural Honduras. Silbert DI, Matta NS and Ely AL. J AAPOS 2014;18:42-44.

The authors compared the SureSight autorefractor (SS), which is battery powered to the plusoptiX A09 photoscreener (PA09) in screening the same group of children. The SS, if as effective as the PA09, would have greater utility in rural areas. 216 children ages <1 to 17 met referral criteria. Nine children (4%) were found to have amblyopia risk factors. PA09 had a sensitivity and specificity of 89% and 80% respectively. SS autorefractor was 89% and 71% respectively. Using VIPS 90% referral criteria altered the sensitivity and specificity to 78% and 99% respectively, while using VIPS 94% referral criteria altered this to 67% and 99% respectively. Vision screeners need to take into account the population they are screening, and its future access to followup care, to determine how stringent referral criteria should be.

Repeat Retinomax screening changes positive predictive value.

The purpose of this study was to quantify the variability between autorefraction readings performed by lay screeners in preschool children and to calculate the clinical effect of this variability. Over a two-year period lay vision screeners performed noncycloplegic in-school autorefraction in low-income urban preschoolers with a Retinomax autorefractor. 636 children completed a follow-up examination. Time from original screening to repeat autorefraction and comprehensive examination averaged 96 days. 49% were Hispanic. African-Americans had disproportionally low follow-up. There was a greater variation in sphere (0.70 intraclass correlation) than cylinder (0.83 OD 0.84 OS). 467/636 children (73%) met referral criteria again at repeat screening. Overall 275 (43%) met the case definition for amblyogenic risk factors. However, this broke down to 57.4% of those who met referral criteria at repeat autorefraction, versus 4.1% who passed the repeat autorefraction. Proportion of children who converted from a referral at first screening to pass at repeat screening was greatest for
anisometropia, and lowest if they had multiple referral indications. Variability can be due to slight variations in working distance, variable accommodation and different screeners. Repeatability metrics found in this study only apply to children who were referred from the initial screening autorefraction. Eye care providers were not masked to previous screening results. This study included a high percentage of minorities.


This study evaluated the Spot photoscreener in detecting amblyopia risk factors in children compared to the 2003 and 2013 AAPOS referral criteria. 151 patients aged <1-6 years old were examined. This study population had a 70% rate of amblyopia or amblyopia risk factors, based on 2003 criteria. A positive predictive value of 88%, negative predictive value of 61%, a sensitivity of 80% and a specificity of 74% were found compared to cycloplegic pediatric ophthalmology examination. Agreement of the Spot photoscreener with pediatric ophthalmic exam occurred in 79% of the cases. With 2013 criteria, 65% of patients were found to have amblyopia risk and Spot results agreed with 2013 AAPOS referral criteria 85% of the time. PPV 86%, NPV 75%, sensitivity 87% and specificity 74%. Spot could not obtain autorefraction readings in 12 patients, who were then referred. This study population was not compatible to the general population, because of the skew towards more pathology. Spot results are fair, but 19/74 children felt to have clinical amblyopia and/or strabismus passed Spot photoscreening.


The Handy Eye Chart (HEC) is a valid measure of pediatric patient visual acuity between ages 6-18. It is intended to be used in preliterate, developmentally challenged, or nonverbal children. The Handy Eye Check (HECh) is a mobile medical application, allowing use of the ATS protocol using (HEC). Test-retest analysis was performed to determine reliability, and HECh validity was tested by comparing visual acuity results obtained with this method, to those obtained with the validated (HEC). Consecutive patients over a 1-month period were invited to participate. Sixty children were enrolled. Results support validity and reliability of HECh. Mean logMAR acuity and best-corrected logMAR acuity were not different to a statistically significant degree. Correlation coefficient was .92 indicating a strong linear correlation. Test-retest showed all patients within 0.2 logMAR absolute difference and 81% were within 0.1 logMAR absolute difference. This application may have use as a vision screening test in health departments, schools and primary care provider offices.
Prevalence of Vision Disorders by Racial Ethnic Group among Children Participating in Head Start


This is a National Institute of Health sponsored multi-center, cross-sectional study designed to compare the prevalence of amblyopia, strabismus and significant refractive error among African-American, American Indian, Asian, Hispanic and non-Hispanic white preschoolers in the Vision In Preschoolers study (VIP study).

Participants were 3-5 year old preschoolers in the Head Start Program from 5 geographically disparate areas of the United States. The VIP study evaluated a targeted cohort of children 3 to 5 years of age. Children in Head Start Programs are, by federal regulation, families whose household income falls below the poverty line. In the VIP study the children represented a variety of racial and ethnic groups; Black 51%, Hispanic 20%, non-Hispanic white 12%, American Indian 8.5% and Asian 3.7%.

Methods: 4,040 preschoolers from 3 to 5 years of age were enrolled. They were from 5 geographically disparate areas of the United States.

Conclusions: Among Head Start preschool children, the prevalence of amblyopia and strabismus were similar among the 5 racial ethnic groups. The prevalence of significant refractive errors, particularly hyperopia and hyperopic astigmatism, vary by group. The highest rate of farsightedness occurred in non-Hispanic whites and the highest rate of astigmatism and anisometropia occurred in Hispanics.

Color Vision Deficiency in Preschool Children: The Multi-Ethnic Pediatric Eye Disease Study


This is a population-based, cross-sectional study designed to determine the sex and ethnicity specific prevalence of color vision deficiency (CVD) in black, Asian, Hispanic and non-Hispanic white preschool children.

Participants: Multi-Ethnic Pediatric Eye Disease Study is a population-based evaluation of the prevalence of vision disorders in children in Southern California. A total of 5,960 subjects 30 and 72 months of age were recruited for the study of which 4,177 were able to complete color vision testing.

Main Outcome Measures: Testing of color vision in preschool children between 30 and 72 months of age and the presence of color vision deficiency stratified by age, sex and ethnicity.

Conclusions: Testability for color vision deficiency in preschool children is high by 4 years of age. The prevalence of color vision deficiency in preschool boys varies by ethnicity with the highest prevalence in non-Hispanic white and lowest in black children.

This was a prospective study over a seven-month period of patients between ages 3 and 17. The authors attempted to determine whether noncycloplegic autorefractor measurements (Marco-ARK-560A automatic refractor) could predict the clinical cycloplegic outcome and evaluate the effectiveness of autorefraction in children. 88 patients were included in the study and autorefractor measurements were successfully acquired in 100% of study subjects. Autorefractor (dry) found on average 0.29 D less sphere than dry refraction. Autorefractor (dry) readings showed -1.03 D less sphere than autorefractor (wet) and a statistically significant but clinically insignificant difference of vertical astigmatism. Comparing autorefractor (wet) with cycloplegic refraction showed a clinically insignificant difference in vertical astigmatism. Autorefractor (dry) compared to cycloplegic refraction showed -1.05D less sphere. Vertical astigmatism showed a statistical but not clinically significant difference.


This study prospectively compared anterior segment parameters of hyperopic anisometropic amblyopic eyes to their fellow eyes and to emmetropic normal eyes. The third group was felt to be necessary because there is a belief that the ‘fellow’ eyes of amblyopic eyes are also abnormal to some degree. Patients were between 6 and 13 years of age and seen over a six month period. There were 34 hyperopic anisometropes and 36 normal control patients. Pentcam showed no difference in mean anterior and posterior corneal curvature, central corneal thickness, corneal volume, anterior chamber depth, anterior chamber volume and pupil diameter between amblyopic, fellow and normal eyes under photopic, scotopic, and cycloplegic conditions. Ths was a small cohort, and results cannot be generalized to other forms of amblyopia.

Modification of the Titmus fly test to improve accuracy
Kyle Arnoldi, Alla Frenkel, Am Orthopt J Sept 2014;64:64-70

This prospective, controlled, observational study analyzed responses of 23 study subjects with strabismus and 10 non-strabismic control subjects when tested with the Titmus fly test book positioned in the typical horizontal position and then with the book rotated clockwise 90° in a vertical position. Although a 3-D image is not possible in the vertical position, the authors found that 48% of the study subjects and 30% of control group subjects reported a 3-D effect when presented the vertical position. The authors concluded that other factors such as monocular clues and history of multiple past Titmus fly tests influence the subjects’ responses leading to inaccuracy of testing. The authors recommend that if a patient reports a 3-D image when tested with the typical horizontal Titmus book orientation then a retest should be performed with the book oriented vertically. If
the patient reports a 3-D image using the vertical orientation then the patient’s horizontal Titmus test is not valid. Given the limitations of stereopsis testing and the variety of stereo tests available, I believe this quick additional step may be useful to improve accuracy for those who use the Titmus fly test.


The Association for the Blind and Visually impaired (ABVI) established the ReFocus on Children Program to assist school nurses in providing vision screening for at-risk children in the Charleston County School District in S. Carolina. Written consent forms were sent to parents prior to the screening process. Eye examinations were performed on children if they met referral criteria and had parental consent. From 2012-13, 2,750 children ages 3-5 years old were screened with the Plusoptix Vision Screener. Approximately 60 children were screened per hour. Children who met referral criteria had an eye examination by a licensed optometrist or ophthalmologist in the school. Glasses were prescribed free of charge and dispensed on the premises when appropriate. Referral criteria were based on the AAPOS guidelines of anisometropia $\geq 1.5$ D, hyperopia $\geq 3.5$ D, myopia $\geq 3.0$ D, astigmatism $\geq 2.0$ D and anisocoria $\geq 1$ mm. 741 of 2,750 children were referred (27%), 419 (56%) had an eye examination (those with parental consent) and 192 were prescribed glasses. The positive predictive value (PPV) of the Plusoptix screener for those examined was 46%. Children received their glasses within 3 weeks.

Teacher feedback letters were sent to 110 teachers with a 49% response rate. The responses were mostly positive for the screening process. The positive impact of glasses was that the majority of children prescribed glasses wore them regularly, had reduced squinting and improved vision. The negative impact of glasses was reported to be embarrassment, poor care of the glasses and use of them as a toy. Informally, nurses reported the process to be efficient and accurate.

This article is unique because at risk children receive vision screening and treatment with glasses, when appropriate, while in school. This process removes the potential for parental non-compliance with referral recommendations and purchase of glasses due to financial constraints.


The authors evaluated the reliability of the Retinomax K-plus-3 autorefractor in obtaining cycloplegic refractive values as compared to a cycloplegic refraction by a Pediatric Ophthalmologist. Children were enrolled over a 2 ½ year period. 622 eyes of 311 children aged 5 months to 17 years were enrolled. For the pooled data of the different age groups, there was no significant difference in regards to the power or axis of astigmatic error. Spherical equivalent was
significantly different across all age groups. The autorefractor measured a more myopic spherical power than the physician. Overall the autorefractor-measured refractive errors were in good clinically acceptable agreement with the clinician cycloplegic refraction. The inclusion of left and right eye data may introduce a bias.


The Spot Vision screener sensitivity and specificity using two different referral criteria to detect amblyopia and its risk factors was evaluated. Patients were derived from four pediatric ophthalmology practices. During a 3-month period, 233 children were screened but only 155 have data that could be used (60 were lost from accidental file corruption, and another 18 screenings were unsuccessful due to poor cooperation or congenital ocular abnormalities). 64/155 (41%) had amblyopia based on 2 line difference in best-corrected acuity or for preverbal children on fixation preference testing. 70% had amblyopia risk factors. Original manufacturer referral criteria resulted in a sensitivity of 89% and a specificity of 71%. After a software update applied retroactively, specificity increased to 88% and sensitivity dropped to 83%. The data found in this study cannot be applied to a general population, as the rate of ocular pathology is much higher in a clinic population.


This study evaluated the newer software version of the Spot in detecting amblyopia risk factors according to the 2013 AAPOS Vision Screening Committee guidelines. This was a prospective study over an 18-month period of patients 1-16 years of age. 444 children were included with an average age of 72 months. There was a 55% prevalence of AAPOS amblyopia risk factors. 61% of patients were referred. With Spot 1.151 version sensitivity was 88.1% and specificity was 71.9%. With version 2.0.16 sensitivity was 87.7% and specificity was 75.9%. Using 2013 AAPOS guidelines instead of manufacturer guidelines lowers sensitivity and specificity to 84.8% and 70.9% respectively. The Spot was unable to obtain a result in 9% of the children. Higher specificity was found for children age 31-48 months compared to 12-30 months of age. PPV also increased with age at testing. The testing of a high-risk population would be expected to decrease testability and alter the PPV and NPV.


The purpose of this study was to assess binocular detection grating acuity using the LEA GRATINGS test to establish age-related norms in healthy infants during their first 3 months of life. This was a prospective, longitudinal study, over a 10-month period. Infants were examined at one month (n=386), two months (n=253)
and three months (n=178). Eleven of the 178 were excluded for actually being older than 3 months, so 167 completed evaluation. 133 infants were available, and not excluded for a 12-month ophthalmic examination. Binocular responses to gratings showed development toward higher mean values and spatial frequencies. This study did not look at monocular values.

**Intraocular Pressure in Children: The Effect of Body Position as Assessed by Icare and Tono-pen Tonometers.**

This prospective study evaluated the effects of the body position on IOP results assessed by the Icare and tonopen. 47 children with 94 eyes were assessed. Mean seated IOP was 16.4 for applanation, 17.5 for Icare, and 18.0 for tonopen. Mean supine IOP was 18.4 for the Icare and 18.8 for the tonopen. The Icare tonometer correlates well with goldmann tonometry in seated children. The Icare correlated well with the tonopen in seated and supine positions.

**Normative Reference Ranges for Binocular Summation as a Function of Age for Low Contrast Letter Charts**

**Purpose:** To study binocular summation (BiS), defined as the superiority of binocular over monocular viewing on visual threshold tasks, with readily available clinical tools.

**Methods/Results:** 129 normal subjects aged 3 to 85 years were prospectively enrolled and underwent monocular and binocular testing using 2.5% and 1.25% Sloan low contrast acuity charts (LCA), Pelli-Robson contrast sensitivity charts, and Early Treatment Diabetic Retinopathy Study (ETDRS) VA charts. BiS was calculated as the difference between the better eye and binocular scores. Monocular and binocular scores decreased with increasing age for all metrics.

**Conclusion:** Of the clinical tests evaluated, 2.5% and 1.25% Sloan LCA charts most readily demonstrated BiS in young normal subjects. BiS declined with increasing age and increased interocular differences. Median values presented in this study may be useful for future clinical studies utilizing LCA.

**3. REFRACTIVE ERROR**

**Effect of Bifocal and Prismatic Bifocal Spectacles on Myopia Progression in Children Three-Year Results of a Randomized Clinical Trial**

This is a randomized clinical trial comparing the effect of single vision spectacles, bifocals, and prismatic bifocal spectacles on the progression of myopia in a cohort of children with a high rate of progression of myopia. Main outcome
measure was myopia measured under cycloplegia with an autorefractor and secondary outcome measure was axial length measured by A-scan at 6 month intervals for 36 months. The authors also sought to determine if treatment effect is dependent on accommodation lag and/or near phoria status. On hundred thirty five Chinese Canadian children (8-13 years old) with documented progression of myopia of at least 0.5 D in the last year were included. Three treatment arms included single vision lenses, executive bifocals with +1.5D and executive bifocals with +1.5 D and 3 BI prism in each near segment. Results suggest a significant inhibition of myopia progression in the bifocal treatment groups and a significant reduction in progression of axial length. Treatment effect is maintained over the 3 year study period. Baseline phoria was not predictive of response to bifocals. A subset of myopes with low accommodation lag showed the greatest response with prismatic bifocal lenses.


This studies purpose was to determine whether unilateral ONG is associated with increased prevalence of anisometropia in children with NF1 disease. This consisted of a retrospective review of all children with NF1 <16 years of age seen over a 5-year period. Anisometropia was defined as an interocular difference of >=1.00 D, spherical equivalent, or a difference of >=1.00 D of cylinder. Of 75 NF1 children, 50 had normal neuroimaging and 25 had ONG. There were no differences found in any refractive parameters.

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This study investigates the relationship between myopic progression and intermittent exotropia in school-aged children. A chart review was performed investigating early school-aged patients (7-12 years) with myopia. 210 patients were included and divided into three groups; (A) Patients with intermittent exotropia and myopia at presentation who underwent bilateral lateral rectus muscle recession; (B) Patients with intermittent exotropia and myopia at presentation who were observed for exotropia; and (C) Patients with myopia and straight ocular alignment. The study examined the rate of myopic progression per year, the preoperative and postoperative rates of refractive growth, and the rate of high myopia development at the end of the early school period. The authors found no significant difference in the rates of myopic progression (Group A - 0.43 ± 0.14 diopters (D) per year, Group B - 0.49 ± 0.17 D/year, Group C - 0.42 ± 0.24 D/year), preoperative and postoperative rates of refractive growth in Group A, or rates of high myopia development. The authors conclude that surgical correction for intermittent exotropia did not influence the rate of myopic
progression and there was no significant difference in the rate of myopic progression in patients with intermittent exotropia and myopia versus myopia alone. The study has a few limitations including its retrospective design, data is from a single institution, and many refractions were manifest refractions and not cycloplegic refractions.

**Does Vitamin D Mediate the Protective Effects of Time Outdoors On Myopia? Findings from a Prospective Birth Cohort**

More time outdoors is associated with a lesser risk of myopia, but the underlying mechanism is unclear. We tested the hypothesis that 25-hydroxyvitamin D (vitamin D) mediates the protective effects of time outdoors against myopia in children participating in the Avon Longitudinal Study of Parents and Children (ALSPAC) population-based birth cohort at age 7 to 15 years; maternal report of time outdoors at age 8 years and serum vitamin D2 and D3 at age 10 years. Total vitamin D and D3, but not D2, levels were higher in children who spent more time outdoors. In models including both time outdoors and sunlight-exposure–related vitamin D, there was no independent association between vitamin D and incident myopia (Total, HR = 0.83 [0.66–1.04], P = 0.11; D3, HR = 0.89 [0.72–1.10], P = 0.30), while time outdoors retained the same strong negative association with incident myopia as in unadjusted models (HR = 0.69 [0.55–0.86], P = 0.001). Total vitamin D and D3 were biomarkers for time spent outdoors, however there was no evidence they were independently associated with future myopia.


Identify risk factors for inadequately corrected refractive error in the United States.

Cross-sectional study including 12,758 participants 12 years of age and older from the 2005 to 2008 National Health and Nutrition Examination Survey. The primary outcome was the proportion of individuals with inadequate refractive correction for whom refractive correction would result in a visual acuity of 20/40 or better. The primary predictor was race/ethnicity. Secondary predictors included age, sex, annual household income, education, insurance, type of refractive error, current corrective lens use, presenting and best corrected visual acuity, cataract surgery, glaucoma, and age-related macular degeneration.

50.6% of subjects had a refractive error which was correctable to 20/40 or better with refraction while 11.7% with correctable refractive error were inadequately corrected. Odds of inadequate refractive correction were significantly greater in Mexican Americans and non-Hispanic blacks than in their non-Hispanic white counterparts in all age groups, with the greatest disparity in the 12- to 19-year-old group. Other risk factors associated with inadequate refractive correction in adults but not in teenagers included low annual household income, low education, and lack of health insurance.
Racial disparities in refractive error correction were most pronounced in those under 20 years of age, as well as in adults with low annual household income, low education level, and lack of health insurance.

**Emmetropization, visual acuity, and strabismus outcomes among hyperopic infants followed with partial hyperopic corrections given in accordance with dynamic retinoscopy**

D Somer, E Karabulut, F G Cinar, U E Altiparmak and N Unlu

*Eye* 28: 1165-1173

In this study, the authors utilize dynamic retinoscopy to see if they can determine which infants with hyperopia are at risk for the development of esotropia later in life. Infants age 3-12 months were enrolled in the study if they had hyperopia greater than 5D. Dynamic retinoscopy at a near target was performed and the infants were defined as normal accommodators or hypoaccommodators. In the hypoaccommodator group, they received specs to correct enough of the hyperopia to allow near focus. They were followed for three years. None of the infants with normal accommodation developed esotropia and of those with hypoaccommodation untreated 47% developed esotropia. They found that prescribing spectacles early had no effect on the emmetropization process. They conclude that dynamic retinoscopy should be performed to identify hyperopic infants at risk for strabismus, and those with poor accommodation should be followed more closely and given some correction at an earlier age.

**Accommodation-induced intraocular pressure changes in progressing myopes and emmetropes**

L Yan, L Huibin and L Xuemin

*Eye* (2014) 28, 1334–1340

This is a provocative study that supports the idea that mechanical changes during near work may be implicated in the progression of myopia. Young myopes (ave-6.50D) were compared to emmetropes. Intraocular pressure was measured after 3 minutes of induced accommodative effort. The myopes demonstrated increased IOP but the emmetropes demonstrated slight reduction in IOP. Both demonstrated shallowing of the anterior chamber structures during accommodation. This study adds to the debate as to whether myopia progression is mediated by mechanical or retinal mediators.

**Children with Down syndrome benefit from bifocals as evidence by increased compliance with spectacle wear.**


Children with Down syndrome are often hypoaccommodators, so the authors evaluated whether the addition of a bifocal lens increases spectacle compliance. Compliance information was obtained in 57 children by telephone contact an average of 51 months after glasses were obtained. 27 children were prescribed bifocals (26 were hyperopic and 1 was myopic). 30 children were prescribed single vision glasses (23 were hyperopic and 7 were myopic). Over half of the
patients in each group had strabismus and the difference between the two groups was not statistically significant. 39 of 57 patients underwent dynamic retinoscopy. 7/39 showed good accommodation and were prescribed single vision glasses. Compliance with glasses wear was 43%. 32/39 showed poor accommodation, and 27 of these patients were prescribed bifocals. Compliance with glasses wear was 89% (24/27) in the bifocal group and 40% (2/5) in the hypoaccommodation, no bifocal group. This study was largely retrospective and made no attempt to assess behavioral or intellectual levels of the enrolled subjects that could affect compliance. Dynamic retinoscopy was not performed quantitatively. Over half of the single vision glasses group did not have dynamic retinoscopy performed. Although the role of hypoaccommodation in Down syndrome is well-known, the data in this study might be skewed by a number of factors. Most of the myopic subjects were in the single vision group and we have no data separating compliance of myopes. Also the bifocal group all showed poor accommodation whereas the single vision group was a mixture of hypo-, normal and nontested accommodators.


This cross-sectional study tried to determine the association between ocular sun exposure and myopic refractive error. Sun exposure was determined by conjunctival ultraviolet autoflourescence. 1344 white subjects (mostly) between ages of 19- 22 years was examined. An inverse relationship was found between UV autoflourescence and myopia. Median area of autoflourescnece was significantly lower in myopic than in nonmyopic patients (31.9 mm2  vs. 47.9 mm2 ). This supports the inverse association between outdoor activity and myopia.

Myopia and Level of Education: Results from the Gutenberg Health Study Alireza Mirshahi, Katharina A. Ponto, Rene Hoehn, Isabella Zwiener, Ophthalmology October 2014; 121(10):2047-2052

A population-based cross-sectional study including 4,658 eligible enrollees between 35 and 75 years of age. The purpose of this study is to analyze the association between myopia and educational level in an adult European cohort. Main Outcome Measures: Prevalence and magnitude of myopia in association with years spent in school and level of post-school professional education. Conclusions: Higher levels of school and post-school professional education are associated with a more myopic refraction. Participants with higher educational achievements more often were nearsighted than individuals with less education. Comment: Myopia is a complex disorder that has a great medical impact on the affected individuals. Myopia causes visual impairment world-wide because of associated ocular comorbidities including rhegmatogenous retinal detachment, myopic macular degeneration, premature cataract and glaucoma. Both genetic and environmental factors have been shown to play some role in the pathogenesis of myopia. Recently environmental factors have been linked to the
prevalence of myopia including near work, outdoor activity during childhood, adolescent education, residence urban versus rural and possibly intelligence. There are considerable differences in the prevalence and severity of myopia in various parts of the world and different races and ethnicities. Previous studies have been done in the Danish and Greek literature comparing myopia with educational levels. This study was designed to evaluate nearsightedness in the European cohort. Risk factors for myopia now include exposure to outside activity, genetics, near work and urban versus rural environments.

4. VISION IMPAIRMENT


Children with cerebral palsy are known to be at increased risk for visual impairment. In a population-based sample drawn from a geographically defined registry, the profile of visual impairment in children with cerebral palsy was investigated. The authors found that close to half (49.8%; 106/213) of the patients had a visual impairment. The majority of these individuals had strabismus (55.7%; 59/106) and a slightly lesser fraction had refractive errors (20.7%; 22/106) or severe visual loss (18.9%; 20/106). The vast majority of children with severe visual loss had spastic quadriplegia (83%; 17/20) or were nonambulatory (i.e., Gross Motor Function Classification Scale IV/V, 80%; 16/20). This paper is useful to our profession in that knowledge of this profile will assist practitioners to heighten their appreciation of potential visual disturbances in certain subsets of children with cerebral palsy.


This study evaluated prevalence of parent-reported ADHD diagnosis in a cohort of pediatric low vision subjects compared to the general population. 264 patients met the inclusion criteria (19 were removed because they had no functional vision). Overall prevalence of parent reported ADHD was 22.9%. ADHD diagnosis were significantly less likely to have nystagmus and more likely to have better acuity. The prevalence of ADHD in the 19 students with near or total vision loss was 10.5%. There was no statistically significant difference in ADHD based on ocular diagnosis. The prevalence of ADHD was 1.5 times that in the state of Alabama (where the study was performed), and 2.3 times the national prevalence. This study had a good sample size but was limited to one geographic region. There is possible selection bias, as the parents in this study enrolled their children in a school for visually impaired children and might have been more likely to investigate other etiologies for behavior issues. ADHD rates were inversely related to visual impairment. This inverse relationship may be real or may be a byproduct of behavior issues being attributed to vision issues.
Cross-sectional study on childhood cerebral visual impairment in New Zealand. Chong CF, and Dai S. J AAPOS 2014;18:71-74

This study investigated the prevalence, etiology, and avoidable causes of CVI in New Zealand. Records of children enrolled in Blind and Low Vision Education Network, New Zealand (BLENNZ) were reviewed retrospectively. 657 children <=16 years of age had an acuity of less than 6/18. Of these 182 had CVI. Prevalence of CVI with acuity of 6/18 or worse in New Zealand is estimated at 0.02%. The majority of visually impaired CVI children had associated comorbidities, with developmental delay being most common. Approximately 50% of CVI blindness was caused by perinatal/neonatal causes: the top three were perinatal hypoxia, traumatic nonaccidental injury, and prematurity. 41% of all low vision CVI and 50% of CVI-related blindness was potentially avoidable. Maori children were overrepresented in CVI related blindness cases.


Low vision in children is an understudied area and most research has been done using adults. Most studies are descriptive and have small sample sizes. Reading is the only area that has been studied in depth, but few conclusions can be drawn because of the limitations of these studies. This study summarizes the findings of 22 studies on low-vision rehabilitation in children. Databases were searched based on categories of low-vision rehabilitation, age younger than 18 years, and population. Sample sizes were small, with the largest non-survey study having 56 participants. Most were case studies and had less than 20 subjects. Reading was the most studied outcome and large-print, magnifiers, and CCTVs were the most common interventions studied. Visual-motor skills, visual-attention skills, visual-memory skills, and pattern recognition were also the subject of some studies. The nature of the studies did not lead to definitive conclusions.

Perceiving 3D in the absence of measurable stereo-acuity

Some individuals with nil stereoacuity subjectively report that they are able to see 3-D effect with modern 3-D movies and televisions. In this prospective observational cases series, 3-D perception was evaluated in 7 adult subjects (mean age 53 years old) who had no measureable stereoacuity by standard clinical examination such as RanDot testing. The subjects were presented 3-D videos over a range of stereoscopic stimuli (range 2578 – 8593 arc seconds) as well as 2-D videos. Objective identification of the stereoscopic video images was poor in all but 2 subjects although all subjects subjectively rated the “popping out” of images highly. In addition to static stereoacuity, the paper provides interesting discussion of the array of binocular/monocular and static/dynamic visual cues that provide depth perception and how modern cinema capitalizes on these visual processes to provide a more realistic experience.

High concentrations of unconjugated bilirubin are neurotoxic and cause brain damage in newborn infants. Aim of this study was to use a quantitative measure of neural activity, the swept parameter visual evoked potential (sVEP) to determine the relationship between neonatal bilirubin levels and visual responsivity several months later. 16 full-term infants with high bilirubin levels (>10 mg/dL) and 18 age-matched infants with no visible neonatal jaundice, all enrolled at 14 to 22 weeks of age. Infants who had a history of neonatal jaundice showed lower response amplitudes (P < 0.05) and worse or immeasurable sVEP thresholds compared with control infants for all three measures (P < 0.05). Swept parameter visual evoked potential thresholds for Vernier offset were correlated with bilirubin level (P < 0.05), but spatial acuity and contrast sensitivity measures in the infants with neonatal jaundice were not (P > 0.05). Elevated neonatal bilirubin levels affect measures of visual function in infancy up to at least 14 to 22 weeks of postnatal age.

Can vergence training improve reading in dyslexics?

Purpose: To investigate whether computerized orthoptic vergence training improves reading ability for dyslexic children.
Methods/Results: Twelve dyslexic subjects, aged 13–14 years, were trained with RetCorr, a computerized vergence training program. Reading speed was assessed before and after treatment. The results were compared with an age-matched control group. The dyslexic subjects conducted on average 11.75 sessions (±2.53 SD) of orthoptic training over a 5-week period. On average, the number of words read per minute before training were 87.83 (±16.80 SD) and after training 95.58 words (±18.08 SD). The difference was statistically significant. In the control group, the change was from 85.00 (±19.68 SD) words to 89.37 words (±19.71 SD) over the same time period. This difference was not significant.
Conclusion: Vergence treatment might help dyslexics. A limitation of this study is the small number of subjects.

5. NEURO-OPHTHALMOLOGY

Handheld Optical Coherence Tomography During Sedation in Young Children With Optic Pathway Gliomas

Determining vision loss in young children with optic pathway gliomas can be difficult. The authors postulate that retinal nerve fiber layer (RNFL) thickness may
be a surrogate for visual acuity/visual field. OCT measures retinal nerve fiber layer thickness. Study objective includes determining if measurement of circumpapillary RNFL can predict which children had vision loss from optic pathway gliomas. Main outcome measures were area under the curve of the receiving operating characteristic (ROC), sensitivity, specificity, positive and negative predictive values of quadrant specific and total RNFL thickness. Children with a sporadic or neurofibromatosis-related optic pathway glioma (OPG) at a tertiary hospital who could cooperate for visual acuity testing, but required sedation for MRI, were included. Hand held OCT measurements during sedation were taken. Thirty three children (64 eyes) were included (median age 4.8 years) with OPG and a cohort of children, normally sighted without OPG, were used as controls (median age 8.7 years) In children with vision loss (visual acuity or visual field) all quadrants had reduction of RNFL compared with children with no vision loss (p<0.01). A longitudinal multicenter trial is needed to define the temporal relationship between RNFL loss and vision loss.

**Optic Nerve Sheath Fenestration for the Treatment of Papilledema Secondary to Cerebral Venous Thrombosis.**


Case report of a 16 year old presenting with acute onset headache, decreased vision, papilledema and MRV that demonstrated thrombosis of the left transverse and sigmoid sinuses and left internal jugular vein. She was initially treated with subcutaneous enosparain and, thereafter, with acetazolamide. Workup revealed positive Factor V Leiden and prothrombin G20210A mutations, elevated Factor XII and mildly lowered antithrombin III and protein S levels. She subsequently developed papilledema and 6th nerve palsy in association with elevation in ICP (50 cm H2O). Marked diminution in acuity and visual field loss was ultimately controlled with bilateral optic nerve sheath fenestration, as medical management proved inadequate. This reported emphasized the need for bilateral, rather than unilateral ONS fenestration in her case, and the caution exercised in performing this procedure on an anti-coagulated patient.

**Optic Nerve Sheath Decompression: A Surgical Technique with Minimal Operative Complications.**


This impressive retrospective documented outcomes and complications of optic nerve sheath fenestration on 578 eyes of 331 patients. Mean follow-up was 18.7 months. Although procedures were performed for a wide variety of indications, 88% were performed to remediate IIH, progressive NAION and complications from optic nerve head drusen. Acuity was stable or improved in 94.4% and continued to worsen in 5.6%. None suffered sight threatening complications such as traumatic optic neuropathy, CRAO, or retro-orbital hemorrhage. The only surgical complications were esodeviation in 15 patients, exodeviation in 6 patients, corneal dellen in 2 and pyogenic granuloma in 1. Diplopia was the most common post-operative complaint (6%) typical resolved with prism or strabismus.
surgery. The approach was medial and trans-conjunctival. Risk and benefits compared to other approaches were discussed. They note that ONS fenestration is no longer recommended for those with progressive NAION because of the high rate of spontaneous resolution and recovery of vision.


Observer to observer diagnosis and (Frissen) grading of papilledema, even among expert observers, is fair to poor. This paper discusses how OCT, enhanced by other forms of image analysis, could improve diagnosis and grading of papilledema. Information extracted from fundus photos (on sharpness of disc border, texture of RNFL and discontinuity of blood vessels) combined with information from OCT (RNFL thickness and volume) would be needed. The combination would permit development of a continuous scale grading disc edema. The author notes that inaccuracies in RNFL measurements in the presence of moderate to severe papilledema can be overcome with utilizing segmentation of total retinal thickness and 3D graphing of total disc volume. Another aspect of papilledema that needs to be including in this continuous scale is appreciation of the importance of deformation of Bruch’s membrane surrounding the neural canal due to a pressure differential between the retrobulbar optic nerve and the vitreous. The degree of angulation, and a change from positive to flat can indicate successful treatment of papilledema, although the presence of a positive angle at the outset foes not always imply the presence of papilledema. Shape characteristics noted on OCT can sometimes distinguish drusen from papilledema, along with results from CT, ultrasound and autofluorescence. Finally is vision loss secondary to optic atrophy versus maculopathy can be distinguished by OCT by identifying neurosensory detachment in the para-foveal area. Lastly, phase contrast OCT enables visualization of optic nerve capillaries without the need for contrast agents.


The goal of this study was to assess the utility and safety of rituximab in pediatric autoimmune and inflammatory disorders of the CNS.. The multicenter retrospective study enrolled a total of 144 children and adolescents (median age 8 years, range 0.7–17; 103 female) with NMDA receptor (NMDAR) encephalitis (n = 39), opsoclonus myoclonus ataxia syndrome (n = 32), neuromyelitis optica spectrum disorders (n = 20), neuropsychiatric systemic lupus erythematosus (n = 18), and other neuroinflammatory disorders (n = 35). Rituximab was given after a median duration of disease of 0.5 years (range 0.05–9.5 years). Infusion adverse events were recorded in 18/144 (12.5%), including grade 4 (anaphylaxis) in 3. Eleven patients (7.6%) had an infectious adverse event (AE), including 2 with grade 5 (death) and 2 with grade 4 (disabling) infectious AE (median follow-up of 1.65 years [range 0.1–8.5]). No patients developed progressive multifocal leukoencephalopathy. A definite, probable, or possible benefit was reported in
125 of 144 (87%) patients. A total of 17.4% of patients had a modified Rankin Scale (mRS) score of 0–2 at rituximab initiation, compared to 73.9% at outcome. The change in mRS 0–2 was greater in patients given rituximab early in their disease course compared to those treated later. While limited by the retrospective nature of this analysis, the authors proposed that the data support an off-label use of rituximab, although the significant risk of infectious complications suggests rituximab should be restricted to disorders with significant morbidity and mortality. This study provides Class IV evidence that in pediatric autoimmune and inflammatory CNS disorders, rituximab improves neurologic outcomes with a 7.6% risk of adverse infections. Given that rituximab is occasionally also used in pediatric ophthalmology disorders such as JIA-uveitis, this information should be useful to our profession.


The goal of this study was to evaluate clinical, genetic, and radiologic features of patients with muscle-eye-brain disease. The data of patients who were diagnosed with muscle-eye-brain disease from a cohort of patients with congenital muscular dystrophy in the Division of Pediatric Neurology of Dokuz Eylül University School of Medicine and Gaziantep Children's Hospital between 2005 and 2013 were analyzed retrospectively. From a cohort of 34 patients with congenital muscular dystrophy, 12 patients from 10 families were diagnosed with muscle-eye-brain disease. The mean age of the patients was 9 ± 5.5 years (2-19 years). All patients presented with muscular hypotonia at birth followed by varying degrees of spasticity and exaggerated deep tendon reflexes in later stages of life. Three patients were able to walk. The most common ophthalmologic and radiologic abnormalities were cataracts, retinal detachment, periventricular white matter abnormalities, ventriculomegaly, pontocerebellar hypoplasia, and multiple cerebellar cysts. All of the patients had mutations in the POMGNT1 gene. The most common mutation detected in 66% of patients was c.1814 G > A (p.R605H). Two novel mutations were identified. The authors suggest that muscle-eye-brain disease is a relatively common muscular dystrophy in Turkey. It should be suspected in patients with muscular hypotonia, increased creatine kinase, and structural eye and brain abnormalities. The c.1814 G > A mutation in exon 21 of the POMGNT1 gene is apparently a common mutation in the Turkish population. Individuals with this mutation show classical features of muscle-eye-brain disease, but others may exhibit a milder phenotype and retain the ability to walk independently. Congenital muscular dystrophy patients from Turkey carrying the clinical and radiologic features of muscle-eye-brain disease should be evaluated for mutations in POMGNT1 gene. In addition, this article points out various ophthalmic findings that we can look out for in our muscular dystrophy patients.

Miller Fisher syndrome is usually a monophasic disorder. Recurrent Miller Fisher syndrome is extremely rare, and all patients with recurrences have been adults. This paper describes two children with recurrent Miller Fisher syndrome. Episodes occurred at the age of 11.5 and 13 years in patient 1 and at the age of 8 and 13 years in patient 2. The article reviews the clinical patterns of the first and recurrent episodes of Miller Fisher syndrome and shows that they were somewhat overlapping. In both patients, steroids were effective in controlling clinical deterioration of Miller Fisher syndrome recurrences. The authors concluded that recurrent Miller Fisher syndrome is a rare disorder that may occur in children. These observations and a review of the literature suggest that there may be a small group of patients in whom steroids may be a therapeutic option when intravenous immunoglobulin fails to control clinical symptoms.


Both cervical and occipital pain has been reported in pediatric patients with migraine. There are no descriptions of anatomical changes on conventional brain magnetic resonance imaging that can explain the pathophysiology of headache with cervical and occipital pain in this age group. The aim of this paper was to evaluate the frequency of cervical and occipital pain in children and adolescents with migraine as opposed to other types of headache and to seek corresponding anatomic abnormalities on brain magnetic resonance imaging. The authors studied a cohort of 194 patients with headache attending the ambulatory headache clinic of a pediatric tertiary medical center. Patients were divided into two groups: migraine headache (n = 125) and other types of headache (n = 69). Occipital pain was reported by 16.4% of the patients and cervical pain by 4.1%; neither type of pain was characteristic of migraine headache in particular. Brain magnetic resonance imaging did not show any anatomic changes specific to migraine or other headache types, regardless of the presence of occipital or cervical pain. Therefore, the authors concluded that occipital and cervical pain are not characteristic symptoms of any headache group in the pediatric age group, and their presence or absence does not correspond to changes on conventional brain magnetic resonance imaging.


This study reports the prevalence of comorbid medical conditions and the longitudinal course of ocular tics in children from a pediatric neuro-ophthalmology practice. Medical records of consecutive children evaluated over an 18-year period were reviewed. Fifty-one of a potential 86 patients were eligible for inclusion (exclusions were for other neurologic conditions, other causes for tics and incomplete records). Eight patients declined to participate. Of the remaining
43 patients, almost 2/3 were male and the tic had been present on average for 9.6 months prior to initial presentation. Blinking (63%) and eye rolling (51%) were the most common ocular symptoms. 16% had nonocular tics and 9% had vocal tics. 32 patients were then followed prospectively with an average follow-up of 6.1 years. This group had a slightly higher rate of resolved ocular tics. 44% had persistent tics although they often lessened over time. 9% developed new ocular tics and 16% developed new vocal tics. One patient was diagnosed with Tourette’s during the follow-up period and three patients were diagnosed with ADHD. No patient was diagnosed with OCD.

**Differentiating Mild Papilledema and Buried Optic Nerve Head Drusen Using Spectral Domain Optical Coherence Tomography**


This is a comparative case series designed to evaluate clinical utility of spectral domain optical coherence tomography (SD-OCT) in differentiating mild papilledema from buried optic nerve head drusen (ONHD).

**Participants:** 16 eyes in 9 patients with ultrasound-proven buried ONHD, 12 eyes of 6 patients with less than or equal to Frisen grade 2 papilledema owing to idiopathic intracranial hypertension. Two normal fellow eyes of patients with buried ONHD were included.

**Results:** We found no difference in retinal nerve fiber layer thickness between buried optic nerve head drusen and papilledema in any of the 4 quadrants. The diagnostic accuracy among the readers was low and ranged from 50% to 64%.

**Conclusions:** We found the spectral domain OCT is not clinically reliable in differentiating buried optic nerve head drusen and mild papilledema.

**Headache and refractive errors in children.**


Children with headaches are often referred to the ophthalmologist by the primary care provider to exclude ocular causes for the headache. The purpose of this study was to investigate the association between uncorrected or miscorrected refractive errors in children and headache, and to determine whether correction of refractive errors contributes to headache resolution. Results of an ophthalmic examination, including refractive error, were recorded at initial visit for headache. If resolution of headache on subsequent visits was not documented, a telephone call was placed to their caregivers to inquire whether headache had resolved.

Of the 158 patients, 75.3% had normal or unchanged eye examinations, including refractions. Follow-up data were available for 110 patients. Among those, 32 received new or changed spectacle correction and 78 did not require a change in refraction. Headaches improved in 76.4% of all patients, whether with (71.9%) or without (78.2%) a change in refractive correction. The difference between these two groups was not statistically significant (P = .38).

The authors conclude that headaches in children usually do not appear to be caused by ophthalmic disease, including refractive error. The prognosis for improvement is favorable, regardless of whether refractive correction is required.
Interpretation of Lumbar Puncture Opening Pressure Measurements in Children

This review of the literature on pediatric idiopathic intracranial hypertension suggests that cerebrospinal fluid opening pressure ≤28 cm H₂O is likely normal for children. Sedation, particularly with ketamine, but even with other agents, typically increases opening pressure about 3-4 cm H₂O and this likely secondary to induced hypercapnia. Agitation increases opening pressure. Leg position (flexed or extended with patient in the lateral decubitus position) has minimal to no impact on opening pressure. Resolution of headache directly after sedated LP may be secondary to sedative analgesics and is not necessarily diagnostic

Protective environmental factors for neuromyelitis optica

This is a case-control study of pediatric patients with neuromyelitis optica (NMO) (n=36), multiple sclerosis (MS) or clinically isolated syndrome (n=491), and healthy subjects (n=224) examining the environmental risk factors associated with the development of NMO. Demographics of patients with NMO were similar to previous studies. Delivery via Caesarean section was more prevalent among those with NMO with an odds ratio of 1.98 in comparison to MS or clinically isolated syndromes, and 1.95 compared to healthy controls, but was not statistically significant [p=0.14; p=0.12]. Enrollment in daycare was protective against NMO (OR 0.33) in comparison to healthy controls [p<0.01]. Breastfeeding was also protective in comparison to healthy controls (OR 0.05, p=0.05). In those whose sera was collected for analysis, EBV, HSV-1, CMV, and HLA-DRB1*15 positivity were not associated with increased risk of NMO in comparison to healthy controls. The authors conclude that similar to previous findings in studies of MS, exposure to other young children may be protective against the development of NMO. They consider that this disease risk modification could be due to increased exposure to infectious agents. Further study of the role of environmental factors may help to define the underlying disease process.

Head impulse gain and saccade analysis in pontine-cerebellar stroke and vestibular neuritis

This is a prospective non-consecutive cohort study evaluating the angular vestibulo-ocular reflex (aVOR) gain and compensatory saccade properties elicited by the head impulse test (HIT) in pontine-cerebellar stroke (PCS) and vestibular neuritis (VN). The authors found bilaterally reduced aVOR gain, greater in AICA strokes than in PICA/SCA strokes. In VN, the authors found
unilaterally decreased aVOR gain. Cumulative amplitudes were larger in VN (8.5deg) compared to PICA/SCA strokes (2.1deg) and AICA strokes (4.2deg). Saccade asymmetry >61% was found in 97% of PCS and none of VN. Gain asymmetry >40% was found in 94% of PCS and 10% of VN. Overall, these results demonstrate that there are differences in aVOR gain and saccade amplitudes between PCS and VN. Comparison of left-right responses when performing the HIT can help localize and characterize the lesion.

**Functional-structural correlations in the afferent visual pathway in pediatric demyelination**

This is a cross-sectional evaluation of 37 children (ages 8-18) diagnosed with a demyelinating disorder, performed at least >6mos after diagnosis, in comparison to healthy controls. Evaluation included high-contrast visual acuity (HCVA), low-contrast visual acuity (LCVA) with Pelli-Robson chart, visual fields, color vision, and OCT of the optic disc and macula. The ganglion cell layer (GCL) was measured using automated software, and thickness was reported. The authors found that the retinal nerve fiber layer (RNFL) was 26μ (25.6%) lower in patients with demyelinating disease (76.2μ) in comparison to controls (102.4μ)[p<0.0001]. Mean GCL thickness was 20% thinner in patients with demyelinating disease [p<0.0001]. 100% of children with a RNFL thickness <87μ (15% less than controls) had abnormal scores on the Pelli-Robson chart. 100% of children with a GCL thickness of <76μ (10% less than controls) had abnormal scores on the Pelli-Robson chart. There was a trend for the RNFL to be thinner among patients with demyelinating disease who suffered optic neuritis, versus those who had not [p=0.08]. The GCL was not affected by the presence or absence of optic neuritis among those with demyelinating disease. RNFL thickness declined in a stepwise manner dependent upon number of optic neuritis episodes (9μ per episode). In contrast to previous studies in adults, the history and number of episodes of optic neuritis was not associated with decrements in GCL thickness. Further study of the utility of OCT as an objective measure of neuronal damage in the evaluation of pediatric demyelinating disease is needed.

**Pediatric optic neuritis: does a prolonged course of steroids reduce relapses? A preliminary study.**

Optic neuritis is an important pediatric disorder causing visual impairment. Because of the absence of pediatric-specific studies, data extrapolated from the adult-based optic neuritis treatment trial are used to guide management of pediatric patients. Recent literature promotes a prolonged course of oral steroids to prevent relapses. However, there are no published data to support this view. The authors retrospectively reviewed 26 patients who were treated in their hospital and received a longer course of steroids, relative to those treated several years ago. The patients (age 4.5-19 years) received either a short course (2 weeks) or a prolonged course (more than 2 weeks) of steroids. Some patients were not treated. Mean follow-up was 70 weeks (3 weeks-10 years).
Comparisons were made among the groups receiving 2 weeks of steroid treatment (16 of 26 patients) and greater than 2 weeks of steroid treatment (seven of 26 patients) to evaluate relapse rate, eventual visual acuity, and reported side effects. There were no significant differences in the relapse rates, reported side effects, and final visual acuity in the two treatment groups. Therefore the authors concluded that in their cohort, a prolonged course of steroids was not associated with reduced relapse rate, increased side effects, or improved visual outcome. This cohort was small, but the results do not identify any reason to deviate from the common approach of optic neuritis treatment, which is 2 weeks of steroids.

"Alice in wonderland" syndrome: presenting and follow-up characteristics.

These authors investigated the distribution of symptoms and etiologies of patients with "Alice in Wonderland" syndrome (visual perception of change in one's body size) and "Alice in Wonderland"-like syndrome (extrapersonal illusions) at presentation and to determine their prognosis. They retrospectively reviewed the charts of children diagnosed with "Alice in Wonderland" syndrome by a pediatric neuro-ophthalmologist between July 1993 and July 2013. Patients seen before 2012, or their parents, were contacted for follow-up information. A total of 48 patients (average age 8.1 years) diagnosed with "Alice in Wonderland" syndrome or "Alice in Wonderland"-like syndrome were identified. Common visual symptoms were micropsia (69%), teleopsia (50%), macropsia (25%), metamorphopsia (15%), and pelopsia (10%). Magnetic resonance imaging and electroencephalography were unrevealing in 21 of 21 and 23 of 23 cases, respectively. The etiology was infection in 33% of patients and migraine and head trauma in 6% each. No associated conditions were found in 52%. Of the 15 patients with follow-up, 20% had a few more events of "Alice in Wonderland" syndrome or "Alice in Wonderland"-like syndrome, which eventually stopped after the initial diagnosis; 40% had no more events, and 40% were still having "Alice in Wonderland" syndrome or "Alice in Wonderland"-like syndrome symptoms at the time of the interview, while four patients (27%) developed migraines and one patient (7%) seizures since the diagnosis. The authors concluded that "Alice in Wonderland" syndrome and "Alice in Wonderland"-like syndrome typically affect young children, and the most common visual complaints are micropsia and teleopsia. The most common associated condition is infection, but half of these individuals have no obvious trigger. Magnetic resonance imaging and electroencephalography are not helpful. The symptoms of "Alice in Wonderland" syndrome and "Alice in Wonderland"-like syndrome usually resolve, but in more than one third of the cases, they continue. One quarter of patients without a history of migraine may subsequently develop migraine.
The International Classification of Headache Disorders-III beta includes a number of episodic syndromes associated with migraine. Those who treat pediatric headaches are aware of a number of other phenomena (such as the Alice in Wonderland syndrome) which are thought to occur as precursors of migraine. There is no available data on the course of these phenomena over the decades following childhood headache diagnosis. Twenty-eight patients who were observed by one of the authors in 1983 were contacted by telephone in 1993, 2003, and 2013. Details were gathered regarding the presence and characteristics of ongoing headaches and about the presence of sleepwalking, motion sickness, and distortions of either time or space perceptions. Ongoing headaches were reported by 71%. Sleepwalking was only present in one patient in 2013. More than a third still complained of motion sickness, and more than one quarter still experienced distortions of time. Distortions of space were still reported by nearly 20%. Reporting any of these phenomena was not consistent over time, with some patients reporting distortions for the first time in adulthood. There was no clear correlation with migraine, and patients with tension-type headaches also reported the phenomena. The authors concluded that motion sickness and distortions of both space and time persist into the fifth decade for many patients initially observed with headaches in childhood. The correlation with migraine is less clear than previously thought.

Is there a role for optokinetic nystagmus testing in contemporary orthoptic practice? Old tricks and new perspectives
Eleni Papanagnu, and Michael C. Brodsky, Am Orthopt J Sept 2014;64:1-10

This review article highlights clinical indications for assessing optokinetic nystagmus (OKN). Some of the more useful indications for OKN testing described in this paper were:

1. To aid in the diagnosis of myasthenia gravis - Orient the OKN drum diagonally and elicit diagonal OKN, then position the drum axis vertically and elicit horizontal OKN to for a period of time sufficient to fatigue horizontal rectus muscles. Lastly, orient the drum again diagonally and attempt to elicit diagonal OKN again. In patients with myasthenia the last step will yield only vertical OKN instead of diagonal OKN due to fatigue of the horizontal rectus muscles.
2. To assess vision in infants with congenital nystagmus - orient the OKN drum axis horizontally and assess vertical OKN. Absent vertical nystagmus indicates poor visual prognosis.
3. To aid in the diagnosis of dorsal midbrain syndrome – Orient OKN drum axis horizontally and elicit convergence-retraction nystagmus.
Cyclotropia to differentiate longstanding and acute fourth cranial nerve palsy

The author of this retrospective case-control study compares the amount of hypertropia and torsion in acute fourth nerve palsy patients with presumed congenital fourth nerve palsy. There was a strong correlation between degree of cyclotropia and amount of hypertropia in subjects with acute cases fourth nerve palsy but no such correlation among the congenital cases. The ratio of cyclotropia to hypertropia was four times greater for acute palsy than for congenital palsy. This may be a useful measure to help differentiate between the two clinical diagnoses.

Etiology and clinical profile of childhood optic nerve atrophy at a tertiary eye care center in South India

There was no data regarding the etiology of optic nerve atrophy in children of India. This was a retrospective case series involving a total of 324 children. Among these 160 (49%) presented with defective vision, 71 (22%) with strabismus, 18 (6%) with only nystagmus. Rest had a combination of two or three of the above symptoms. Sixty-five patients (20%) had a unilateral affection. Hypoxic ischemic encephalopathy seen in 133 patients (41%) was the most frequent cause of childhood optic atrophy, followed by idiopathic in 98 (30%), hydrocephalus in 24 (7%), compressive etiology in 18 (5%), infective in 19 (6%), congenital in 6 (2%), inflammatory in 5 (2%) patients, respectively. Hypoxic ischemic encephalopathy appears to be the most common cause of optic atrophy in children in this series. Surprisingly this is similar to other western studies. One of the issue here is this is not a population based study.


This was a 5-year retrospective review of subjects <18 years of age. Patients were divided into ultrasound first (UF) versus ultrasound after other diagnostic studies (UA). 20 patients were in the UF group and 26 were in the UA group. Over 70% of patients were female. The UA groups costs average 1173$ while the UF costs averaged 305$. The major problem I have with this study is its retrospective nature. To truly analyze cost differences to set up a preferred protocol, patients would need to be enrolled randomly into two diagnostic protocols. The problem with the retrospective nature of this study is that the more worrisome patients may have ended up in the UA group so the two groups would not truly be comparable.

This study assessed the ability of SD-OCT measured peripapillary retinal nerve fiber layer (RNFL) thickness to detect optic neuropathy compared to fundus examination in patients with craniosynostosis. They compared indication of optic neuropathy by RNFL thickness and fundus exam with evidence of altered visual function (acuity and field), and investigated the correlation of fundus examination abnormalities with historical evidence of elevated ICP. There was a moderate correlation between logMAR acuity and optic neuropathy on fundus exam (very low sensitivity but excellent specificity). SD-OCT was more sensitive at detecting optic neuropathy (88%) versus optic atrophy (60%). SD-OCT was a significant predictor of papilledema. Abnormal visual fields along with optic neuropathy on fundus examination guaranteed predicted SD-OCT abnormalities. Peripapillary RNFL thickness measured by SD-OCT confirmed fundus examination findings of optic neuropathy with a sensitivity of 77% and specificity of 83%. RNFL thickness measurements were more sensitive at detecting optic neuropathy than visual field testing. Axial length was not measured. Peripapillary total RNFL thickness or volume were not obtained. Elevated ICP was based on historical data.

Visual Outcomes in Pediatric Optic Neuritis

This retrospective study attempted to evaluate visual outcomes in children presenting to a tertiary care center with a first episode optic neuritis. These patients had at least 3 months of followup over a 10 year period. Out of 59 patients, 46 had 3 months of followup and 36 had 1 year of followup. Mean age was 12.6 years and 72% were female. 41% had bilateral disease. 52% had or developed an underlying disease including MS, encephalomyelitis, and neuromyelitis optica. 91% received treatment with 85% getting steroids. At one year, 81% were 20/20 vision and 89% were at least 20/40. Poor vision at 1 year was associated with vision of less than 20/20 at 3 months. No other factors predicted outcome.

Intra- and Inter-visit Reproducibility of Ganglion Cell-Inner Plexiform Layer Measurements Using Handheld Optical Coherence Tomography in Children with Optic Pathway Gliomas.

This prospective longitudinal cohort study attempted to analyze the reproducibility of the handheld OCT in sedated children with gliomas and or NF1. 42 patients with 45 eyes were examined for intra-visits. The superior quadrant differed between subjects by 4.4% in patients with vision loss and 2.1% in patients without vision loss. 25 patients qualified for the inter-visit cohort, showing
a range from 1.6% to 5.2%. The handheld OCT was considered reproducible to measure ganglion cell-inner plexiform layer thickness.

**The Role of Magnetic Resonance Imaging in Diagnosing Optic Nerve Hypoplasia.**

This was a case control study of 26 patients with clinically confirmed optic nerve hypoplasia. 31 normal subjects were also measured. Optic nerve diameter increased by 0.05 mm per year of age. A lower limit of 2.24 mm +0.052 x (age in years)mm excluded all cases of hypoplasia except one. This study provides a formula for clinicians to objectively assess for optic nerve hypoplasia.

**Reproducibility of Retinal Nerve Fiber Layer Thickness Measures Using Eye Tracking in Children With Nonglaucomatous Optic Neuropathy.**

This prospective longitutdinal study, examined the reproducibility of assessing the retinal nerve fiber layer using SD OCT in children with optic neuropathy. 42 subjects with 62 eyes were included. Intervisit reproducibility remained good for those with normal and abnormal vision. SD OCT with eye tracking is highly reproducible on RNFL thickness.

6. **NYSTAGMUS**

**INFANTILE NYSTAGMUS AND VISUAL DEPRIVATION: FOVEAL INSTABILITY AND REFRACTIVE DEVELOPMENT IN A LOW VISION REGISTER SERIES**

A retrospective analysis of data from the Danish Register for Blind and Weaksighted Children with prime diagnosis of infantile nystagmus identified 90 records of children, now aged 10-17 years old. Of these, 48 children with nystagmus had a single diagnosis, whereas 42 had clinical colabels (Down syndrome [13], dysmaturity [9], and mental retardation, encephalopathy [20]). Results: Median binocular visual acuity was 0.3 in the full series, and median refraction was emmetropia in all subgroups. Compared with Danish control data, myopia was over-represented, and generally of juvenile onset. The Down syndrome subgroup was separated from the remainder by an even higher myopia prevalence. Astigmatism above 1 D cylinder value was recorded in 52% of all cases. Conclusions: The prevalence of myopia and astigmatism was higher among children with nystagmus than in controls.
The Effect of Colored Overlays on Reading Performance in Infantile Nystagmus
N Barot, R J. McLean, I Gottlob, F A. Proudlock,
Ophthalmology March 2014; 121:804-805

Infantile nystagmus is an involuntary oscillation of the eyes with onset within 6 months from birth. This can result in vision loss owing to constant retinal motion and lead to significant psychosocial problems. It has been suggested that colored filters might influence the magnocellular pathway contributing to reading by reducing inhibitory S-cone inputs and/or changing the relative balance of the L-cone and M-cone inputs. (S-cone inputs are blue in color; L-cone inputs are red in color and M-cone inputs are green in color.)

Twenty-five participants with albinism and 20 age-matched controls were recruited from neuro-ophthalmology clinics in the Leicester royal Infirmary, UK. All participants with idiopathic nystagmus reported onset of nystagmus within the first 6 months of life with no history of persistent oscillopsia.

Methods: Reading performance was assessed using a Radner reading chart consisting of a series of short sentences read in descending order of font size. Subjective improvements made by the colored overlays were assessed by filling out a questionnaire.

Results: The most popular overlay color choices were yellow and lime green for all participants. The colored overlays made no significant difference to any objective reading parameters measured using the Radner reading chart for the albinism group, the idiopathic infantile nystagmus (IN) group (referred to as the idiopates) or the age-matched control group. Subjective improvements made by the colored overlays were assessed by asking whether they subjectively perceived that the overlay helped and if so, how. A sample size was based on previous reported test/retest values for the Radner test. Idiopathic infantile nystagmus (IN) patients favored yellow overlays. Upon questioning, 60% of the participants with albinism and 50% of the patients with idiopathic infantile nystagmus reported that overlays “helped them read” compared with only 30% of the control participants.

Conclusions: Although the colored overlays did not significantly affect the number of mistakes made by any group, participants with albinism made significantly more errors than participants with idiopathic infantile nystagmus with the use of the colored overlay. There was no objective improvement in reading performance in infantile nystagmus when using colored overlays either for participants with albinism with idiopathic infantile nystagmus.

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A Randomized Controlled Trial Comparing Soft Contact Lens and Rigid Gas-Permeable Lens Wearing in Infantile Nystagmus
Pavitra Jayaramachandran, Frank A. Proudlock, Nita Odedra, Irene Gottlob,
Ophthalmology September 2014; 121(9):1827-1836

This article comes from the Ophthalmology Group, University of Leicester, Faculty of Medicine & Biological Sciences, Leicester Royal Infirmary, Leicester, United Kingdom. This is a randomized, controlled cross-over trial with an intention-to-treat design. This study is designed to perform the first randomized
controlled trial comparing soft contact lens with rigid gas-permeable lens (RGPL) in infantile nystagmus using spectacle wear as a baseline. Twenty-four patients (12 idiopathic, 12 with albinism) were randomized into 1 of 2 treatment arms: A) spectacles with soft contact lens, rigid gas-permeable lens and spectacle wear or B) spectacles, rigid gas-permeable lens, soft contact lens and spectacle wear. The main outcome measure was mean intensity of nystagmus at the null region viewed at 1.2 meters. Secondary outcome measures included the same measurement at 0.4 meters viewing and across the horizontal meridian. There was no significant difference between soft contact lenses and rigid gas-permeable lens wearing for any nystagmus characteristics when compared with spectacle wearing.

Conclusions: Nystagmus was not significantly different between soft contact lens wear and rigid-gas permeable lens wear in infantile nystagmus. Contact lens wearing does not significantly reduce the nystagmus when compared with baseline spectacle wearing. The wearing of soft contact lenses leads to small but statistically significant deterioration in visual function compared with both rigid gas-permeable lenses and spectacle correction at baseline.

Electroretinographic Characteristics In Children With Infantile Nystagmus Syndrome And Early-Onset Retinal Dystrophies
Alma Kurent, Branka Stirn-Kranjc, Jelka Brecełj

This study attempted to differentiate early-onset retinal dystrophies on the basis of electroretinogram (ERG) characteristics in children with infantile nystagmus syndrome (INS). Thirty-seven children with INS and early-onset retinal dystrophies were included, with diagnosis according to clinical and ERG findings. There were: 9 children with Leber congenital amaurosis, 6 children with congenital stationary night blindness, 8 children with achromatopsia, 1 child had blue-cone monochromatism, 6 children with cone–rod dystrophy without systemic disorder, and 7 children with systemic disorder. Clinical and electrophysiologic findings were in agreement across all of the children. In children with INS, some early-onset retinal dystrophies can be differentiated through ERGs, also with skin electrodes.

7. PREMATURITY.


In the multicenter ELGAN study sample of 1057 infants born before the twenty-eighth week of gestation who had a developmental assessment at 2 years corrected age, the authors identified 73 who were unable to follow an object across the midline. These infants were compared to the 984 infants who could follow an object across the midline. In this sample of very preterm newborns,
those who had impaired visual fixation were much more likely than those without impaired visual fixation to have been born after the shortest of gestations (odds ratio, 3.2; 99% confidence interval, 1.4-7.5) and exposed to maternal aspirin (odds ratio, 5.2; 99% confidence interval, 2.2-12). They were also more likely than their peers to have had prethreshold retinopathy of prematurity (odds ratio, 4.1; 99% confidence interval, 1.8-9.0). At age 2 years, the children with impaired fixation were more likely than others to be unable to walk (even with assistance) (odds ratio, 7.5; 99% confidence interval, 2.2-26) and have a Mental Development Index more than three standard deviations below the mean of a normative sample (odds ratio, 3.6; 99% confidence interval, 1.4-8.2). The authors concluded that risk factors for brain and retinal damages, such as very low gestational age, appear to be risk factors for impaired visual fixation. This inference was further supported by the co-occurrence at age 2 years of impaired visual fixation, inability to walk, and a very low Mental Development Index.

In this study, authors evaluated measurements of CCT and IOP in 45 premature and 45 full-term newborns. IOP was determined with topical anesthesia using a Tono-Pen AVIA, applanation tonometer and a wire lid retractor in premature newborns undergoing screening for retinopathy. Full-term newborns were used as a control group. The mean IOP was 16.2 ± 2.7 mmHg (ranging 10-22 mmHg) in premature and 16.6 ± 2.3 mmHg (ranging 10-22 mmHg) in full-term newborns. The mean CCT was found 600 ± 50 μm (ranging 515- 790 μm) in the premature group and 586 ± 48 μm (ranging 475-730 μm) in the full-term group. Mean CCT was greater in premature newborns than in full-term newborns, but the difference between groups was not statistically significant (P = 0.7). Mean IOP measurement in two groups was found very similar and the difference also was not statistically significant (P = 0.27). There was no correlation between IOP and CCT, gestational age, gestational weight, age at measurement, weight at measurement neither right nor left eye in both groups in multiple regression analysis. Authors found that premature infants have slightly thicker corneas but no high IOP measurements than full-term newborns. It could be concluded that in premature at the mean gestational age of 36 weeks CCT is not different from that of full-term newborns.

The authors prospectively collected data on 6075 deaths among 22,248 live births with gestational ages of 22 0/7 to 28 6/7 weeks. They compared overall and cause-specific mortality across three periods from 2000 through 2011. In this cohort, the number of deaths per 1000 live births was 275 (95% confidence interval [CI], 264 to 285) from 2000 through 2003 and 285 (95% CI, 275 to 295) from 2004 through 2007; the number decreased to 258 (95% CI, 248 to 268) in the 2008-2011 period (P=0.003 for the comparison across three periods).
Overall, 40.4% of deaths occurred within 12 hours after birth, and 17.3% occurred after 28 days. Deaths related to pulmonary causes, immaturity, infection, and central nervous system injury decreased, while necrotizing enterocolitis-related deaths increased.

Ophthalmologists typically become involved in the care of these babies once they require ROP exams. It is helpful to know that the overall mortality rate for <29 weekers is approximately 25%. However, most of the mortality takes place in the first 12 hours after birth, and by the time the baby reaches age 28 days, the mortality rate decreases to 17% of 25.8%, or 4.4%.


This article comes from the Department of Ophthalmology, Duke University Eye Center. This is a prospective, cross-sectional, longitudinal study designed to evaluate the effects of prematurity on early optic nerve development and the usefulness of optic nerve parameters as indicators of the central nervous system pathology.

Forty-four preterm infants undergoing retinopathy of prematurity screenings and 52 term infants were studied.

Conclusions: This is the first analysis of optic nerve parameters in premature infants using spectral-domain OCT. It demonstrated that by age of term birth, vertical cup diameter and vertical cup-to-disc ratio are larger in preterm infants who were screened for ROP than in term infants. In this prospective pilot study, optic nerve parameters in these preterm infants associate weakly with CNS pathology and future cognitive development.

**Correlation Of Intraocular Pressure With Central Corneal Thickness In Premature And Full-Term Newborns**

Eyyup Karahan, Mehmet Ozgur Zengin, Ibrahim Tuncer, Neslihan Zengin


This study evaluated the relation of central corneal thickness and intraocular pressure in preterm and full-term newborns. Mean IOP was 17.5 (± 2.1 mm) Hg in premature newborns and 16.3 (± 1.9) mm Hg in full-term newborns. Mean CCT was 576.5 (± 16.8) µm in premature newborns and 562.7 (± 18.5) µm in full-term newborns. The results showed that the CCT does not affect IOP significantly in preterm infants.
8. ROP

The effect of erythropoietin on the severity of retinopathy of prematurity

Y Kandasamy, P Kumar and L Hartley  
*Eye* (2014) 28, 814–818

In this retrospective study conducted in a single intensive care nursery in Australia, over 10 years, 688 infants were screened for ROP. When controlling for other risk factors for the development of ROP, the authors found that the use of erythropoietin increased the severity of ROP compared to those infants who did not receive the treatment. The authors comment that there is variable evidence regarding the affect of this medication on the natural history of ROP, and state that the benefits of its use must be weighed against the possible increase risk of more severe ROP.

Refractive errors after the use of bevacizumab for the treatment of retinopathy of prematurity: 2-year outcomes

Y-H Chen et al  
*Eye* (2014) 28, 1080–1087

In this lead article in *Eye* from August, the authors investigate the incidence of myopia at age 2 in children with ROP treated with intravitreal bevacizumab with or without laser vs laser alone. They conclude that those treated with intravitreal injection alone had a much lower incidence of myopia vs those treated with injection plus laser (10 vs 47%). However, there are major study design issues to be considered including the fact that the study was not prospective, or controlled or randomized and none of the patients treated with laser alone returned for followup. Finally, the authors stated that axial length was determined by use of IOLmaster in these 2 year old patients, but technique was not discussed.

Fluorescein angiographic observations of peripheral retinal vessel growth in infants after intravitreal injection of bevacizumab as sole therapy for zone I and posterior zone II retinopathy of prematurity

SG Tahija, R Hersetyati, GC Lam, S Kusaka, PG McMenamin  

This study investigates the vascularization of the peripheral retina using fluorescein angiography in infants who had been treated with intravitreal bevacizumab as sole therapy for zone I and posterior zone II retinopathy of prematurity (ROP). The study is a retrospective evaluation of 20 eyes in 10 neonates who received treatment between August 2007 and November 2012. All included eyes had resolution of posterior disease after a single injection of bevacizumab and were followed for a minimum of 24 weeks. The authors used a distance of 2 disc diameters from the ora serrata to the vascular termini as the upper limit of allowable avascular retina in children. Their review revealed that 11 of 20 eyes had not achieved normal retinal vascularization. 9 of these eyes demonstrated fluorescein leakage at the vascular-avascular border. The authors conclude that although bevacizumab appears effective in bringing resolution of zone I and posterior zone II ROP and allowing growth of the peripheral retinal vessels, complete normal peripheral retinal vascularization was not achieved in half of the patients. They believe ophthalmologists should remain cautious as these infants may remain at risk due to avascular peripheral retinas even many years after treatment.

This is a retrospective study reviewing records of infants born between 2001 and 2010 in a level IIIIC NICU. 780 neonates were examined during this time period. 3332 met study gestational age and birth weight criteria for the study (greater than 30 weeks but less than 1500 gm. 211 babies (99.5%) were observed and vascularized to zone 3. Of these 211, 202 showed no ROP at all. 9 showed mild ROP of stage 2 or less. Only one child required laser treatment, he was 905 gm at birth. This study implies that birth weight may not be as strong an indicator of ROP when the baby is 30 weeks gestational age or more.


The purpose of this study was to evaluate whether digital retinal images obtained using an indirect ophthalmoscopy imaging system could be accurately graded by masked experts for clinically significant ROP (CSROP). This was defined as pre-plus or plus disease. 253 infants were included (average gestational age 27 weeks, average postmenstrual age at examination 35 weeks). 7% had plus disease, 13% had pre-plus disease and 80% had a normal posterior pole. There were two graders of the images. Using the reference standard of plus disease identified by indirect ophthalmoscopy, sensitivity grading CSROP of the two graders averaged 97% while specificity averaged 87.5%. One clinical diagnosis of plus disease was missed, the rest were all classified as pre-plus or plus based on the images. Using pre-plus or plus as the reference standard, sensitivity dropped to 77% but specificity increased to 96%. Intra-grader reliability averaged 92.5% and inter-grader reliability was 95%. The presence of pre-plus or worse disease may be a reasonable surrogate for significant ROP in the periphery. This would allow a screening protocol that only required posterior pole images, which could then be evaluated to determine whether or not a full examination was needed.

Predicting the need for laser treatment in retinopathy of prematurity using computer-assisted quantitative vascular analysis. Wu KY, Wallace DK and Freedman SF. J AAPOS 2014;18:114-119

ROPtool is a computer program that evaluates the presence of plus disease, based on retinal vessel tortuosity and dilation. The authors attempted to determine if any parameters helped predict the need for laser treatment for ROP prior to the diagnosis of plus disease. Video recordings were performed over a seven-year period. 442 ROP examinations from one eye of 84 infants were included. The laser treated group (EL) had 132 exams in 28 infants and the no treatment group (NL) had 310/56 respectively. Approximately 30% of images
were of insufficient quality to analyze. Maximum tortuosity indices from any one vessel across all examinations, and median highest mean tortuosity index (TI) were significantly greater in the EL group. Other parameters (dilation, sum of adjusted indices, and changes per week) were not statistically significant. However there was a trend towards significance between the two groups in the largest increase per week in maximum tortuosity index, the largest increase per week in mean TI, and the maximum SAI from any one vessel across all examinations from one examination to the next. To clarify, the highest max and highest mean TIs were able to predict the need for laser treatment at an earlier postmenstrual age (PMA) than pre-plus disease in the EL infants. Highest predictive value is when the infant is around 38 weeks. This technique is better when the ROP progresses slowly. Younger infants (ex. 33 weeks PMA) may have rapid plus disease development even one week after having normal tortuosity values. This could be an early alert tool but it is somewhat limited by the large number of poor images, and its lower efficaciousness in younger, more rapidly progressive cases.


This study reports retinal vascular changes after ROP treatment with anti-VEGF intravitreal bevacizumab. Patients were recruited from 2008 to 2012. There were 47 eyes of 26 patients. One month after treatment, there was a marked decrease in vascular tortuosity in 96%. Angiographic evidence of a foveal avascular zone was observed in 53%, beginning one month after injection. At one month, all eyes had marked regression of neovascularization and flattening of the demarcation line, with subsequent growth of vessels to the capillary-free zones. However 70% developed vascular loops at the site of the regressed demarcation lines. 30% developed persistent areas of capillary closure posterior to the demarcation line, which eventually disappeared. 83% developed perivascular leakage, which gradually decreased. Some patients did not develop retinal vessels in the far periphery. This study had no control group, but does offer insight into the remodeling and retinal changes that occur after injection of bevacizumab.


The authors investigated the risk factors specific for type 1 ROP in zone I by comparing systemic parameters between infants with type 1 ROP in zone I to zone II age-matched controls. Rate of progression from the detection of any ROP to the detection of type I ROP was also compared. Medical records of 566 consecutive preterm infants with gestational age <=30 weeks were reviewed. The zone I ROP group showed type 1 ROP at significantly earlier postnatal age and postmenstrual age, as well as a shorter interval between initial ROP detection and type 1 ROP. Initial ROP detection did not differ between the two groups. Duration of mechanical ventilation and the proportion of infants treated
with mechanical ventilation > 30 days were significantly different between the two groups. Mechanical ventilation > 30 days caused a 4-fold increase in type I ROP. The study was limited by its retrospective nature, and inconsistent management protocols during the study period.


This study evaluates the relationship between ROP and brain disorders. Between 2002 and 2004, infants who were born before 28 weeks at 14 participating institutions were enrolled. Children with severe ROP were more likely to have been born at very low gestational age (23-24 weeks) and growth restricted. They were also more likely to have ventriculomegaly and a hypoechoic lesion on brain ultrasound. Severe ROP was associated with a Bayley Scale of Infant Development Index >3 SD below mean at age 2 years, a diagnosis of quadriparetic or diparetic cerebral palsy, head circumference >2 SD deviations below expected mean, and a low mental development index (MDI). Retinal ablative surgery did not alter Bayley Scales of Mental and Psychomotor Development. The authors postulate that ROP and structural/functional brain damage share risk factors.


The purpose of this study was to evaluate the risk of ROP and related outcomes in a cohort of low (<=25 weeks) gestational age infants. During a 21-month period, 1206 infants were admitted to the NICU, of which 78 were <26 weeks GA. Twenty died. 34% had PDA, 17% had severe RDS, 12% had bowel perforation, 8% had necrotizing enterocolitis and 29% had other conditions. Laser treated and untreated groups both had high rates of complications during their NICU course. Worst ROP examination occurred at a median PDA of 36.1 weeks. Twenty infants required laser treatment. Aggressive posterior ROP was associated with an earlier need for laser treatment. Infants who presented with any of the four diagnosis mentioned earlier had slightly earlier onset of ROP. Lower gestational age was associated with an earlier need for laser. Advancing gestational age lowered risk of plus disease. Current screening guidelines are felt to be appropriate for this subset of infants. Earlier progression to ROP was paradoxically related to higher birth weight. Sample size was small, and a retrospective study design was used.


Exudative retinal detachments have been reported after conventional laser therapy for retinopathy of prematurity. This case series reports two neonates
treated with laser for retinopathy who subsequently developed exudative retinal detachments that responded well to intravitreal bevacizumab. One of the babies was also treated with intravenous dexamethasone. The authors hypothesize that the instability of the inner blood retinal barrier seen in stage 3+ ROP, combined with further inflammatory insult secondary to laser therapy, may lead to a vasoactive response that results in subretinal exudate accumulation and detachment. They also hope that if future studies demonstrate an acceptable safety profile for intravitreal bevacizumab use in ROP, that its use will minimize the need for laser and its potential sequelae.

**Impact of the day-30 screening strategy on the disease presentation and outcome of retinopathy of prematurity. The Indian twin cities retinopathy of prematurity report number 3.**

A retrospective case-control study from a prospectively collected ROP data-base was analyzed. Cases (group 1a) included ROP babies that were screened directly in neonatal intensive care units, and controls (group 1b) were babies referred directly to the institute from other neonatal centers during the same period. Historical controls (group 2) were ROP cases seen in the years preceding establishment of this ROP program and database. Primary outcome measure was the risk of eyes presenting with stage 4 or worse ROP, and main secondary outcome measure was the final anatomic outcome. Of the 643 cases screened, 322 eyes of 161 babies had ROP. The median age of 7.19 months at presentation for the 46 patients (92 eyes) in group 2 was higher than the median age of 1.29 months for the 115 patients (230 eyes) in group 1. Within the group 1, group 1a had lower median age at presentation than group 1b (0.91 months versus 2.30 months). The relative risk of an eye presenting in the stage 4 and 5 in group 2 was 4.7 times higher (95% confidence interval 3.07 - 7.32) than in group 1. Eyes that could be given treatment in group 2 were significantly less (P < 0.0005) than in group 1. The relative risk of poor outcome in group 2 was 3.83 times higher (95% confidence interval 2.75 - 5.34) than in group 1. Group 1a eyes had the best outcomes. Early screening before one month of age in neonatal centers detects the disease early where prompt treatment can lead to favorable outcomes. The study provides early results of a model strategy for ROP screening.

**Three-Dimensional Assessment of Vascular and Perivascular Characteristics in Subjects with Retinopathy of Prematurity**

This is a cross-sectional study of 57 premature neonates. Ten of the neonates had plus disease in at least one eye and 47 patients did not have plus disease. Purpose: To evaluate vascular features detected with spectral domain optical coherence tomography (SD-OCT) in subjects undergoing retinopathy of prematurity screening.
Main Outcome Measures: Prevalence of spectral domain OCT vascular abnormalities, the vascular abnormality score (VASO) and intergrader agreement
and the presence of elevation on surface maps. (The best demonstration of all 3 of these concepts is on the cover of *Ophthalmology*, volume 121, number 6, June 2014.)

Conclusions: We present a novel three-dimensional analysis of vascular and perivascular abnormalities identified in spectral domain OCT images of eyes with retinopathy of prematurity. Spectral domain OCT characteristics that are more common in eyes with plus disease provide the first “in vivo demonstration of the effects of vascular dilation and tortuosity on perivascular tissue.” The vascular abnormalities for “VASO and surface maps also delineate the severity of vascular pathology in plus disease.” Further studies evaluating these findings in eyes with pre-plus versus normal posterior pole vessels may determine the usefulness of spectral domain OCT in the early detection of vascular abnormalities in ROP.

Reviewers’ Comment: This article is well worth reading. The photographs and the spectral domain OCT scans are very illustrative.

**Intravitreal Bevacizumab versus Laser Treatment in Type 1 Retinopathy of Prematurity: Report on Fluorescein Angiographic Findings.**

Lepore D, Quinn GE, Molle F, Baldascino A, Orazi L, et al


Results of FA in 13 patients at 9 months after treatment comparing intravitreal injection of bevacizumab with fellow eyes treated with laser photocoagulation for zone I Type 1 ROP. Among 23 eyes available for FA at 9 months, all bevacizumab eyes had peripheral abnormalities including large avascular areas, abnormal branching and shunts, and hyperfluorescent lesions or abnormalities of the foveal avascular zone. These abnormalities were not observed in the majority of lasered eyes.

Conclusion – long lasting structural abnormalities appear to be more common in bevacizumab treated eyes than in lasered eyes and the effect on function of these abnormalities must be studied.

**Validity of a telemedicine system for the evaluation of acute-phase retinopathy of prematurity.**


Purpose: Evaluate the validity of a telemedicine system to identify infants who have sufficiently severe ROP to require evaluation by an ophthalmologist. 1257 infants with BW<1251 enrolled in 13 North American Centers from May 2011- Oct 2013. Trained non-physician retinal imagers obtained images and submitted them for grading by non-physician readers. Primary outcome was comparison of grading results for referral warranted ROP (zone I ROP, stage 3 or worse ROP, and/or plus disease) with the results of diagnostic examination by the ophthalmologist.
Sensitivity for detection of RW-ROP was 90% and specificity of 87% for a single exam for an infant. These results support the validity of remote evaluation by trained non-physician readers of digital images obtained by trained non-physician imagers for at risk infants.

The 44th Richard G. Scobee Memorial Lecture: Insights in ROP

This lecture reviews the history leading to current ROP screening and management and discusses current controversies in ROP diagnosis, prognosis and treatment. Issues highlighted are

1. zone 3 ROP with and without previous zone 2 ROP
2. 1 clock hour of neovascularization ROP in zone 2 that encroaches on zone 1 vs ≥ 1 clock hour of neovascularization of ROP which is all in zone 1
3. subjectivity of diagnosing plus disease in zone 1 ROP
4. additional early screening of infants born before 25 weeks GA (2013 guidelines)
5. conclusion of screening at 50 weeks (2013 guidelines) vs 45 weeks (2006 guidelines)
6. follow-up of patients after intra-vitreal bevacizumab (IVB) injection for zone 1 ROP
7. blindness after laser for zone 1 ROP
8. theoretical systemic risk of IVB vs risk of systemic effects of IVB vs alternative such as IV ranibizumab


Determine genetic variants associated with severe retinopathy of prematurity (ROP) in a candidate gene cohort study of US preterm infants. Severe ROP was defined as threshold disease in the discovery cohort and as threshold disease or type 1 ROP in the replication cohort. Whole genome amplified DNA from stored blood spot samples from the Neonatal Research Network biorepository was genotyped. Three analyses were performed to determine significant epidemiologic variables and SNPs associated with levels of ROP severity. Eight hundred seventeen infants in the discovery cohort and 543 in the replication cohort were analyzed. Severe ROP occurred in 126 infants in the discovery and in 14 in the replication cohort. In both cohorts, ventilation days and seizure occurrence were associated with severe ROP. After controlling for
significant factors and multiple comparisons, two intronic SNPs in the gene BDNF (rs7934165 and rs2049046, P < 3.1 x 10(-5)) were associated with severe ROP in the discovery cohort and were not associated with severe ROP in the replication cohort. However, when the cohorts were analyzed together in an exploratory meta-analysis, rs7934165 increased in associated significance with severe ROP (P = 2.9 x 10(-7)).


Extracellular matrix (ECM) and cellular membrane proteoglycans (PGs) play important roles in neural differentiation and cell adhesion. Vascular endothelial growth factor, an important signal protein in vascular and retinal neural cell development, is retained in the ECM due to its high affinity for PG. Bevacizumab, an anti-VEGF agent, has been extensively used for treating retinal diseases in adult and newborn patients, although its effect on the developing retina remains largely unknown. The purpose of this study was to investigate the effect of bevacizumab on neurocan, phosphacan, and syndecan-3 PG levels in newborn rat retina.

No significant difference in the staining intensity and mRNA expression of phosphacan and syndecan-3 was observed between treated and control groups. However, a significant decrease in neurocan content and mRNA expression was observed in bevacizumab-treated retinal explants compared with controls. Bevacizumab did not affect phosphacan and syndecan-3 levels but decreased neurocan content and gene expression. Therefore, it may interfere with early postnatal retinal cell differentiation.


Timing of natural involution of acute retinopathy of prematurity (ROP) not requiring treatment and determined the risk factors associated with delayed involution. Retrospective case series of 82 eyes that didn't progress to type 1 ROP. The location, extent, and severity of ROP were documented by investigators during serial retinal examinations. Acute ROP not requiring treatment began to involute at a mean of 40.4 weeks of postmenstrual age and finished at a mean of 50.6 weeks. Involution began at the same mean postmenstrual age for each zone of disease (P = 0.48) and finished earlier in zone III than in zone II (P < 0.01). An analysis by severity of ROP found that involution began the earliest with the mildest disease and latest with the most serious disease. Zone II disease took longer to finish involution (16.04 +/- 12.35 weeks) than zone III (8.30 +/- 7.3 weeks), and stage 3 (23.88 +/- 10.58 weeks) took longer to finish involution than stage 1 (2.03 +/- 0.96 weeks) and stage 2 disease (7.69 +/- 4.75 weeks, P < 0.01, respectively). Multivariable logistic regression analysis showed that continuous positive airway pressure
(CPAP, $P < 0.0001$), active stage 3 disease ($P = 0.006$), and anemia ($P = 0.03$) were significant risk factors associated with delayed involution.


In this lead article in *Eye* from August, they authors investigate the incidence of myopia at age 2 in children with ROP treated with intravitreal bevacizumab with or without laser vs laser alone. They conclude that those treated with intravitreal injection alone had a much lower incidence of myopia vs those treated with injection plus laser (10 vs 47%). However there are major study design issues to be considered including the fact that the study was not prospective, or controlled or randomized and NONE of the patients treated with laser alone returned for followup. Finally the authors stated that axial length was determined by use of IOLmaster in these 2 year old patients, but technique was not discussed.


Pictor is a portable, noncontact digital fundus camera evaluated for its utility as a potential ROP screening tool. This was a retrospective review of ROP records over a 6-month period. 48/54 infants with retinal images met inclusion criteria. Clinical exam showed a 6% rate of plus disease, a 7% rate of pre-plus disease and 86% normal posterior poles. Two graders found image quality good in 96%/97% and at least 3 gradable image quadrants in 80%/86%. Using the reference standard of indirect-ophthalmoscopy reported plus disease- sensitivity of grading pre-plus or plus disease was 100%/83%, specificity was 79%/85%. Using the reference standard of indirect-ophthalmoscopy reported pre-plus or plus disease- sensitivity of grading pre-plus or plus disease was 92%/81%, specificity was 86%/90%. Intragrader reliability was 95% for both graders. The Pictor is able to evaluate the posterior pole for pre-plus or plus disease but does not have as wide a view as some other cameras. The camera weighs one pound and is easily transported. It is noncontact and no lid speculum is needed.

**Evaluating the association of autonomic drug use to the development and severity of retinopathy of prematurity.** Hussein MA, Coats DK, Khan H, et al. *J AAPOS* 2014;18:332-337

This study was a 2-year retrospective review of the outcome of ROP in premature infants treated in the NICU with agents affecting the autonomic nervous system. The authors postulate this may influence ROP outcomes. This study does not prove cause and effect but rather looks at the possibility of an association. Rates of ROP and ROP needing treatment were 54% / 15% (n=97/98)when dopamine was administered. When dopamine was not used the rates were 24% / 2% (n=249/252). These differences were significant. Caffeine dose was also significantly associated with development of any ROP and with
the need for treatment. Higher doses of caffeine were highly predictive. This study lacked a control group not using caffeine and the study was retrospective.


Using spectral domain OCT (SD-OCT), the authors measured iridocorneal angle characteristics in ROP patients versus non-ROP controls. This was an observational case-control study. The ROP group included 27 eyes (n-14) and the non-ROP group included 21 eyes (n=13). Mean corrected age at the time of imaging was 18.1 weeks and 25.7 weeks respectively. Scleral spur visualization was slightly better in the ROP group (74% vs 62%). A convex iris configuration was more common in the ROP group (56% vs 23%). Identification of the trabecular meshwork and Schwalbe line was also more common in the ROP group (93%/85% versus 76%/71%). Presence or absence of glaucoma was not evaluated. These patients were unsedated and therefore patient fixation could not be controlled. This could affect measurement. Ambient lighting during testing was not controlled. Only one quadrant was evaluated because imaging was technically difficult. Also the mean corrected age was not equal in the two groups and this could also affect results.


This study reports baseline plasma levels of VEGF-A, sVEGFR-2 and sTie2 in infants with treatment requiring ROP and to investigate the effect of laser photocoagulation on plasma levels of angiogenic factors. Consecutive infants with prethreshold type ! ROP over a 12-month period were enrolled. 48 eyes of 30 infants were included (8 eyes of 4 infants had zone I disease and the rest had zone II disease). The difference between laser spots in zone I vs zone II cases was significant. 6 eyes of 3 infants developed ASI, 5 of which resolved within 3 weeks of medical treatment. No correlation was found between gestational age and baseline VEGF-A, sVEGFR-2 and sTie2. Median plasma levels of all 3 angiogenic factors declined when checked before, 1 day and 1 week after laser photocoagulation. No correlation was found with the number of laser spots, number of days on a ventilator, O2 supplementation and baseline plasma levels. The authors found plasma levels of these angiogenic factors declined after laser treatment but this does not prove causality because there was no control group and the decline could be a result of advancing age.
Foveal Structure-Function Correlation in Children with History of Retinopathy of Prematurity.

This study attempted to correlate visual acuity with macular OCT anomalies detected after ROP. This was a retrospective study reviewing medical charts. Two years of charts for all children with ROP between ages of 2 and 18 years was reviewed. They reviewed 44 eyes of 44 patients. 64% had 20/40 or better visual acuity even though they possessed abnormal morphology on 91%. They examined only the better seeing eye of these patients. Abnormal findings included retention of the inner retinal layers and absent foveal depression on OCT. It appears that cone maturation is a better predictor of visual acuity. In addition, there was a suggestion that higher myopia resulted in lower visual acuity.


This observational prospective study presented the outcomes of babies with stage 4b or 5 retinopathy of prematurity who underwent vitrectomy in a tertiary care center of a developing country. Neonates with stage 4b ROP underwent a 3-port lens-sparing vitrectomy. Those with stage 5 ROP also underwent lensectomy and retrolental membrane dissection. Patients were assessed on their last follow-up for anatomic, visual, and functional results. The study included results of 20 babies with stage 4b and 11 babies with stage 5. Anatomic success was achieved in 18 eyes (90%) with stage 4b. In stage 5 eyes, anatomic success was achieved in 5 eyes (45.45). The authors conclude that anatomic, visual, and functional recovery was found in a good percentage of eyes. They also concluded that compared with the developed world, tertiary care centers in the developing world are more likely to see larger, older babies and previously unablated eyes with retinopathy of prematurity requiring surgery.


This is an article from the Department of Ophthalmology, Catholic University of Sacred Heart, Rome, Italy and Division of Pediatric Ophthalmology, The Children’s Hospital of Philadelphia, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania. This is a single randomized control trial of inborn babies with Type 1 Zone I retinopathy of prematurity born in a single institution in Rome, Italy. One eye was randomized to receive intravitreal injection of 0.5mg of Bevacizumab and the fellow eye received conventional laser photoablation. The purpose of this study was to compare the structural outcome
at 9 months of eyes treated with intravitreal injection of Bevacizumab with fellow eyes treated with conventional laser in zone 1 retinopathy of prematurity. Digital fundus photographs and fluorescein angiography (using the Ret-Cam system) was performed before treatment and 9 months after treatment.

Conclusion: Thirteen infants were enrolled; 1 died at 3 months after birth, 1 laser-treated eye progressed to stage 5 retinal detachment and the remaining 23 eyes had favorable structural results at 9 month follow-up and provided fluorescein angiographic results. At 9 months of age all eyes treated with Bevacizumab injection were noted to have abnormalities at the periphery (large avascular area, abnormal branching and shunt vessels) or the posterior pole (hyper-fluorescent angiogram lesions and absence of foveal avascular zone). These posterior and peripheral lesions were not observed in the majority of the lasered eyes.

Comment: This study documents the significant vascular and macular abnormalities of eyes in the Bevacizumab group. Long lasting implications of these abnormalities for visual function of the child need to be studied.

Please look carefully at the photographs on page 2215, 2216 and 2217. These clearly show the capillary dropout, particularly in the foveal avascular zone and the retinal periphery.


Retinopathy of prematurity affects only premature infants, but as premature births increase in many areas of the world, ROP has become a leading cause of childhood blindness. Blindness can occur from aberrant development angiogenesis that leads to fibrovascular retinal degeneration. In this Translational Science Review, Dr. Hartnett carefully goes through the concepts of the human phases of retinal development starting from a loss of internally derived factors during the preterm birth to postnatal repeated fluctuations supplemental oxygen and poor infant growth, disregulated signaling pathways. The phase of early ROP showed delayed physiologic retinal vascular development. In the vascular phase stage III, there is intravitreal neovascularization and in stage IV there is fibrovascular phase characterized by scarrring of the retina and the pupil. In figure 2, Dr. Hartnett goes through the phases of oxygen-induced retinopathy (OIR). She goes through feline studies and mouse models which have been performed in the past. Figure 3 shows pathways involved in disordered angiogenesis showing the influence repeated oxygen fluctuations, increased VEGF, decreased Müller cell erythropoietin, programmed cell death with phase 1 physiologic retinal vascular development. Figure 4 shows disordered angiogenesis.

Comment: This is an extremely well done Translational Science Review where Dr. Hartnett, who is a world internationally renowned authority in retinopathy of prematurity, put together a combination of clinical photos of humans, photos of retinal development in animal models and pathways in disordered angiogenesis. She also helps put into focus the concepts of insulin growth factor-1 and insulin growth factor-1BP3 and Omega-3 fatty acids.
Validity of a Telemedicine System for the Evaluation of Acute-Phase Retinopathy of Prematurity

Retinopathy of prematurity (ROP) remains a significant public health issue and a scarcity of trained ophthalmologists who can screen for ROP is problematic, especially in underserved areas of the United States. This study evaluated the efficacy of telemedicine to reach underserved areas of the country and identify referral warranted ROP (RW ROP). Referral warranted ROP is defined as Zone 1 ROP, Stage 3 ROP or Plus disease. This is a multicenter trial comparing digital image acquisition and analysis by non-ophthalmologists of at risk infants with gold standard retinal exams performed by experienced ophthalmologists. Most images were acquired by nurses (44%). This observational study was comprised of 1257 infants with a birth weight less than 1251 gms.

The infants had a median of 3 examinations and imaging. Diagnostic examination identified characteristics of RW-ROP in 18.2% of eyes (19.4%of infants). Remote grading of images of an eye at a single session had sensitivity of 81.9% and specificity of 90.1%. When both eyes were considered for the presence of RW-ROP, the sensitivity was 90.0%, with specificity of 87.0%, negative predictive value of 97.3%, and positive predictive value of 62.5% at the observed RW-ROP rate of 19.4%.

The authors conclude that the telemedicine system studied demonstrated strong validity in identifying referral warranted ROP. Further safeguards need to be explored to reduce the number of false negatives seen in this study so potentially blinding ROP is not missed.

Evaluation of Compounded Bevacizumab Prepared for Intravitreal Injection

Although this study does not mention use of bevacizumab for treatment of retinopathy of prematurity per se, their analysis of samples of bevacizumab from 11 compounding pharmacies across the United States is relevant for the treatment of any retinal disease with this antiVEGF agent. The authors highlight recent cases of endophthalmitis from contaminated bevacizumab from a pharmacy in Florida and the scandal involving contaminated steroids which led to the death of several patients treated with steroid injections obtained from a compounding pharmacy in Massachusetts. The authors conducted a sophisticated analysis of samples of bevacizumab obtained from 11 compounding pharmacies and compared them with bevacizumab (25 mg/mL) provided by Genentech, the manufacturer. No microbial contamination or endotoxin was detected by any of the assays in any of the samples. However, the concentration was lower, sometimes significantly lower, than the stated 25 mg/mL concentration stated on the syringe. The authors conclude that bevacizumab prepared by compounding pharmacies may not yield the stated concentration, and the therapeutic implication for the patient receiving treatment is not yet fully known.
Refractive Outcomes Following Bevacizumab Monotherapy Compared With Conventional Laser Treatment

The authors studied the original cohort of infants who were randomized to bevacizumab or laser in the BEAT-ROP trial and determine their refractive error at a mean age of 2 ½ years by performing a cycloplegic refraction. The cohort was comprised of 131 infants (255 eyes, including 21 eyes which required a second treatment for recurrence of ROP). Mean spherical equivalent refractions were as follows: zone I, −1.51 diopters (D) in 52 eyes that received intravitreal bevacizumab and −8.44 D in 35 eyes that received laser treatment (P < .001); and zone II posterior, −0.58 D in 58 eyes that received intravitreal bevacizumab and −5.83 D in 66 eyes that received laser treatment (P < .001). Very high myopia (−8.00 D) occurred in zone I in 2 of 52 (3.8%) eyes that received intravitreal bevacizumab and in 18 of 35 (51.4%) eyes that received laser treatment (P < .001). Very high myopia occurred in zone II posterior in 1 of 58 (1.7%) eyes that received intravitreal bevacizumab and in 24 of 66 (36.4%) eyes that received laser treatment (P < .001).

The authors postulate that myopia is more prevalent and severe in infants treated with laser because the development of the anterior segment may be retarded by laser and conversely, uninhibited by treatment with bevacizumab.

NATURAL HISTORY OF RETINOPATHY OF PREMATURITY – TWO YEAR OUTCOMES OF A PROSPECTIVE STUDY Chen, Yi-Hsing MD et al Retina, January 2015, 35(1)141-148

Most of the published literature regarding the natural history of retinopathy of prematurity (ROP) has been on white populations. This study provides data regarding the natural history and associated risk factors for ROP in a Taiwanese neonatal population. This was a prospective study conducted at two tertiary medical centers in Taiwan. Premature infants were screened and treated for ROP. A total of 698 eyes were included. The authors found ROP and type 1 ROP to occur slightly earlier in this population than previously published in the ET-ROP study. They also found treatment requiring ROP occurred even in infants over 1250 grams. The incidence of ROP and treatment-requiring ROP in all patients with ROP were 29.7% and 37.2%. When only including patients with birthweight of 1,250 g or less, the incidences were 62.2% and 39.1%, respectively. In patients with ROP with birth weight over 1,250 g, 25% of them developed treatment-requiring ROP. The median postmenstrual ages for the development of Stage 1, Stage 2, and Type 1 ROP were 33.0, 34.0, and 34.7 weeks, respectively. Gestational age at birth and birth weight were the most important factors associated with treatment-requiring ROP. Suboptimal oxygen control, different genetic dispositions among different races, inconsistencies in ROP diagnosis, and earlier screening might account for these different statistics.
9. STRABISMUS


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 Schiotz 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.

Changes in fusional vergence amplitudes after laser refractive surgery for moderate myopia

In this prospective study, the authors analyze the effect of bilateral laser refractive surgery on fusional vergence amplitudes and near point convergence in normal orthotropic myopic patients. Myopic spectacles decrease the demand for convergence because they are effectively “base in.” A refractive surgery patient would no longer have the benefit of “base in” spectacles postoperatively.
Thus, decreases in fusional convergence postoperatively might become symptomatic.

Thirty moderately myopic patients (2.0 to 6.0 D) underwent bilateral LASIK or LASEK and had an orthoptic evaluation postoperatively at 1 week and 1 and 3 months. Patients with manifest strabismus, previous strabismus surgery, amblyopia, absent or impaired binocularity, or planned monovision were excluded. The mean age of patients was 29 years ± 4 (SD). The convergence amplitude at near decreased 1 week and 1 month postoperatively, after which it progressively stabilized to near preoperative values. There was a slight increase of 6 mm in the near point convergence at 3 months (P<.001). The authors concluded that although fusional vergence amplitudes at near and near point convergence changed after laser refractive surgery, the observed changes were transient or small and not clinically significant.

Binocular function in patients with pseudophakic monovision

This retrospective comparative case series evaluated stereopsis and fusion in patients five years after undergoing pseudophakic monovision (one eye set for plano and the other for -2 D). Patients were divided into two groups: those with preoperative small-angle exophoria (≤10 PD) or moderate-angle exophoria (>10 PD) at near. The study comprised 60 patients with a mean age of 70.2 years ± 7.7 (SD). 37 or 61% of the patients had stereopsis of at least 100 arcsec on the Titmus test postoperatively, while wearing no refractive correction. Stereopsis was worse in the patients with X’>10 PD compared to those with X’≤10 PD (P<.001), and these patients were also more likely to fail the Worth 4 dot test. In the X’>10 PD group, 10 patients (62.5%) developed intermittent exotropia after surgery. The authors caution against pseudophakic monovision in patients with a preoperative exophoria > 10 PD. Based on this retrospective study, it is unclear whether the threshold of concern is truly X’ 10 PD or whether it falls along a continuum.


This was a retrospective study to see if prisms help improve a patients quality of life. The adult strabismus 20 questionnaire was used. It is a patient derived strabismus specific HRQOL questionnaire. 4 functions are looked at: self-perception, interactions, reading function, and general function. 34 patients were included. Overall the mean magnitude of prism perscribed was 8 pd. 23 had fresnel prism and 11 were given ground prisms. Patients were followed for 4.5 months. 23 patients were considered prism success, and 11 were failures. The HRQOL only showed improvement if the prism was successful and it only seemed to affect reading function and general function. So prisms and fresnel can be a successful non surgical treatment.
The Sensitivity of the Bielschowsky Head-Tilt Test in Diagnosing Acquired Bilateral Superior Oblique Paresis.

This was a retrospective chart review of 25 patients who were identified with true bilateral superior oblique palsies. This study evaluated the pattern of deviation on the Lancaster RG test as the standard for diagnosing bilateral 4th nerve palsies and then examined the sensitivity of the Bielschowsky tilt test. Inclusion criteria included: V pattern eso or exo, bilaterl SO underaction, objective fundus extorsion, subjective extorsion greater in downgaze than in upgaze on lancaster RG plot. The lancaster plot did detect all cases of bilateral SO palsy. Based on the Bielschowsky test, 10 (40% ) were diagnosed as bilateral palsies; 60% were marked as unilateral though. The Parks 3 step test only worked in 6 (24%) of patients. The authors stress that no single test should be used to determine a bilateral 4th nerve palsy.


This study was a cross sectional population based study looking at 7537 children aged 6-17 years.Examinations were performed on these children and 4000 children ages 10 and older were given a questionnaire. Prevalence of strabismus was 6.8 % with 2.7% exotropia, 0.2% esotropia, and intermittent exotropia 3.9%. Strabismus was more common in the urban setting and in females. The questionnaire was answered by 3903 children. Alcohol use, depression symptoms, and anxiety were more common in the strabismus group and was significant. Further evaluation should be done, if this information is correct, trying to label strabismus repair as “cosmetic” would be inappropriate since it appears to be linked to other diseases.

Muscle path length in horizontal strabismus. Rabinowitz R and Demer JL. JAAPPOS 2014;18:4-9

This study determined whether abnormalities in horizontal rectus muscle path lengths are associated with commonly encountered intermittent or alternating esotropia and exotropia. Digital MRI measurements were obtained in central gaze only (both eyes in normal patients and on the fixating eye in strabismic patients). Investigators were unmasked, but did not have a strong prior hypothesis. Control data were obtained from 13 orthophoric adults and 12 adult strabismus subjects (8 esotropic 4 exotropic). Mean medial and lateral rectus paths were not significantly different in controls, exotropes, or esotropes. Three patients with divergence paralysis esotropia had moderate but not significantly longer lateral recti paths than controls. Overall sample sizes were small, but no significant trends were detected.
Reproducibility of horizontal extraocular muscle insertion distance in anterior segment optical coherence tomography and the effect of head position. Park K-A, Lee JY and Oh SY. J AAPOS 2014;18:15-20

The purpose of this study was to assess inter- and intraexaminer reproducibility of muscle insertion distance measurements using AS-OCT and the effect of eye position on the measurement. Thirty healthy adults were evaluated (one was excluded from analysis because of poor image quality). Lateral and medial rectus insertion distances measured, were not statistically different when different gaze positions were compared. Reproducibility was excellent for intra- and interexaminer distance measurements of the medial and lateral rectus muscles. This test is relatively inexpensive and rapid. It may have utility in measuring rectus muscle location as a preoperative tool in patients who have had prior surgery or have possible abnormal muscle insertions such as with pathologic myopia. This study only included adults of one ethnicity with healthy normal eyes, and only measured the horizontal recti.

Clinical progression of untreated bilateral Brown syndrome. Sorrentino D and Warman R. J AAPOS 2014; 18:156-158

The authors describe the natural progression of untreated bilateral Brown syndrome. This consisted of a 25-year retrospective review. Nine patients were included with a mean follow-up of 7.9 years. At most recent follow-up, one patient had resolution in one eye. There was little visual impairment during follow-up and the course was benign.

Change in convergence and accommodation after two weeks of eye exercises in typical young adults. Horwood AM, Toor SS and Riddell PM. JAAPOS 2014;18:162-168.

This study evaluated objective changes in convergence and accommodation produced by short courses of different exercises regimens. Attention was placed on the influence of practice, placebo, and encouragement. 156 healthy, young, adult students were analyzed. Two participants were switched to the no treatment group after admitting they did not perform any exercises (which violates randomization doctrine). The authors found that disparity was the strongest driver of responses. True treatment effects were small. Encouraging effort produced significant increased vergence and accommodation. Encouragement effect was the strongest influence on changing subject responses. This may be the sole reason why in-office therapies may hold more benefit than home treatments. This improvement effect of in-office therapy must be balanced against time commitments and increased costs. These patients were all normal and derived information may not apply to patients with accommodative or convergence problems. The authors could not objectively prove whether or not
participants had in fact performed the exercises prescribed. Also the treatment period may have been too short.


Health-related quality of life (HRQOL) of strabismus on Singaporean children was assessed using the Intermittent Exotropia Questionnaire (IXTQ) and the Adult Strabismus 20 Questionnaire (AS-20). Differences in responses between the child and parent/proxy were also assessed. Three groups of children were included: strabismus (gp S), eye condition other than strabismus (gp A), and no eye condition (gp B). Each group had 60 children. IXTQ scores in children in gp S were significantly lower than the other two groups, and gp A scores were significantly lower than gp B. AS-20 scores were similar in gp S and gp A, but both groups were significantly lower than gp B. These same findings were found in parental/proxy scores. In gpS parental/proxy scores tended to underestimate their child’s worries about what others thought of their eyes, feeling different, and concerns about making friends. Sex of the child and type of strabismus did not affect results, however scores were generally lower for younger children. AS-20 has not been validated for use in children, and using the IXTQ on children with non-strabismic conditions may not be appropriate. Presence or absence of glasses wear was not included in this study but this variable could affect data scores.


The authors attempted to find the latest possible age to correct infantile esotropia while also preserving the opportunity to obtain stereopsis. This was a retrospective review of children who were aligned within 10 PD of orthophoria after surgery, over a 12-year period. Thirty-eight patients with a mean follow-up time of 72 months were included. Half (n=19) developed stereopsis better than 1000 arcsec, and 13% showed a stereopsis of >=400 arcsec. No patient operated on prior to 13 months failed to achieve some degree of stereopsis and no patient operated on after 39 months developed stereopsis. Power of stereopsis was correlated with age at surgery, but not other parameters. 16 months was the cut-off age for predicting development of stereopsis. Alignment within 5 PD or 10 PD of stereopsis did not affect stereopsis results. Surgery before 16 months resulted in a 80% stereopsis rate and a median stereoacuity of 480 arcsec. Surgery after 16 months resulted in a 30.4% stereopsis rate and a median stereoacuity of 1000 arcsec. Duration of misalignment is also critical but this was not specifically assessed in this study. This study showed a moderate correlation between early surgery and stereopsis.

The purpose of this study was to ascertain whether hypertropia is a typical concomitant of abducens nerve or a coexisting lesion. Consecutive patients’ medical records with isolated unilateral abducens palsies over a 24 year period, were reviewed retrospectively. 79 patients met inclusion criteria. 15 of 79 cases (19%) demonstrated hypertropia in central and/or lateral gaze by alternate cover or Krimsky testing. On Hess screen testing, this increased to 32/56 (57%). The mean maximum hyertropia in lateral or central gaze on clinical examination was 5.0 PD, and 5.8 PD on Hess screen testing. Both hyper- and hypotropias occurred. In most cases the vertical strabismus was worse in abduction. 30 control subjects had no hypertropia on Hess screen. The authors suggest another potential etiology for hypertropia in the setting of isolated abducens, other than an associated 4th nerve palsy or skew deviation. Compartmental paralysis or paresis of the superior or inferior zones of the affected lateral rectus muscle could produce a vertical strabismus, and this effect would be seen more in abduction than adduction (consistent with this report). Limitations of this study include: retrospective data, variable testing methods to measure vertical strabismus, all patients not neuro-imaged, tertiary center.


This study reports ocular alignment outcomes in patients with refractive accommodative esotropia with a minimum follow-up of 10 years. The medical records of consecutive patients seen over a 13-year period were reviewed retrospectively. 107 patients met inclusion criteria. 35/107 had amblyopia. Mean follow-up was 12.02 years. At first examination past 10-year follow-up, 79% of patients were orthophoric or esotropic within 10 PD, 13% had consecutive exotropia, 5% had decompensated esotropia and 3% had high AC/A ratio esotropia. Kaplan-Meier survival analysis demonstrated orthophoria/esotropia <10 PD- 89% @ 5 years, 80% @ 10 years, and 71% @ 15 years. There was a slightly higher rate of consecutive exotropia with higher hyperopia, but this was not statistically significant. No parameters could be linked to decompensation, or conversion to a high AC/A ratio. The investigator was not masked in this study and AC/A ratio was not measured routinely. Technique of cycloplegic refraction was not uniform.


Approximately 90% of physicians use smartphones. This article is a description of ways to use an iPhone to measure anomalous head postures, including head tilts, face turns, and chin up/down positions. Previous studies have illustrated that visual estimation of the degree of anomalous posturing is inaccurate, especially for right head tilts and right face turns. The Compass application, which comes installed on all iPhones, can be used to provide a more accurate measurement. Face turns can be estimated by standing above the patients head
and holding the iPhone parallel to the floor, head tilts toward the shoulder can be estimated by orienting the phone in front of the patient’s face, and chin-up or chin-down postures can be estimated by standing at the patient’s ear side and measuring the degree of flexion or extension. Alternatively, the free iHandy Level app can be used to estimate anomalous head postures.

**Abducens nerve in a patient with Duane retraction syndrome.**

This is a case report that describes an 8 year old with Duane's type II retraction syndrome and an absent abducens nerve on MRI. He had an exotropia since early childhood but had good vision in both eyes. He had 2 prism diopters of exophoria at distance and 20 prism diopters of left exotropia at near in the primary position. This case is likely the first report of a complete absence of the abducens nerve in type 2 DRS. The authors do mention, however, that it is possible that this patient represents an extreme case of Duane’s type III with a predominant limitation of adduction compared with abduction.


Fifty-two students participated in this analytical–descriptive study. Accommodative amplitudes were measured using four common clinical techniques, namely: Push-up, push-down, minus lens, and modified push-up. The highest amplitude was obtained using the push-up method (11.21 ± 1.85 D), while the minus lens technique gave the lowest finding (9.31 ± 1.61 D). A repeated-measures Analysis of Variance (ANOVA) showed a significant difference between these methods (P < 0.05), further analysis showed that this difference was only between the minus lens and other the three methods (the push-up (P < 0.001), the push-down (P < 0.001) and the modified push-up (P < 0.001)). The highest and the lowest mean difference was related to the push-up with the minus lens, and the push-down with the modified push-up, while the highest and the lowest 95% limits of agreement were related to the push-up with the modified push-up and the push-up with the push-down methods. There was almost a perfect agreement between the push-up and the push-down method, whereas, a poor agreement was present between the modified push-up and the minus lens technique, and a fair agreement existed between the other pairs. The quick and easy assessment of the amplitude using the push-up and the push-down methods compared to other methods, and the obtained perfect agreement between these two methods can further emphasize their use as a routine procedure in the clinic, especially if a combination of the two techniques is used to offset their slight over- and underestimation.
Incidence, Types, and Lifetime Risk of Adult-Onset Strabismus
J M. Martinez-Thompson, N N. Diehl, J M. Holmes, B G. Mohney, *Ophthalmology*
April 2014; 121:877-882

This is a retrospective reviewed population-based cohort designed to describe the incidence and types of adult-onset strabismus in a geographically defined population, mainly Olmsted County, Minnesota. Participants: Residents, 19 years of age and older who were newly diagnosed with some form of strabismus from January 1, 1985, to December 31, 2004, were included in this study. Methods: The medical records of all potential cases identified by the resources of the Rochester Epidemiology Project were reviewed. Main Outcome Measures: Incidence rates for adult-onset strabismus and its different types. Results: 753 cases of new onset adult strabismus were identified during a 20 year period. The average annual age and gender adjusted incidence rate was 54.1 cases per 100,000 individuals 19 years of age and older. The foremost common types of new onset strabismus were paralytic strabismus 44.2, convergence insufficiency 15.7, small angle hypertropia 13.3 and divergence insufficiency 10.6. Conclusions: Paralytic strabismus was the most common subtype of new onset adult strabismus in this population based cohort (limited to Olmsted County, Minnesota). All of the most common forms of adult onset strabismus increased with age especially after the sixth decade of life.

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Measurement of Ocular Cyclotorsion in Superior Oblique Palsy Using a Single Maddox Rod
Yehoshua Almog, Arie Y. Nemet, Yokrat Ton,

The authors compare cyclotorsion measured with double Maddox rod technique (red and white Maddox lenses in a darkened room “eliminating environmental clues”) to that measured with a single Maddox rod in ambient lighting allowing the patient to compare subjective tilt with environmental clues such as the door frame or office furnishings. Non-blinded testing of 48 adult patients with superior oblique palsy demonstrated excellent correlation between the two techniques. The authors suggest that the single Maddox test may be simpler to perform, particularly when comparing torsion in different directions of gaze.

Clinical characteristics and outcomes of Möbius syndrome in a children's hospital.

Möbius syndrome is a congenital disorder with facial and abducens palsy that is frequently seen by pediatric ophthalmologists due to ptosis and esotropia. Although a few case series studies have examined comorbid conditions in
Möbius syndrome, follow-up and outcome data are sparse. The authors set out to examine the clinical characteristics and outcomes of Möbius syndrome in 10 patients. Neonatal history, neurological examination, comorbid anomalies, medical home care, outcomes, and neuroimaging were summarized. The patients' mean age was 7.3 ± 6.2 years. On neurological examination, absent blink reflex, jaw ankylosis, absent gag reflex, and tongue atrophy were frequently observed. Specific therapies required for patients included medical home care (six patients), suction apparatus (six), tube feeding (five), gastrostomy (two), tracheostomy (three), oxygen therapy (three), and home ventilator (two). Pontine and medulla hypoplasia were detected on the basis of anteroposterior diameter in four and seven patients, respectively. Two patients had congenital hydrocephalus with aqueductal stenosis. Global developmental delay occurred in five patients. Three patients died. The authors concluded that the rate of both the use of home medical devices and death was high in their patients and that Möbius syndrome is extremely diverse, not only in clinical manifestation, but also with regards to outcome. Pediatric ophthalmologists should recognize that early multidisciplinary intervention is important to ensure an optimal outcome and that aqueductal stenosis is an occasional comorbid anomaly resulting from the associated midbrain abnormality.


This is an important paper that should be read by all strabismologists. In this retrospective study the authors investigate the "cure" rate for exotropia comparing those who had surgery to those who did not. After seven year followup the cure rate for the surgical group was 30% and for the non surgical group 12%, not a statistical difference. More important than the numbers is the authors discussion of the challenges of studying this challenging condition. They are commended for presenting long term results, as such data is rare in our literature.


This study investigates the factors influencing the development and severity of DVD. The medical records of consecutive patients over a 13-year period were reviewed. 90 patients were enrolled with a mean follow-up of 65.3 months. Initial visit was at a mean age of 16.8 months, which brings into question the claim that all children had infantile esotropia. DVD was detected in 58% of which 34 were spontaneous and 18 were latent. There was no difference between the spontaneous DVD and the latent DVD in regards to the timing of DVD development. Spontaneous DVD patients had a significantly higher preoperative angle of esotropia compared to latent or no DVD. >60 PD esotropia preop and delayed surgery were associated with an increased risk of spontaneous DVD. Amblyopia and stereopsis were not found to be risk factors, however nil stereopsis was associated with spontaneous DVD. The degree of stereopsis lessened the risk of DVD. Only 2 patients in this study underwent surgery prior
to 12 months of age, which would not represent surgical patterns in the United States. Some DVD data was missing in some patient records.


The authors used a population-based medical record retrieval system to assess prevalence of dissociated strabismus in children with any form of ocular misalignment. A ten-year period was reviewed. 627 childhood strabismus cases were identified. At initial exam, 12 children (1.9%) were found to have DVD. Rates were 6.6% (2/30) for infantile esotropia, (1.1%) 2/175 children with accommodative esotropia and 1 child in each of the other categories. 2/627 had DVD without horizontal strabismus. Over a mean follow-up of 10.4 years, an additional 44 patients were diagnosed with DVD. DVD was ultimately diagnosed in 53.3% of children with infantile esotropia (16/30), 25% (11/44) children with CNS esotropia, and no more than 2 children in any of the other categories. The association with CNS esotropia has not, to the authors knowledge, been reported previously in the literature.


This study attempts to characterize binocular summation (BiS) and binocular inhibition (BI) in strabismic pediatric and adult patients to determine the relationship to overall quality of life as measured by 3 quality of life scales. 108 patients were enrolled, with various strabismus types. Half had subjective diplopia. For lower-contrast ETDRS these patients displayed binocular inhibition, but this was not noted with high-contrast ETDRS. The percentage of patients exhibiting both BiS and BI increased as contrast levels were reduced. When compared to BiS patients, BI patients exhibited significantly lower scores on the VFQ-25 questionnaire and lower quality-of-life scores. AS-20 scores were also lower for BI patients for ETDRS visual acuity. Subnormal scores were more common on the AS-20 than on the VFQ-25, regardless of diplopia status. This study should have looked at data separated by whether the patient did or did not have diplopia to better ascertain the role of strabismus itself versus diplopia in affecting quality of life scores. Also no attempt was made to separate data by strabismus type so it is unclear whether BI, BiS, and quality of life scores are different between subgroups.

**Sensitivity of the three-step test in the diagnosis of superior oblique palsy.** Manchandia AM, Demer JL. J AAPOS 2014;18:567-571.

No prior studies have validated three-step testing sensitivity against other indicators of superior oblique function. Patients were included if they had superior oblique atrophy on coronal plane MRI (this was used as the diagnostic criteria).
The authors did not distinguish acquired cases from other causes. 73 patients had superior oblique atrophy on MRI but 23 were excluded from the study for unreported causes. The possibility of spread of comitance affecting results was not addressed. Mean superior oblique cross section was only 52% of the contralateral side, but was similar whether the patient fulfilled one, two or three steps of the three-step test. Patients who fulfilled all three steps had no difference in the amount of central hypertropia, excyclotorsion or age but significantly greater contralateral and ipsilateral gaze hypertropia. Step one of the three-step test was present in 92% of patients. Step two was present in 84% of patients. Step three was present in 92% of patients. Steps one and three combined was more sensitive than the three-step test. Patient age, maximum superior oblique cross-section and palsy etiology did not affect fulfillment of the three-step test. Those patients not fulfilling the complete three-step test had significantly less elevation in adduction. Overall the three-step test was not found to be highly specific or sensitive.

Disparity-driven vs blur-driven models of accommodation and convergence in binocular vision and intermittent strabismus.

The authors investigate vergence and accommodation to blur disparity and proximity. They present evidence in support of a conceptual model that suggests individual biases in near-cue use predict clinical characteristics. Clinically significant problems may result from excessive bias or inflexibility of response to cues. They enrolled healthy children ages 4-12. Different blur and disparity biases characterize clinical patterns despite identical AC/A and CA/C ratios. The authors classify normal, high AC/A-low CA/C, and low AC/A-high CA/C based on whether there is disparity bias or blur bias. Biases may be altered over time or with orthoptic exercises.

Surgical Correlation of Childhood Intermittent Exotropia and the Risk of Developing Mental Illness.

This retrospective observational study assessed whether successful surgical intervention for intermittent XT had any affect on the development of mental illness. A genetic link between mental illness and XT had been reported. This study wanted to assess whether successful surgical intervention or timing of intervention, influenced mental illness outcomes. All patients diagnosed with XT between the years of 1975 thru 1994 were considered. 96 of 184 children (52%) were diagnosed with a mental illness at a mean age of 23.3 years. 35 of the 96 children (36%) who had developed mental illness had undergone strabismus surgery. Successful surgery was not associated with less mental illness. Of the 88 patients who did not develop mental illness, strabismus surgery was not more commonly performed and it was performed at an older age. The conclusion: strabismus surgery regardless of success or age of surgery did not alter the development of mental illness.
Quantitative Assessment of Inferior Oblique Muscle Overaction Using Photographs of the Cardinal Positions of Gaze.  

This cross-sectional diagnostic study was to report a novel way to measure the degree of inferior oblique overaction off of photos. 142 eyes of 120 patients were enrolled in the study. Photographs were taken and measurements were taken off the photos. Mean angle of inferior oblique overaction was 17.8 degrees. The angle showed significant correlation with the clinical grading scale and with hypertropia in adducted position. The mean angles were classified into grades of 1, 2, 3, and 4 and the angles were 10.5, 16.8, 24.3, and 40 degrees.

An Objective Photographic Analysis of Ocular Oblique Muscle Dysfunction.  

This prospective observational study, attempted to create a more objective method to measure ocular oblique muscles. 12 healthy patients and 27 patients with oblique overaction were included. Corneal contour in 9-gaze photos was transcribed into an ellipse. By analyzing how the corneal contour appeared with eye movement, the angular difference between the two eyes was analyzed to measure oblique overaction. An angular difference of 5 degrees was 1 unit of overaction. They found that this analysis correlated nicely with clinical grading of overaction. This method may be a good way to objectively evaluate IOOA.

Depressive Symptoms Associated with Poor Health-Related Quality of Life in Adults with Strabismus
Sarah R. Hatt, David A. Leske, Laura Liebermann, Kemuel L. Philbrick, Ophthalmology October 2014; 121(10):2070-2071

This article comes from the Department of Ophthalmology and Department of Psychiatry at the Mayo Clinic in Rochester, Minnesota. This is a prospectively enrolled study of adults ranging from 18-88 years, 4% of the patients were female and a large percentage of patients were Caucasian. This study employed the use of health-related quality of life questionnaire (HRQOL) and adult strabismus-20 (AS-20) HRQOL questionnaire. All adults were given the adult strabismus-20 or AS-20 questionnaire. Adults also received the DS-14 distress personality questionnaire as well as the diplopia questionnaire.

Conclusion: The association of subthreshold depressive symptoms with reduced quality of life scores (HRQOL) should be considered when evaluating adults with strabismus when interpreting patient reported outcomes. Further studies are needed to elucidate whether depression develops as a result of pure HRQOL associated with strabismus or whether depression is an independent cause of reduced HRQOL in strabismus patients.

Extraocular Muscle Repositioning and Diplopia Associated with Ophthalmic Plaque Radiation Therapy for Choroidal Melanoma  
This study comes from the The New York Eye Cancer Center, New York, New York. This is a single-center retrospective cohort study of 329 eyes of 329 consecutive patients clinically diagnosed with choroidal melanoma. The objective is to evaluate extraocular muscle surgery associated with plaque brachytherapy diagnosed with choroidal melanoma. Two hundred fifty-four of the 329 patients (77.2%) required muscle surgery, 107 patients required surgery on 2 or more muscles. Of 373 muscles repositioned, the lateral rectus muscle and inferior oblique muscle were the most common, correlating to intraocular tumor location. Only 6 tumors originated from the iris and ciliary body required muscle surgery for plaque placement. Of the 312 patients with a preoperative visual acuity better than 20/400, diplopia was reported at the first postoperative visit by 41 patients. Among the 312 patients, persistent diplopia occurred in 1.9%.

Conclusions: Extraocular muscle surgery is frequently required for plaque brachytherapy. Although transient diplopia occurred in 11.2% of patients, persistent diplopia occurred in 1.9% of patients.

Comment: There are excellent photographs of the 4 different types of brachytherapy plaques used. There is also an intraoperative photograph (page 2269) showing the tumor edges as typically identified by transillumination are marked with dots.

A Randomized Trial Comparing Part-Time Patching with Observation for Children 3 to 10 Years of Age with Intermittent Exotropia

This is a multicenter, randomized clinical trial of 358 children 3 to less than 11 years of age. The purpose is to determine the effectiveness of prescribed part-time patching for treating intermittent exotropia in children.
Results: Of the 324 participants (91%) completing the 6-month primary outcome examination. Main Outcome Measures: Deterioration occurred in 6.1% in the observation group and 0.6% in the part-time patching group.
Conclusions: Deterioration of previously untreated childhood intermittent exotropia over a 6-month period is uncommon with or without patching. There is a slightly lower deterioration rate with patching. Both management approaches are reasonable for treating children 3 to 10 years of age with intermittent exotropia.
10. STRABISMUS SURGERY

Surgical Outcomes Following Rectus Muscle Plication
A Potentially Reversible, Vessel-Sparing Alternative to Resection

Plication and resection of an extraocular muscle are both strengthening procedures. In this study authors determine the surgical dose effect of plication and compare that with resection. The study is a retrospective review comprised of 22 patients who underwent bilateral plication of the medial or lateral rectus or plication combined with recession of the antagonist muscle (13 ET/9XT), 31 who underwent bilateral resection of the medial or lateral rectus or resection combined with recession of the antagonist (12 ET/19 XT) and 6 patients who had vertical rectus plication. Mean follow-up was much less for plication group versus resection group(137 vs. 1243 days). Outcomes studied included binocular alignment at first and last postop visits. Mean initial correction for lateral rectus plication was 5.17PD/mm and for resection 6.63PD/mm. Surgical dose effect of medial rectus plication (4.9PD/mm) and resection (5.1PD/mm) were similar. Advantages of plication include simplicity of procedure, reversibility, and sparing of anterior ciliary circulation. The technique is described. The muscle is secured in the usual fashion with Vicryl suture at the desired position as if for a resection. An iris spatula is used to fold the muscle under and up to the original insertion and secured with scleral passes at each pole of the original insertion. An adjustable suture may be used.

Superior Rectus Transposition vs Medial Rectus Recession for Treatment of Esotropic Duane Syndrome

The authors compared the effectiveness of superior rectus transposition(SRT) +/- ipsilateral medial rectus recession (MRrc) with unilateral or bilateral MRrc in the treatment of esotropic Duane’s syndrome. This was a retrospective review which identified 36 patients who had 37 procedures(18 in the SRT group and 19 in the non-SRT group). Main outcomes included binocular alignment, ocular ductions, head position, stereopsis, and fundus torsion measured pre-operatively and at the 2-month and final postoperative visits. The authors conclude that SRT was more effective in improving abduction than MRrc alone. No vertical or torsional complications were noted. In 24 patients followed for greater than 6 months mean esotropia decreased from 8.2 to 6.1 PD in SRT group and increased in MRrc group from 7.2 to 10.9PD.
Adjustable Nasal Transposition of Split Lateral Rectus Muscle for Third Nerve Palsy

The authors describe a novel surgical technique to improve eye alignment in patients with third nerve palsy. The surgeon needs to extensively split the lateral rectus (LR) anteriorly to posteriorly and secure the split LR each with a Vicryl suture. Then the split muscle is threaded beneath the vertical rectus and oblique muscles on its way to the medical rectus. The two portions of the LR are ultimately secured at the poles of the medial rectus with an adjustable noose knot suture. The study describes the pre-op characteristics and postoperative course of 6 patients who had the procedure. Three out of 6 patients achieved orthotropia. Mean pre-op deviation was 68 PD of exotropia. Two patients with vertical misalignment improved because of the ability to adjust one pole of the LR versus the other. One patient had undercorrection and transient choroidal effusion. MRI imaging post-operatively identified the split lateral rectus to be posterior to the globe in all cases except in the one patient who was undercorrected and had a choroidal effusion. In this patient, the split lateral rectus followed a course in apposition to the globe. Case selection is important since prior surgery on the lateral rectus could render the muscle stiff and scarred and not amenable for the long course it needs to take to be secured to the medial rectus.

Contralateral lateral rectus muscle recession in patients with Duane retraction syndrome type 3

The authors describe a new approach to the treatment of patients with type 3 Duanes Retraction Syndrome. In this syndrome there is limitation of both abduction and adduction. They describe a 8 patients with DRS type 3, all who were exotropic in the primary position. By performing lateral rectus recession in the contralateral eye, they achieved good alignment without over or undercorrection. If upshot or downshoot is present, Y splitting of the ipsalateral lateral rectus was performed.

Muscle belly union associated with simultaneous medial rectus recession for treatment of myopic myopathy: results in 33 eyes
M Fresina, A Finzi, P Versura and E C Campos Eye (2014) 28, 557–561;

This is the largest clinical series describing the treatment of esotropia and hypotropia associated with high myopia. The authors described 26 patients with high myopia (spherical equivalent -22.0D +/- 9) who underwent union of ½ width lateral rectus muscle to ½ width superior rectus muscle with non absorbable suture 12-15 mm from original insertions. All had simultaneous medial rectus recession. Scleral fixation was not performed. There was marked improvement in alignment (45 ET preop to 7 ET postop) and few complications. Such patients
should receive orbital MRI preop to confirm presence of inferior displacement of the lateral rectus and medial displacement of the superior rectus.

**Intermittent exotropia: relation between age and surgical outcome: a change-point analysis**  
A Awadein, R M Eltanamly and M Elshazly  
*Eye* (2014) **28**, 587–593

In this combined retrospective and prospective study, the authors examine the relationship between amount of surgery and surgical outcomes in 311 patients with intermittent exotropia all treated with bilateral lateral rectus recessions. They found that adhering strictly to the standard surgical tables, young children can develop overcorrections and older patients undercorrections. By decreasing recessions by 1mm for children less than 6 years, the success rate remained stable while leading to fewer overcorrections. By increasing recession by 1.5 mm in patients over 12, the success rate increased from 41 to 80%. Bottom line, surgical tables should be used as guidelines, and modified by multiple factors, with age of patient being an important consideration.

**The Results of Brown Syndrome Surgery with Superior Oblique Split Tendon Lengthening**  
Moghadam AAS, Sharifi M, Satar Heydari S.  

This retrospective study reports the outcome of superior oblique tendon split lengthening (10 mm) surgery for patients with severe congenital Brown syndrome. Through a superonasal approach the superior oblique was split with a Stevens hook for 10 mm. The posterior half of tendon was cut at nasal side and anterior half at temporal side and the two end were re-anastomosed by a double-armed Mersilene 5/0 (Ethicon) suture. Surgery was performed on 15 eyes with a mean postoperative follow-up of 12.93 ± 1.79 months. Average hypotropia in primary gaze improved from 16.2 ± 5.5 prism diopters preoperatively to 5.9 ± 4.0 prism diopters postoperatively. The limitation in adduction improved postoperatively. One patient was undercorrected, but none developed major complications including superior oblique palsy, granuloma, or extrusion of suture material. The authors conclude that superior oblique tendon split could be an alternative method for surgical management of congenital Brown syndrome. The study is limited by small number of patients and limited follow-up.

**Standardising Reported Outcomes of Surgery for Intermittent Exotropia – A Systematic Literature Review**  
Chiu AKC, Din N, Ali N.  

The purpose of this study is to assess the extent of standardization of reported outcomes in studies of surgery for IXT. A systematic literature review was conducted of outcomes of surgery for IXT published in the last 10 years. The databases used were Medline and EMBASE. Fifty-six studies met the inclusion criteria (thirty-two retrospective and twenty-four prospective). Results showed that outcome measures varied widely between studies and variously included
ocular alignment, stereopsis, visual acuity, re-operation rate, and postoperative drift. Even for ocular alignment, there was no agreed definition of postoperative success. The authors suggest redefining the criteria for success in IXT surgery based on which outcomes, and what level of outcome, translate into noticeable benefit to patients, rather than what matters to surgeons or researchers. They suggest 4 core outcomes for all future studies: alignment, near stereoacuity, control score, and quality of life score.

Adjustable Augmented Rectus Muscle Transposition Surgery with or Without Ciliary Vessel Sparing for Abduction Deficiencies

This is a retrospective review of patients undergoing adjustable partial or full tendon VRT augmented by resection of the transposed muscles. Seven patients had abducens palsy and one Duane syndrome. Both vertical rectus muscles were symmetrically resected by 3–5 mm. Ciliary vessels were preserved in most of the patients by either splitting the transposed muscle or by dragging the transposed muscle without disrupting the muscle insertion. Preoperative esotropia of 30.6 ± 12.9Δ (range, 17–50Δ) decreased to 10.6 ± 8.8Δ (range, 0–25Δ) at the final visit (p = 0.003). Three patients required postoperative adjustment due to an induced vertical deviation, coupled with overcorrection. At the final follow-up visit 3.8 ± 2.6 months postoperatively, one patient had a vertical deviation <4Δ, and none had overcorrection or anterior segment ischemia. Three patients required further surgery for recurrent esotropia. Limitations of the study include the small number of patients, surgery for all patients was not exactly the same, and follow-up time is short.

Congenital esotropia after surgery for intermittent exotropia: the clinical course and factors associated with the onset

This retrospective study reviewed 526 cases of exotropia surgery. They looked at risk factor for consecutive esotropia. ET was defined as postoperative measurement of greater and/or equal to 10 PD. Consecutive ET occurred in 26 cases (4.94%). Findings that showed higher association with consecutive ET included divergence excess XT, bilateral lateral rectus recession, esodeviations of greater than 20 ET at postop day 1, younger age at surgery. Out of the 26 patients, 15 became orthophoric with patching and fresnel treatment. Eleven failed to show improvement and seven had repeat surgery for correction.

Diclofenac versus fluorometholone after strabismus surgery in children H. Yang, S. Han, J. Hwang.BJO 2014; 98: 734-738.
This retrospective study looked at 60 Korean children who underwent strabismus surgery for XT and received either FML 0.1% vs. diclofenac 0.1% after surgery for up to 4 weeks. IOP increased in 23% of the group on the FML within 4 weeks of surgery. There was no significant difference in discomfort, conj inflammation or injection in the two groups.


This study was performed on adult patients with strabismus. They had a total of 31 patients with a mean age of 22 years. Fourteen patients had esotropia and 17 patients had exotropia. They evaluated the patients preoperatively and postoperatively for standardized testing to evaluate for social phobia diagnosis and severity of anxiety and depression. All patients showed a significant decrease in all subscale scores and total scores of both tests. Significant improvements occurred in the quality of life and disability score as well. This paper is important as more insurance companies decide that strabismus surgery is cosmetic for our adult patients and claim it serves no benefit to them.


This was a retrospective study looking at 2 muscle surgery for large angle exotropia greater than 40 diopters with either 10 mm bilateral lateral rectus recession vs. recess / resect unilaterally. 86 children were reported on. Patients were followed for 2 years. 29 patients (60.4%) in the BLR group had successful alignment. 16 had recurrence, and 3 had overcorrection. In the RR group, 26 (68.4%) had a good outcome, 10 had recurrence and 2 had overcorrection. Both groups were equal in outcome. In patients where the XT was greater than 45 diopters, the RR group appeared more successful. Surgical outcome was considered satisfactory if the alignment was between 10 pd of exo and 5 diopter of eso. Reoperation was performed if they were over 14 XT.

**Cyanoacrylate tissue adhesive on a polyglactin scaffold in strabismus surgery: a laboratory study.** Bona MD and Arthur BW. J AAPOS 2014;18:21-25

To avoid scleral perforation, studies have used tissue adhesives. However this brings up concerns about inadequate bonding and retraction of the muscle belly within the muscle fascial sheath. The authors combine incorporating tissue adhesive on a polyglactin scaffold, with suture retention of the muscle. Cadaver eyes were used. Bond strength increased with increasing surface area and polymerization time. These factors were independent and additive, without a potentiating effect on each other. Polyglactin 910 knitted mesh was used as the scaffold and butyl-cyanoacrylate was the tissue adhesive. This combination
appears to hold promise as it eliminates scleral needle passes, but appears to provide strong bonding to avoid muscle belly slippage.

**Factors related to strabismus decompensation after a period of prolonged postoperative stability.** Adler E, Ding K and Siatkowski M. J AAPOS 2014;18:50-55.

This study identified clinical and demographic factors associated with late decompensation of horizontal strabismus after good postoperative alignment of at least 12 months. Medical records of surgeries performed by a single surgeon over a 10-year period were reviewed retrospectively. At least two years of follow-up were required. 185 cases were included (172 different patients) with a mean follow-up of 62.2 months. 31% of cases (n=57) decompensated. The three key factors which increased the risk of decompensation were: pre-operative oblique dysfunction, and deviation size (distance and near) at the first >12 months postoperative visit. For distance deviations, 4 PD to <8 PD had a higher rate of decompensation than 0 PD to <4 PD. For near deviations the >=8 PD had a higher rate of decompensation than the 0 PD to <4 PD group. The authors made no effort to separate type of strabismus (eso or exotropia) or type of surgery performed.


This study describes a new surgical technique to treat acquired Brown syndrome. The goal was to release adhesions. Depending on the location of the adhesions, either the trochlea was reconstructed or a trochlea adhesiotomy was performed. Results of surgeries from a two-year period were reviewed retrospectively. Intraoperative forced duction testing confirmed the location of the lesion. Six patients with a mean age of 46.8 years were operated on. Five patients had Brown syndrome secondary to trauma, one secondary to frontal sinusitis. Two patients received trochlea adhesiotomy alone, the other four had trochlea reconstruction surgery. Mean follow-up was 15 months. Five of the 6 patients had improved Hess chart scores postoperatively and 4 of 5 had improved binocular single vision (this was not testable in one patient who was 4 years old). Primary position hypotropia improved in 5 patients. Iatrogenic superior oblique palsy did not develop in any patient. This surgical technique allowed direct visualization of the trochlea, allowing determination of the exact adhesion site, and preserving superior oblique function. No artificial materials were required.


The purpose of this study was to identify which specific aspects of function-related quality of life reported on the Adult Strabismus 20 questionnaire (AS-20) improve postoperatively in nondiplopic patients with childhood-onset strabismus. This was a retrospective study looking at AS-20 results preoperatively and 1-year postoperatively. Twenty patients were included with a median age of 46.5 years.
Nine of 10 AS-20 function-related items showed statistically significant improvement pre- to postoperatively. The top five items that improved were, “I feel stressed because of my eyes”, “I worry about my eyes”, “In need to take frequent breaks when reading because of my eyes”, “I can’t enjoy my hobbies because of my eyes”, and “My eyes feel strained”. This study shows that adult strabismus patients can obtain function-related benefits, in addition to psychosocial related benefits from surgery. This cohort was small and no included patients had diplopia. No surgical failures were included so a comparison between surgical success patients and failure patients cannot be made in regards to the effect of surgery on AS-20 results.


Consecutive patients over a 3-year period received one of the two procedures unilaterally and the data was reviewed retrospectively. It is unclear in the paper whether the surgical technique used in a given case was decided randomly or not. If not this could bias results. Both groups were followed for 12 weeks. There were 15 patients total. Seven patients underwent Y-split of the lateral rectus and 8 underwent anchoring of the lateral rectus muscle to the lateral palpebral ligament. Preoperative deviation size and head postures were similar in the two groups. Both groups showed post-operative improvement in head posture and primary position deviation. Upshoots and downshoots improved in 7/7 Y-split patients and 7/8 anchor patients. One patient in the anchor group developed a post-operative esotropia. The anchor surgery took an average of 8.3 minutes, while the Y-split surgery took an average of 15.3 minutes. This study was small, retrospective and followup was short. It is unclear if randomization took place.


This study compares oculocardiac reflex (OCR), postoperative vomiting, and visual status in strabismus patients treated using the same anesthetic method. Surgical results from a three-year period were reviewed retrospectively. 111 patients were included (12 were excluded for incomplete data). The mean age at surgery was 17.9 years. 41 patients had OCR. Of these 93% had bradycardia and 7% had dysrhythmia. OCR occurred on manipulation of the first muscle, second muscle, third muscle, 24%, 28%, 38% respectively. There was a significant association between the presence or absence of OCR during traction on the first muscle with traction on the second muscle. There was no significant difference in OCR rates between medial and lateral rectus muscles, or between esotropia and exotropia. The two most important predictors of OCR were the number of muscles operated on and having coarse stereopsis (instead of fine stereopsis). Younger age and female sex were also associated with greater risk.
of OCR. In addition, OCR and more operated muscles were associated with postoperative vomiting.


The authors developed an analysis tool that takes into account surgeon-determined goals for intervention. Over a 6-year period 777 patients met inclusion criteria. Patients underwent surgery to establish binocularity, restore eye contact, resolve diplopia and remediate torticollis. Surgical success was defined based on the reason for surgery. Overall 71% of patients had an excellent outcome and 14% had a good outcome. Risk factors for reduced surgical success included prior strabismus surgery, preoperative angle $\geq 50$ PD, and surgery performed prior to 12 months of age. Prior surgery specifically reduced the success in the establish binocularity group. This study is interesting in that the cause for surgery determines outcome success and success can include nonsurgical methods in addition to the surgery. For example the reconstructive group success was based on near deviation, which is what people ‘see’, and diplopia resolution success allowed postoperative prisms (this would be a ‘good’ outcome). Surgical success results may have had bias since there was no masking, and surgical techniques were not uniform.

**Surgical management of long-standing antielevation syndrome after unilateral anterior transposition of the inferior oblique muscle.** Han J, Han SY, Lee JB and Han S-H. J AAPOS 2014;18:232-234.

This study reports the surgical management of 3 patients with long-standing antielevation syndrome after unilateral anterior transposition of the inferior oblique muscle. Postoperative followup was at least 3 months. One patient underwent a denervation-extirpation of the inferior oblique, followed by a contralateral superior rectus recession. One patient underwent a denervation-extirpation, followed by an ipsilateral inferior rectus recession and a contralateral superior rectus recession. The final patient underwent a denervation-extirpation, simultaneously with a ipsilateral inferior rectus recession and a contralateral superior rectus recession. It appears denervation-extirpation alone is not beneficial in these types of patients, based on a very small series of patients.


This study is a retrospective chart review of the one year surgical results for 39 patients who had a diagnosis of early-onset exotropia and subsequent surgical intervention. All patients underwent bilateral lateral rectus recession by the same surgeon as the primary procedure. “Success” at one year was defined as exodeviation less than 8 prism diopters or esodeviation of less than 5 prism diopters without having undergone a re-operation. 75% of their patients fit this criteria. The age of surgery and the pre-operative duration of misalignment were evaluated and suggestions for appropriate timing for surgical intervention were
made. The odds of successful outcome diminished significantly with preoperative duration of misalignment over 24 months, but age at surgery had no effect on outcome. Their multiple logistic regression model illustrated a risk estimate of “failure” over 6-fold if duration of deviation was greater than 24 months before surgical intervention.


The purpose of this study was to present the results of single-stage adjustable surgery under topical anesthesia in the treatment of symptomatic small-angle strabismus. Thirteen patients with small angle strabismus and symptomatic uncorrected diplopia or asthenopia were consecutively recruited. Small angle strabismus was defined as less than 20 prism diopters horizontally and 10 prism diopters vertically in best refractive correction. Patients received unilateral surgeries using the same surgical protocol, which was either recession or resection, and all procedures were performed by the same surgeon. Surgery was performed successfully in all patients without complications. Out of a total of thirteen patients, two reported mild pain when incisions were made through the conjunctiva, and five felt pain during traction on the extraocular muscles. Administration of oxybuprocaine controlled the discomfort in these patients. Afterwards, all patients reported complete resolution of the primary symptoms, the procedure was tolerated well, and no complications occurred.

**Effect of strabismus surgery on torticollis caused by congenital superior oblique palsy in young children**


A non-comparative interventional case series of 13 cases of congenital superior oblique palsy with head tilt, who underwent simultaneous superior oblique tuck and inferior oblique recession were studied. Purpose was to evaluate the outcome of strabismus surgery for congenital superior oblique palsy (SOP) in relation to correction of head tilt and hypertropia. Mean pre- and post-operative hypertropia (p.d.) in forced primary position was 19 ± 7 and 2 ± 6, respectively (P < 0.0001). The head tilt reduced from mean of 17 ± 9 to 2 ± 2 degrees (P < 0.0001). Success, defined as hypertropia <5 PD and head tilt less than 5 degrees, was achieved in 69% (9/13. C.I. 42–88%) and 85% (11/13. C.I. 56–96%), respectively. The success rate for achieving both criteria was 61.5% (C.I. 35–88%). Five patients required additional surgery; usually a contralateral inferior rectus muscle recession, which was successful in all cases. One case developed asymptomatic Brown syndrome (7.69% - C.I. 6.7–22.2). Simultaneous superior oblique tuck and inferior oblique muscle recession can successfully treat selected cases of congenital superior oblique palsy. About one-third required an additional procedure, which led to total normalization it is cautioned that simultaneous superior oblique tuck
and inferior oblique recession may not be the standard of care in all the cases. This form of surgical treatment needs to be chosen on a case-to-case basis of the head position.

SUB-TENON BLOCK DOES NOT PROVIDE SUPERIOR POSTOPERATIVE ANALGESIA VS INTRAVENOUS FENTANYL IN PEDIATRIC SQUINT SURGERY

This study of 67 children, aged 2-12, compared the efficacy of a sub-Tenon block in decreasing perioperative pain, intraoperative oculocardiac reflex (OCR), and postoperative nausea and vomiting (PONV) as compared to IV fentanyl in pediatric strabismus surgery. There was no statistical difference in the postoperative pain scores in the recovery room in the first 2 hours after surgery. However, the incidence of oculocardiac reflex and postoperative nausea and vomiting was significantly higher in the IV group in the first two hours.

Resident and Fellow Participation in Strabismus Surgery: Effect of Level of Training and Number of Assistants on Operative Time and Cost T W Winter, R J Olson, S A Larson, T A Oetting, Ophthalmology March 2014; 121:797-801

This is a comparative case series of 993 children and adults between the ages of 6 months and 75 years evaluated between July 1, 2008, and December 31, 2012, by any of 3 attending surgeons assisted by a resident in the postgraduate year 3 (PGY3) and a fellow in the postgraduate year 5 (PGY5) or both. Main Outcome Measures: Operative time in minutes and associated operative cost (dollars). Conclusions: Operative time in strabismus surgery increased with the addition of resident PGY3 participation and further increased with both assistants (PGY3 and PGY5) over either assistant alone. Operative times earlier in the year did not vary from those later in the year for PGY3 or PGY5 assistants. The difference in quarterly and individual PGY3 but not PGY5 assistant operative times suggests that efficiency in strabismus surgery varies by assistants with less experience or interest.


The purpose was to evaluate the results of bilateral lateral rectus (BLR) recession which is based on ‘augmented surgical amounts’ of classical surgical table of Parks’ for basic and pseudo-divergence excess type intermittent exotropia [X(T)]. 37 patients were included. The mean age was 6.78 ± 2.87 years
(range: 2–12 years). Mean preoperative deviation was 29.72 ± 8.07 PD (range: 15–45 PD) at distance and 20.94 ± 11.65 PD (range: 10–45 PD) at near (P < 0.0001). There were 21 (56.8%) patients in Group 1, 9 (24.3%) patients in Group 2, 1 (2.7%) patient in Group 3 and 6 (16.2%) patients in Group 4. Initial esotropia was achieved in 30 (30/37) of the patients. 28 of them had good results at the end of the 6 months. Overall “motor surgical” success rate was found to be 89.2% (33/37 patients), with 1 (2.7%) overcorrection and 3 (8.1%) recurrences at the end of the 6 months.

This study demonstrated that early overcorrection of 10–20 PD after X(T) surgery can achieve acceptable motor outcomes in the first 6 months postoperative period.


This is a prospective surgical study investigating surgical outcomes of different surgery procedures for convergence insufficiency (CI) – type intermittent exotropia (IXT) in children. The study investigated 45 children with 6 months of follow-up. The children were randomly divided into three groups: the unilateral medial rectus resection (UMR) group (15 patients), the bilateral medial rectus resections (BMR) (14 patients), and the improved unilateral recession-resection (R&R) group (16 patients). In the UMR and BMR groups the resections were based on the distance exodeviation. In the R&R group the resection was based on the near exodeviation and the recession was based on the distance exodeviation. A successful surgical alignment was defined as the distance deviation in primary gaze to be between < 10 prism dipters (PD) of esophoria/tropia and < 5 PD of esophoria/tropia. At the 6 month follow-up the success rate in the R&R (87.5%) group was significantly higher than those in the UMR (13.3%) and BMR(42.9%) groups (p = 0.000 and 0.008). There was no significant differences in the mean near-distance differences between the R&R group and the other two groups (p>0.05). The authors conclude that the R&R procedure has a better alignment than the UMR and BMR surgeries for children with CI-type IXT. They also note that all three treatments reduce the near-distance differences in this patient population. The study is limited by its small sample size and short follow-up. The authors also point out that using the distance exodeviation for the UMR and BMR groups may be insufficient as all of the cases that did not meet criteria for success were undercorrections.
The relationship between preoperative and postoperative near stereoacuities and surgical outcomes in intermittent exotropia
Dae Seung Lee, Seong-Joon Kim, Young Suk Yu British Journal of Ophthalmology. 2014;98:10 1398-1403

This is a retrospective chart review of postoperative stereo acuity in patients with intermittent exotropia. 137 records were reviewed. Children less than 5 years of age were excluded and at least 1 year of postoperative follow-up was required. Patients were divided into 3 groups based on the degree of stereopsis: good (40-60 arcsec), moderate (80-200 arcsec), and poor (>200 arcsec). These groups were compared with each other with respect to preoperative and postoperative clinical features. Poor stereopsis was found in 19 (13.9%) patients, moderate in 62 (45.2%), and good in 56 (40.9%) patients. There were no statistically significant differences in preoperative deviations, postoperative deviations, or surgical success rates. The preoperative and postoperative stereoscopic statuses were similar in each group. Patients with better stereopsis tended to be older when the intermittent exotropia was first detected and showed better best corrected visual acuity. The authors conclude that near stereopsis is a useful tool for initial sensory status and postoperative prognosis in patients with intermittent exotropia. This study is limited by the small size and retrospective nature.

Factors associated with the angle of exodeviation in patients with recurrent exotropia
Byung Joo Lee, Seong-Joon Kim, Young Suk Yu


This study compares preoperative and postoperative distance deviation angle in recurrent exotropes to determine factors associated with large-angle recurrent exotropia. The authors included 242 patients with 2 years of postoperative follow-up. Of these 83 patients showed recurrent exotropia. The authors found that the bigger preoperative angle of deviation was associated with a better angle of recurrence. However, in patients with smaller preoperative angles of deviation they found that the angle of recurrence grows closer to the preoperative one. Only six patients showed a postoperative recurrence larger than their preoperative deviation. These patients had a smaller mean preoperative angle. The authors conclude that the incidence of recurrent exotropia with a relatively large angle (greater than or equal to their preoperative deviation) is low among patients who underwent surgery for exotropia (2.5%). They do note that the ratio of relatively large angle recurrence was higher in patients with small preoperative exodeviations and basic type exotropia. This study is limited by its retrospective nature and the small number of patients with large angle recurrences.
Efficacy of diagnostic monocular occlusion in revealing the maximum angle of exodeviation


A retrospective study to determine the efficacy of diagnostic monocular occlusion in revealing the maximum angle of exodeviation compared with repeated measurements taken during three or more consecutive examinations in the outpatient clinic. 185 patients with intermittent exotropia were examined. The angle of deviation was measured at distance and near fixation on three or more consecutive examinations and then 1 day of diagnostic monocular occlusion was performed. After diagnostic monocular occlusion, the mean angle of deviation at distance (23.5 prism diopters (PD)) and near fixation (23.5 PD) was significantly smaller compared with the maximum angle of deviation at distance (27.0 PD) and near fixation (25.2 PD) (p=0.001, 0.022). However 14.1% of patients showed an increase of > 5 PD in their distant angle after occlusion and 30.8% of patients showed an increase of > 5 PD in their near angle of deviation. After occlusion 39.1% (9/23) of divergence excess type, 20.0% (3/15) of convergence insufficiency type and 2.7% (4/147) of basic-type exotropia were converted to other types. Patients were hyperopia were more likely to show a significant increase during near fixation. The authors conclude that diagnostic monocular occlusion could be useful in patients with divergence excess type or convergence insufficiency type exotropia and with hyperopia. In other cases they feel its role is limited in determining the maximum angle of exodeviation when compared with multiple exams. This study is limited by its retrospective nature and the authors report the potential for a selection bias towards patients with poor fusional capacity as most of the patients were scheduled for surgery.

Dual application versus single application of povidone-iodine in reducing surgical site contamination during strabismus surgery.


Contamination rates of patients who underwent strabismus surgery were evaluated over a 10-month period. The dual application (DA) group received an additional 2 drops of povidone-iodine 5% in the conjunctival fornices after draping but prior to incision. 104 patients were included: 44 single-application (SA). In the SA group, 25% had bacterial contamination of either the surgical site or sutures. The most common location was the conjunctival site. All grew coagulase-negative Staphylococcus. The DA group had 10% contamination (3 suture, 3 surgical site). Two plates grew coagulase-negative Staphylococcus, 2 gre Streptococcus, 1 Bacillus and 1 S. aureus. This difference was statistically significant. There were no cases of endophthalmitis and only one infection postoperatively (coag. Neg. staph) and this was a conjunctival abscess in a patient with lagophthalmos. The lid speculum contamination rates were unaffected by additional application of Povidone-Iodine. The DA group largest reduction of contamination rates was at the conjunctival incision site.
Characteristics and surgical results in patients with age-related divergence insufficiency esotropia. Repka MX and Downing E. J AAPOS 2014;18:370-373

This study presents a large cohort of patients with adult-onset divergence insufficiency and reports surgical outcomes. This study included consecutive patients over age 40 years over a 34 year period. 85 patients with a mean age of 74 years with no pathology on imaging were included. The mean angle of esotropia was 12 PD at distance and 5.4 PD at near. 15 cases were diagnosed in the first 25 years and 40 cases were identified in the last six years. There was no specific surgical protocol. There was a tendency for overcorrections at near with bimedial rectus recessions and overcorrection at distance with unilateral R&R. For bimedial rectus recession, conventional surgical tables were inadequate, and surgical dose was found to be a poor predictor of surgical effect. The authors feel recognition and diagnosis of this condition have increased dramatically over the last five years, but this observation cannot be proven by study design. This study has retrieval bias and incomplete data but does highlight a condition that clinicians need to be aware of.


The authors present 5 patients who required further surgery after bilateral modified Harada-Ito procedures. Inferior transposition of the bilateral medial rectus muscles to reduce V pattern eso- or exodeviation was performed but produced a large degree of excyclotorsion and intractable diplopia. All patients were adults with acquired 4th nerve palsies (closed head injury (3), AVM (1), and post-surgical. All 5 required reversal of the medial recti transpositions to relieve the diplopia. The authors suggest that normal excyclotorsion is exaggerated in the presence of bilateral superior oblique weakness. Previous bilateral Harada-Ito procedures should reduce the risk of causing diplopia but may not be powerful enough in patients who already have significant paretic superior oblique muscles.


This study evaluates the efficacy of bilateral superior oblique posterior 7/8 tenectomy (combined with horizontal strabismus surgery) in the setting of A-pattern strabismus with superior oblique overaction in a large retrospective review of 10 years of medical records. 73 patients with an average age of 13.1 years were evaluated. The preoperative pattern average 19.6 PD and collapsed 18.5 prism diopters. The preoperative superior oblique overaction was 2.3 and was reduced to 0.3 2 weeks after surgery. No significant surgical complications occurred over a mean follow-up of 28 months. Residual patterns were greater in the setting of preoperative exotropia. The procedure seems to be self-calibrating,
as the larger patterns collapsed to a greater degree than the smaller patterns. There was no control group and the study was retrospective.


This was a retrospective review of adults 60 years of age or older who underwent this surgery over a three-year period. 19 patients with an average age of 79.8 years were evaluated, but another 30 patients were excluded. Post-op follow-up ranged from 28 days to 1 year. 11/19 patients had under 50 days of follow-up which severely compromises any study results for long-term success. Median distance esotropia was 16 PD pre-op and 0 PD post-op. No lateral incomitance occurred and diplopia resolved in all cases.

**Assessment of torsion after superior rectus transposition with or without medial rectus recession for Duane syndrome and abducens nerve palsy.** Velez FG, Oltra E, Isenberg SJ and Pineles SL. J AAPOS 2014;457-460.

Torsional outcomes after superior rectus transposition surgery were assessed. Patients had esotropic Duane syndrome, or complete 6th nerve palsy and underwent full-tendon superior rectus transposition to the lateral rectus muscle insertion with a posterior fixation myopexy. All patients had at least 8 weeks of follow-up. 11 subjects (4 with Duane syndrome) were included. 7/11 underwent double Maddox rod testing and subjective excyclotorsion improved from 4.7+/−3.8 to 0.0+/−5.0 post-operatively. ¾ patients who were evaluated by fundus torsion showed no change, but one developed marked incyclotorsion. This was a small study with multiple surgeons and a lack of a uniform surgical technique. Diplopia-free fields were not measured and torsional measurements were not standardized. This procedure may induce clinically significant post-operative incyclotorsion.


The authors attempt to augment surgical effect, and thereby lessen the number of muscles operated on, by adding a central tenectomy. Patients were prospectively enrolled over a 3-year period. The effect was similar to a central sag. 16 horizontal muscles of 16 eyes of 12 patients were included, with a mean age of 24.8 years. No overcorrections occurred, ductions were full and no reoperations were required at one-year follow-up. Median achieved corrections at distance and near were significantly higher (for the overall group and for exotropes but not for the esotropic subgroup) than the expected median correction. Mean tenectomy effect was higher for the esotropic group than the exotropic group but there was no statistically significant difference. The goal of this study is to augment effect but avoid crippling ductions in larger-angle strabismus cases. The study has numerous problems though: small size limits
true ability to compare groups, very variable effect of central tenectomy, confusing data, and a lack of a control group.

**Consecutive exotropia: why does it happen and can medial rectus advancement correct it?** Gesite-de Leon B and Demer JL. J AAPOS 2014;18:554-558.

The authors investigated consecutive exotropia: is it due to slippage of the medial rectus? does medial rectus advancement effectively treat it? and what factors lead to a good outcome?. This was a 17-year retrospective chart review. 20 patients met inclusion criteria. Consecutive exotropia surgery occurred at an average of 14.6 years after initial surgery. Of the 14 patients with known prior surgical dosage, 5 had slippage of 2.5 mm. Mean alignment pre-operatively was 28 PD exotropia at distance and 29 PD exotropia at near. Immediate post-operative alignment was 2 PD esotropia. At 4-8 weeks postop, there was an average exoshift of 7 PD. At final follow-up 1.6 years postop, 10 patients (50%) maintained alignment within 10 PD of orthophoria; the rest developed recurrent exotropia. No risk factor could be identified as resulting in better or worse surgical success. Exoshift occurred over time. Of the 13 patients who had preoperative duction deficits, 9 (69%) normalized. No patient displayed a stretched scar. Size of preoperative exodeviation did not predict the presence or degree of muscle slippage, suggesting other factors may be at work.


The authors determined the incidence and degree of lateral incomitance initially and long-term in exotropes who underwent unilateral surgery. Enrolled patients were greater than 7 years old and represented consecutive patients over a two-year period who were prospectively evaluated. Twelve patients (ages 29-74) were enrolled (9 underwent an R&R and 3 underwent a unilateral LR recess). Ten of the 11 patients who were evaluated within 1 wek of surgery had a greater effect from surgery in gaze toward the operated eye with an average incoma of 14 PD. Nine patients were followed for more than 3 months, with no change in the amount of incomitance compared to immediate post-op. Initially, five patients were diplopic in gaze towards the operated eye, and three remained so at long-term follow-up. The study included some patients with larger deviations who might have been better serve by operating on more muscles with corresponding lower surgical dosages. Also this study combines one-muscle and two-muscles cases with no ability to separate results.

**Sustained improvement of reading symptoms following botulinum toxin A injection for convergence insufficiency** Saunte JP, Holmes JM Strabismus. September 2014;22(3):95-99

**Purpose:** To evaluate the use of botulinum toxin A in adults with convergence insufficiency

**Methods/Results:** Retrospective review. Eight patients (median age 36 years,
range 17 to 77 years) with reading symptoms due to convergence insufficiency defined as an exodeviation greater at near, not exceeding 10 PD in the distance measured by prism and alternate cover test, and either convergence near point >6 cm or reduced fusional amplitudes were included. All patients were symptomatic after prior treatment by convergence exercises, base-in prism glasses or strabismus surgery. Five patients received injection of 5 IU botulinum toxin to one lateral rectus muscle, two received 2.5 IU, and one received 2.5 IU to both lateral rectus muscles. At 1 month post injection, all patients had reduction of exodeviation from baseline (median 9 PD, \( p = 0.008 \)) at near; 2 patients had a temporary intermittent esotropia at distance with diplopia. At 6 months, patients still maintained a small reduction of exodeviation (median 4 PD, \( p = 0.3 \)) at near. Reading symptoms improved in 7 of 8 patients at 1-month post injection, and in all patients at 6 months. Interestingly, 3 patients reported improved reading despite returning to the baseline angle at 6 months.

Conclusion: In adult convergence insufficiency, botulinum toxin injection to a lateral rectus muscle improves reading symptoms beyond the duration of the pharmacological effect. Botulinum toxin injection may be useful in management of adult convergence insufficiency, although repeat injections may be needed. The main limitations of this study are the small sample size, short follow-up time and possibility of a placebo effect.

Results of Bilateral Medial Rectus Recession for Comitant Esotropia in Patients with Developmental Delay
Swaminathan M, Shah SV, Mittal S, Gunasekaran A
Strabismus. September 2014;2(3):138-142

Purpose: To determine the results of strabismus surgery for esotropia among children with developmental delay.
Methods/Results: Retrospective review. 25 patients with developmental delay (excluding Down syndrome) and 53 normal children who underwent bimedial recession for comitant esotropia were included. Age, refractive error, and preoperative angle of deviation were comparable in both groups. Amount of surgery performed was compared with standard table to determine the angle of deviation that would have been corrected by the surgery. Response to surgery was defined as percentage of change in angle of deviation after surgery to the operated angle of deviation. Success rate was 60% with an average of 72.13\% \pm 16.08 of angle of deviation operated in patients with developmental delay, whereas in the control group the success rate was 73.5\% with an average of 89.08\% \pm 10.83 of angle of deviation operated. Response to surgery was 134.06\% \pm 51.62 in the developmental delay group vs 89.83\% \pm 22.49 in the control group. Mean amount of surgery performed in patients with optimal outcome was 70.67\% \pm 17.95 in the developmental delay group vs. 90.56\% \pm 9.99 in the control group.

Conclusion: Surgical outcome in patients with developmental delay is unpredictable. An exaggerated response to standard amounts of bimedial recession should be anticipated. Operating for 70.67\% \pm 17.95 of angle of deviation seems more likely to be successful in patients with developmental delay. A limitation of this study is the short follow-up time; surgical success was determined at 6-week postoperative follow-up.

Purpose: To evaluate the effect of uni- and bilateral medial rectus recession on squint angle and ductions in Graves’ orbitopathy patients.

Methods/Results: Retrospective study. 102 patients were included, 24 were operated on one medial rectus and 78 on two medial rectus muscles. Mean recession was 3.3 [2.0–5.0] mm in the unilateral group and 4.5 [2.5–7.0] mm per eye in the bilateral group. Dose-effect response was calculated by dividing the “preoperative – postoperative squint angle” by the amount of recession. The dose-effect response was 1.0 [−0.6–3.8]°/mm in the unilateral and 1.4 [0.2–3.0]°/mm in the bilateral group (p = 0.000). In the bilateral group, the maximal abduction and adduction changed significantly, however, the total duction range remained unchanged. The extent of the preoperative abduction did not influence the dose-effect response, nor did the muscle volume. The results after orbital decompression were comparable with those without previous orbital surgery. Twenty-three patients (23%) needed additional horizontal squint surgery.

Conclusion: The authors found significantly lower dose-effect response ratios as compared to other studies. The amount of abduction deficit did not influence outcome. To the best of the authors’ knowledge this study presents the largest case series of pure medial rectus recessions in Graves’ orbitopathy patients.


This prospective cohort study provides objective information on patients' preoperative expectations and actual discomfort after strabismus surgery. This is a very useful study for any strabismologist because it provides insight into what patients may be expecting regarding their experience with surgery. A questionnaire was used to evaluate the following on a scale of 0 (absent) to 10 (very severe). Patients' expectations of pain, blurred vision, daily life disruption, diplopia, conjunctival redness, foreign body sensation, eyelid swelling, postoperative nausea and vomiting, and post-operative cosmetic satisfaction. Patients answered the questionnaire at 6 hours, 1 day, 2 days, 3 days, 1 week, 2 weeks, 1 month, and 3 months after surgery. Postoperative pain, nausea, and vomiting occurred at significantly lower-than-anticipated levels. Blurred vision, daily life disruption, and conjunctival redness occurred at significantly higher-than-expected levels. Patients felt that conjunctival redness was the most severe symptom occurring immediately after surgery. Patients who required vertical or oblique muscle procedures or had undergone previous ophthalmic experienced higher levels of postoperative pain than they had preoperatively anticipated.

This is a case report of a 9-year-old child who had consecutive cyclic esotropia after surgery for intermittent exotropia. The patient was referred with a complaint of diplopia and inward deviation of right eye on alternate days for 2 years after corrective surgery for his exotropia. The patient had developed an intermittent exotropia at age 5 years. He was treated with correction of the moderate myopia at that time, but the condition progressed and he underwent right lateral rectus recession and medial rectus resection at 7 years of age at local hospital. He was esotropic instantly after surgery and complained of diplopia. He was treated with patching therapy, alternating eyes. A few weeks later, he experienced development of cyclic esotropia, which began to appear on alternate days. The cyclic phase persisted for 2 years, after a 48-hour alternate-day pattern. After strabismus surgery for the esotropic angle, the deviation disappeared and the patient remained orthotropic.

Outcomes of Strabismus Surgery with or without Trainee Participation as Surgeon

This study was done at the Department of Ophthalmology and Visual Sciences, Vanderbilt Eye Institute, Vanderbilt University, Nashville, Tennessee; Department of Ophthalmology, Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, Ohio. This is a retrospective comparative case series involving 543 patients (921 eyes) from different institutions in the Midwest United States undergoing eye muscle surgery with or without training participation. Strabismus surgery was done for horizontal deviations only. The purpose of the study was to compare success rates of strabismus surgery. It involves trainees/ophthalmology residents versus those performed solely by staff surgeons. Results: Trainees were involved in surgery on 396 patients (672 eyes) where staff surgeons were involved in 147 patients (249 eyes). After a minimum follow-up of 8 weeks, there was no significant difference between the success rates of procedures that involved trainees versus staff surgeons.

Comment: The involvement of trainees as surgeons, particularly in training institutions did not result in a worse outcome than surgeries performed by staff. This has importance in the fact that it provides data to support the high quality of surgery provided by trainees. Important data was a definite shift toward competency based education and more scrutiny of patient outcomes. The surgeries involved “primarily horizontal deviations.”
A Comprehensive Clinical Study About Patching After Strabismus Surgery  
Wenqiu Zhang, Jihong Zeng, Jinying Liao, Tao Yang, 

This is a prospective study comparing the perioperative behavior of 61 children who underwent strabismus surgery randomized into two groups: post-operative patching or no patching. They were analyzed by: The Faces Pain Scale–Revised score or numerical rating scales score, Children’s Hospital of Eastern Ontario Pain Scale (CHEOPS) score, crying time, and preoperative and postoperative physiologic parameters. The conclusion of this study is that patching is not necessary for reducing postoperative pain or the risk of infection in children undergoing strabismus surgery.

11. ANTERIOR SEGMENT

Successful Management of Secondary Iris Cysts With Viscoelastic-Assisted Endophotocoagulation  

The authors describe a technique of obliterating secondary iris cysts in a series of 4 patients, one of whom is a 4 year old child. Iris cysts in the pediatric population can grow and occlude the angle resulting in glaucoma or obstruct the visual axis, leading to amblyopia. Surgical management includes aspiration, surgical excision, cryoablation, photocoagulation, or intracystic irrigation of a cytotoxic agent such as ethanol. The ideal approach would have a low incidence of side effects and have a low incidence of recurrence. The authors aspirated the cysts and then injected viscoelastic to isolate the cyst and separate it from the cornea and angle. Viscoelastic was also used to flatten the cyst and then a 20-gauge diode endolaser photocoagulator (QuantelMedical) was introduced. Laser was applied to encircle the cyst and then was applied directly to the roof of the cyst, titrated to cause tissue shrinkage and closure of the potential space. Postoperative medications included topical antibiotics and corticosteroids for 2 weeks. One patient had an early recurrence, which was successfully retreated. With a mean follow up of almost 3 years, no further recurrences were noted. There were no side effects.

Varicella-Zoster Virus Detection in Varicella-Associated Stromal Keratitis  
A Y. Matoba, B Meghpara, P Chevez-Barrios,  JAMA Ophthalmol  

The authors present the first documented case of PCR-confirmed varicella-zoster virus in a 9 year old patient with disciform keratitis. The child had a primary varicella infection 3 months prior to a complaint of blurry vision. Serology confirmed IgG and IgM varicella-zoster virus antibodies. The clinical course led to a penetrating keratoplasty. Host cornea was dissected into an anterior and posterior layer. Histopathology revealed a diffuse lymphocytic infiltrate and PCR for varicella-zoster virus was positive only in the deeper stroma/endothelium.
specimen. The authors conclude that primary varicella infection of the cornea can produce a disciform keratitis and that this should be kept in the differential of stromal keratitis.

**Iris Stromal Cyst Management With Absolute Alcohol–Induced Sclerosis in 16 Patients**  

The management of iris cysts is difficult. Recurrence is common with simple aspiration and other procedures including excision, cryotherapy, intracameral cautery or photocoagulation are associated with significant risks. The authors detail their experience with aspiration and microscopically guided injection of absolute alcohol on the involution of 16 cysts, the effect on vision and side effects from the procedure. Six were congenital stromal iris cysts, 4 were acquired, and 6 were secondary. All had failed prior treatment such as aspiration. At the end of the study period, 14/15 cysts had sclerosed (n=1) or involuted (n=13) with one (n=10), 2 (n=2) or 3(n=2) treatments with aspiration and injection of absolute alcohol. Vision remained stable in 14/15 of patients. Complications included transient corneal edema (n=4) and transient anterior chamber inflammation (n=1).

**Management of Extensive Epibulbar Choristoma Associated With Microphthalmos A Rare Clinical Entity**  

A choristoma is a benign tumor composed of normal tissue elements in the wrong location. Congenital epibulbar choristoma with microphthalmos is a rare entity and the authors describe a novel approach using an autologous skin graft over the partially resected lesion to promote cosmesis and orbital growth without the need for a socket expander. The authors describe this approach in 2 children and advise that all uveal appearing tissue is removed to reduce the risk of sympathetic ophthalmia in the fellow normal eye.

**Successful Long-term Management of Iris Flocculi and Miosis in a Patient With a Strong Family History of Thoracic Aortic Aneurysms and Dissections Associated With an MYH11 Mutation**  

The authors present a case report of a 13 year old boy with visually symptomatic iris flocculi. Flocculi are posterior pigmented epithelial cysts of the pupillary ruff. The patient had associated miosis, nystagia and photophobia. The authors dissect the cysts and perform iris sphincterotomies which alleviate the patient’s symptoms. The authors highlight the association with familial transthoracic aortic aneurysm and aortic dissection (TAAD), which resulted in the early death of several of the patient’s paternal family members. Genetic testing revealed a
mutation in MYH11 (smooth muscle myosin heavy chain 11), a gene known to be associated with TAAD.

**Corneal resistance factor and corneal hysteresis in a 6- to 18-year-old population**  

In this cross-sectional study, schoolchildren ages 6-18 years underwent analysis of corneal biomechanical properties. The purpose of the study was to determine the distribution and normal range of the corneal resistance factor (CRF) and corneal hysteresis (CH) in this population. Corneal biometry data is provided for these 683 Iranian children and compared/contrasted against similar biometry data from other races/populations. Corneal biometrical properties play a role in the understanding of glaucoma and keratoconus. The authors confirm a previously reported observation that corneal hysteresis decreases with increased axial myopia.

**Paediatric and adolescent elevated conjunctival lesion in the plical area: lymphoma or reactive lymphoid hyperplasia?**  
G Beykin, J Pe’er, G Amir, S Frenkel  

This paper investigates the features of ‘salmon patch’-like conjunctival lesions in the pediatric and adolescent population. The authors performed a chart review of patients presenting between 2000 and 2011 with conjunctival ‘salmon-patch’-like lesions in the plical area. Eleven patients aged 6-21 years presented with an elevated pink conjunctival mass in the plical area of one or both eyes. 9 patients underwent excisional biopsy. The other two patients were treated with antiallergic medication with resolution of the lesion and were therefore diagnosed clinically with reactive lymphoid hyperplasia. Of the 9 patients who underwent biopsy, histopathology demonstrated extranodal marginal zone B cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) in 2 cases and reactive lymphoid hyperplasia in 7 cases. Molecular diagnosis showed polyclonal B cells in six patients, monoclonal B cells in two patients, and a questionable status in one patient. The authors conclude that it is clinically difficult to differentiate between conjunctival reactive lymphoid hyperplasia and MALT lymphoma in the pediatric and adolescent population. They suggest that a short treatment course with antiallergic drops may sometimes assist diagnosis.

**Superior rectus underaction following botulinum toxin injection to induce protective upper eye lid ptosis – a comparative study of two techniques**  
Sadiq SA, Dharmasena A.  

This retrospective study compared the incidence of reduced upgaze in transcutaneous versus transconjunctival administration of BTXA (Dysport) to induce protective ptosis in patients with exposure keratopathy due to facial nerve palsy. Group A had 20 patients who received a mean dose of BTXA of 10 units though the upper eyelid skin crease and Group B had 15 patients who were injected an average of 54.8 units into the subconjunctival space at the superior border of the tarsal plate. Reduced upgaze occurred in 9 patients (45%) in Group A and in 2 patients in Group B. Approximately 50% of patients in each group required treatment for diplopia lasting for 12 months or more (Fresnel
prism/temporary ocular occlusion). The authors concluded that injecting BTXA to induce protective ptosis via a transconjunctival supratarsal route was significantly less likely to induce superior rectus underaction than when given via the transcutaneous route. Disadvantages to the study include small sample size and retrospective nature of the study.


Treatment of cornea opacities with endothelial keratoplasty (EK) is more frequently performed in adults than children. Indications for pediatric Descemet stripping endothelial keratoplasty (DSEK) in published case series include: congenital hereditary endothelial dystrophy (CHED), pseudophakic cornea edema, Peter’s anomaly, Descemet membrane breaks caused by forceps delivery, posttraumatic globe repair, bee sting, buphthalmos and failed penetrating keratoplasty (PKP). Potential advantages to performing EK versus PKP include faster postoperative recovery and stabilization of refractive error. It has been suggested that the rejection rate for EK is lower than for PKP, but the data lacks long-term follow-up. The surgeon faces additional challenges when performing EK in children due to significant overlying cornea stromal edema resulting in poor visualization of the anterior segment, shallow anterior chamber with relatively anterior lens position, and inability to strip the Descemet membrane from the cornea stroma encountered in CHED. Larger studies with long-term follow-up are necessary to determine if EK is a feasible alternative to PKP.

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Defining success in infant penetrating keratoplasty for developmental corneal opacities

The authors review the literature and report that penetrating keratoplasty (PKP) outcomes for neonatal corneal opacities are not reported consistently and generally describe graft clarity and do not include visual outcomes or the timing of surgery. The authors also report 2 of their cases of infants with unilateral NCO and relatively visual outcomes. One patient had PKP at 5.5 weeks of age, optical correction and amblyopia therapy resulting in best corrected visual acuity of 20/80. The other patient had PKP at 16 weeks of age, optical correction and amblyopia therapy resulting in acuity of 20/125. The authors conclude that timing of surgery within the critical period of visual development may be important in improving outcomes.


The authors characterize the clinical spectrum of this condition. This was a six-year retrospective review. 68 eyes of 40 patients (73% male) were included (70% bilateral). Median age at presentation was 12 months. Of the bilateral cases, 25% showed general pain insensitivity with anhydrosis. 40% of cases had
parental consanguinity. The most common symptoms were a red eye, a white spot on the cornea, and absent tearing. Most patients presented with a lusterless, asymptomatic sterile corneal ulcer. Other systemic symptoms included loss of touch, loss of pain sensation, trophic skin ulcers, oral mucosal ulcerations, and self-mutilating behavior. Treatment included preservative-free tears, antibiotics, goggles, arm splint, and tarsorrhaphy. Mean time to healing of the sterile ulcer was 30 days. Four children required tissue adhesives for corneal melts and 1 child required an evisceration.

**Clinical characteristics and surgical approach to visually significant persistent pupillary membranes.** Kraus CL and Lueder GT. J AAPOS 2014;18:596-599.

The authors present a series of patients treated for clinically significant PPMs. Their technique is described. Ten eyes of six children were included with a mean age at presentation of 7 months and mean age at surgery of 14 months. All patients had good final visual acuities, with a mean follow-up of 5.3 years. There were no intraoperative complications. One patient had mild anisocoria and 2 patients had mild corectopia. Surgery was indicated based on impaired retinoscopy reflex, obscured view of the fundus, or decreased visual acuity on spatial-sweep visual evoked potentials. The authors used a solitary stab-incision, which allowed for a stable chamber and closure with a single suture. The membrane was gently peeled and then cut with intraocular scissors, eliminating the need for a separate infusion port. No lens opacities resulted.

**The Outcomes of Primary Pediatric Keratoplasty in Singapore**

This study attempted to evaluate the long term survival rate of a corneal graft in pediatric eyes. 105 patients below the age of 16 years was examined. The mean age of the patients was 8.38 years and mean follow up was 34 months. 44 eyes had undergone penetrating keratoplasty, 37 underwent anterior lamellar keratoplasty, 22 underwent lamellar corneal patch graft and 2 underwent DSEK. The Kaplan-Meier survival analysis was used for survival scoring. The PK eyes had a survivival rate of 92.8% at 1 year, 88.9% at 2-4 years and 80.9% at 5-16 years. ALK was 88% at 1 year, 84.3% at 2-7 years, and corneal patch graft was 100% at 1 year and 90% at 4-10 years. When indicated, lamellar keratoplasty should be procedure of choice in pediatric patients.

**Robotically Assisted Amniotic Membrane Transplant Surgery**

The uses of amniotic membrane transplantation in pediatric ophthalmology and strabismus include prevention of cicatrical changes in Stevens Johnson syndrome and similar conditions, for treatment of conjunctival scarring after strabismus surgery and for treatment of persistent epithelial defects. The authors describe the first human cases of robotically assisted ocular surgery using the
daVinci SiSurgical System and its feasibility and safety in performing amniotic membrane transplantation. The 3 patients did well but the operative time was prolonged compared to non-robotic surgery. The authors are confident, however, that with further refinement of robotic systems, the advantages will become apparent, including better precision and maneuverability, scalability of motion, tremor filtration, better ergonomics, the ability to simultaneously manipulate 3 surgical instruments and cameras, improved patient access to surgeons, and enhanced surgical training.

12. Cataract

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This study investigated the retinal macular structural features in two groups of patients using Fourier domain optical coherence tomography (FD-OCT): unilateral and bilateral congenital or developmental cataracts. 41 patients (unilateral n=22) aged 5-16 years were enrolled (one was excluded). In the unilateral group the central CST was significantly thicker in the cataractous eye, even after adjusting for axial length. The central outer layer difference was significant, whereas the inner layer was not. Cataractous eyes CST were significantly thicker than pediatric and adult norms. This did not necessarily correlate with poor visual acuity. The sample size was too small to look at cataract subtypes. Eyes with very poor vision or nystagmus were excluded.

Lenticular Changes in Congenital Iridolenticular Choroidal Coloboma.

This retrospective observational case series looked at 145 eyes of 98 patients with diagnosis of congenital iridolenticular choroidal coloboma. The median age at initial visit was 23 years. 48% had bilateral involvement. The lens showed cataractous changes in 68 eyes (48.9%). 51% of cataracts were nuclear sclerosis. Coloboma cataract (linear opacity in the region of the coloboma) was seen in 29% of cases. Disc or macular involvement in 57 eyes did not influence the cataract.

Personalized Diagnosis and Management of Congenital Cataract by Next-Generation Sequencing

This is a prospective evaluation of diagnostic technology involving 36 individuals diagnosed with nonsyndromic or syndromic bilateral congenital cataracts. All patients came through a single ophthalmic genetics clinic at the Manchester Centre for Genomic Medicine, Institute of Human Development, University of
Manchester, St. Mary’s Hospital, Manchester, United Kingdom. Participants underwent a detailed ophthalmic examination accompanied by dysmorphology assessment. Lenticular, ocular and systemic phenotypes were recorded. Mutations were detected using a custom-designed target enrichment that permitted parallel analysis of 115 genes associated with congenital cataract. Next-Generation DNA sequencing techniques were used. Thirty-six patients and a known positive control were tested.

Main Outcome Measures: Molecular genetic results and details of clinical phenotypes were identified.

Results: Next-generation DNA sequencing technologies were able to determine the precise genetic cause of congenital cataracts in 75% of individuals and 85% of the patients with nonsyndromic congenital cataracts was found to have likely pathogenic mutations. All of these pathogenic mutations occurred in domains known to be vital for “normal protein function.” The detection rate in patients with syndromic congenital cataracts was also high, with 63% having potential disease causing mutations.

Conclusions: This study demonstrates the clinical utility of this test, providing examples where it altered clinical management, directed care pathways and enabled more accurate genetic counseling. The authors feel that this comprehensive screen will extend access to genetic testing and lead to improved diagnostic and management outcomes through a stratified medicine approach.

Comment: Congenital cataracts affect 2.5-3.5 per 10,000 children younger than 15 years of age in the United Kingdom. The cataracts have been estimated to causing lifelong visual loss or deficit in approximately 200,000 children worldwide. Approximately 50% of the congenital cataract cases have a genetic basis resulting in disturbances in the packaging of proteins within lens fibers. The study shows congenital cataract morphologies some of which are familiar and some of which are not. The cataracts in the study were small and not visually significant.

Next-Generation sequencing, when it becomes financially feasible and covered by insurance, will probably replace the current diagnostic work-up that we use for diagnosing bilateral congenital cataracts. Next-Generation sequencing is the synonym for Sanger sequencing. “Segregation analysis of other affected family members was carried where samples were available.” Standard polymerase chain reaction was used to amplify targets where the products underwent sequencing.
13. **CATARACT SURGERY**

Comparison of Contact Lens and Intraocular Lens Correction of Monocular Aphakia During Infancy A Randomized Clinical Trial of HOTV Optotype Acuity at Age 4.5 Years and Clinical Findings at Age 5 Years

This study provides data on visual acuity and clinical course, at age 4.5 years and 5 years, respectively, for the cohort of children who were enrolled in the Infant Aphakia Treatment Study. One hundred thirteen patients with visually significant cataracts identified and operated between age 1 and 6 months of life were randomized to aphakia correction with a contact lens or intraocular lens (Acrysof SN60AT or MA60AC). The authors conclude that there was no significant difference in visual acuity between the 2 groups (median visual acuity 0.9 logMar or 20/159) and half of patients in each group had visual acuity of 20/200 or less. The group who received an IOL had more complications and required additional surgeries. Seventy two percent required at least one additional surgery in the IOL group compared with 21% in the contact lens group (p<0.001). Most common complications were lens reproliferation into the visual axis, pupillary membranes and corectopia. Glaucoma/glaucoma suspect developed in 28% of patients with IOL and 35% with contact lens. Most patients developed strabismus. The authors conclude there is no visual benefit from implanting an IOL in an infant less than 7 months of age.

Treatment Outcomes of Monocular Infantile Cataract at 5-Year Follow-up: Work in Progress

Mike Repka emphasizes that the Infant Aphakia treatment study studied not just a procedure, but an entire treatment paradigm. The treatment of unilateral congenital cataracts begins with surgery but requires the diligence of parents and caregivers to adhere to the regimen of visual rehabilitation. This includes compliance with patching and glasses and frequent follow up visits and sometimes additional surgery. Dr. Repka cites that progress is being made in obtaining better visual outcomes in these patients but innovations in surgical technique, better models of predicting emmetropization in aphakic and pseudophakic eyes, and novel amblyopia treatments will be needed to improve visual outcomes even further.


This randomized clinical trial compared the outcomes of congenital cataract surgery using intraoperative intracameral triamcinolone versus postoperative oral
prednisolone to modulate ocular inflammation. Children younger than 2 years were randomly divided into 2 groups. The study group (31 eyes) received an intraoperative intracameral injection of 1.2 mg/0.03 mL of triamcinolone acetonide. The control group (29 eyes) received 1 mg/kg per day of prednisolone syrup for 15 days postoperatively, which was then tapered over the following 2 weeks. Intraocular pressure (IOP), central corneal thickness (CCT), cell deposits on the intraocular lens (IOL), posterior synechiae, visual axis obscuration, additional surgical procedures, and IOL centration were assessed 12 months postoperatively. The mean patient age at surgery was approximately 10 months in both groups. In both groups, the mean IOP and CCT did not change significantly postoperatively. The groups also had similar incidences of cell deposits and posterior synechiae. No eye developed visual axis obscuration or had additional surgical procedures. All eyes had a clinically centered IOL. The authors conclude that intraoperative intracameral triamcinolone injection and postoperative oral prednisolone for modulating inflammation after congenital cataract surgery behave in a similar fashion. A peer critique of this paper cautioned that children on such high doses of postoperative prednisolone may experience hyperglycemia, adrenal suppression and immunosuppression.


This study evaluated the post-cataract surgery follow-up program implemented to improve follow-up care. Retrospective data prior to the program was compared to prospective data upon initiation of the program. The program consisted of a full-time pediatric counselor and program director, a specific database, a tracking system, and cell phone numbers. 301 children underwent cataract surgery in 2009 prior to the program and 334 children underwent cataract surgery after the program was started. Follow-up rates prior to the program for first, second, and third appointments were 87%, 60% and 37%, respectively. This improved to 96%, 81% and 57% after the program was instituted. Total cost for the program was 17,477 US dollars for one year. Since there was no control group, cause and effect cannot be established.


Using the IATS dataset, the authors developed a regression formula and A-constant. This study’s purpose was to validate these and to provide guidelines for the selection of an initial contact lens power for distance if retinoscopy over a diagnostic lens is not possible. Thirty-four patients were included. Silicone elastomer contact lenses were used in 2/3 of the patients, and RGP contact lenses were used in the rest. The regression formula revealed a contact lens for distance of 70.4- 2.5* AL (R² = 0.7488). In this study the targeted contact lens power for distance based on the 1-month refraction was 26.0 +/- 4.5 D. Therefore including a 2 diopter correction for near, the average prescribed contact lens power
was +28D. This data is helpful in formulating a plan for initial prescribed contact lens power.


Regular follow up and amblyopia treatment are essential for good outcomes after pediatric cataract surgery. Aim was this was to study the regularity of follow-up after cataract surgery in children and to gauge the causes of poor compliance to follow up. 262 children (393 cataracts) who underwent cataract surgery in 2004-8 were studied. Of the 262 children, only 53 (20.6%) had been regularly following up with any hospital, 209 (79.4%) had not. A total of 150 (57.3%) were boys and the average age was 13.23 years (Std Dev 5 yrs). Poor follow up was associated with the older age group (P < 0.001), less education of mother (P = 0.012), father’s occupation (P = 0.031), how much money spent on travel (P = 0.033) and was it paid or free surgery (P = 0.001). It was not related to gender, numbers of children in family, ordinal status of child, and social strata. Distance and cost were major barriers, as was the inability of the eye care center to communicate the importance of follow up. A prospective follow-up visit showed that 93 children needed Nd: YAG LASER capsulotomy, 5 needed low vision aids, 4 contact lens, and 162 a change of spectacles. The average visual acuity improved in 150 (38.8%) eyes >1 line with regular follow-up. Conclusion of this study is that, regular follow-up is important and improves vision; eye care practitioners need to take special efforts to ensure better follow-up.

**HEALTH-RELATED QUALITY OF LIFE IN CHILDREN OPERATED FOR PEDIATRIC CATARACTS**


Purpose: To evaluate health-related quality of life (HRQOL) in children who had surgery for pediatric cataracts. Twenty-five children were divided into 2 groups: younger than 6 years or 7 years and older. A questionnaire had 1 part appraising the child’s perception and 3 parts evaluating the functional, social, and surgical apprehensions of parents was given to the participants. The questions in the first part were answered by parents in group A (proxy test) and by children in group B (self test). The correlations between the results and patient characteristics were evaluated statistically. Functional, social, or surgical scores were not significantly different between age groups. Although pediatric cataracts are known to have a great impact on children’s life socially and functionally, there was no significant relationship between patient characteristics and HRQOL. The authors concluded that social apprehensions were significantly higher in parents of patients with preoperative strabismus in the older group.

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Long term results after primary intraocular lens implantation in children operated less than 2 years of age for congenital cataract

Purpose of this was to study the long-term outcome of cataract surgery with primary intraocular lens (IOL) in children <2 years. Retrospective analysis of bilateral cases that were operated before 2 years age for congenital cataract. Only those with a follow-up of at least 8 years were evaluated. 26 eyes of 13 children with bilateral cataract met the inclusion criteria. Average age at surgery was 14.15 months with a mean follow-up of 102 months. Average preoperative axial length (AL) was 19.93 mm. There was a refractive shift from a mean spherical equivalent of 1.64 D at 2 weeks after surgery to -1.42 D measured at last follow-up. Twenty-four eyes out of 26 (92%) achieved final visual acuity (VA) of 6/18 or more at last follow-up with 19/26 (73%) having acuity of 6/12 or greater. Raised intraocular pressure was documented in one eye only. Average AL recorded at last follow-up was 22.21 mm.

Primary IOL implantation in children <2 years is a safe surgical procedure with excellent long-term results. The myopic shift is well-controlled and final VA achieved is reasonably good. Although this study provides a long term (8 years) outcome, the sample size was very small. Additionally age group was heterogeneous ranging from 3 months to 2 years. Morphology and density of the cataract was unknown.


In this retrospective cohort study of 11 eyes, the authors compare macular thickness before and after cataract surgery and intraocular lens (IOL) implantation in pediatric eyes. Eleven eyes of patients with mean age of 5.8 years (range 3 to 14 years) were included in the study. Eight of the eleven eyes also underwent posterior capsulorrhexis with anterior vitrectomy. There was an increase in mean macular thickness of 12% at 1 and 9% at 3 months, which then reached baseline values after 3 months and was stable over the 12 month follow-up period. The result was statistically significant but not clinically significant. None of the eyes developed cystoid macular edema. This study corroborates finding in prior studies that cystoid macular edema is rare after pediatric cataract surgery.

In this prospective study, authors evaluated the preoperative and early postoperative differences in contrast sensitivity after cataract extraction with IOL implantation in children presenting with lamellar and posterior subcapsular cataract. The study included children presenting with such cataracts after the age of 4 or 5 years. 22 eyes of 13 patients were evaluated, and the ages of the patients ranged from 4 to 14 years. Contrast sensitivity was measured using gratings of varying spatial frequencies under both scotopic and mesopic conditions. Contrast sensitivity improved after cataract surgery under all testing conditions. Contrast sensitivity even improved in the 4 eyes that did not achieve improvement in visual acuity.

This study suggests that measurements of contrast sensitivity could be used preoperatively to help gauge the cataract’s effect on visual function, and thus be used in making the decision on whether to remove or observe the cataract. In addition, contrast sensitivity is an outcome measure that can be used to gauge the success of pediatric cataract surgery. Cataract surgeons operating on adult patients frequently take into account measures other than high contrast visual acuity in determining whether to recommend cataract surgery, and this manuscript suggests pediatric surgeons could do so as well.

This study does not address other factors determining on whether to operate on lamellar and posterior subcapsular cataracts, such as the impact of loss of accommodation. There is also a possibility that improvements in contrast sensitivity postoperatively compared to preoperatively could have been partially due to a learning effect, as the study did not include control eyes.


In this prospective observational study from India, 21 children (37 eyes) with congenital rubella syndrome who had cataract surgery were evaluated for postoperative complications and for visual outcomes. The mean age of the 21 children (37 eyes) undergoing cataract surgery was 4.0 months ± 2.1 (SD). Intraocular lens implantation was performed in 12 eyes (32%), while 25 eyes (68%) were left aphakic. The median follow-up was 61 months. Posterior synechiae were observed in 22 eyes (60%) and visual axis opacification in 9 eyes (24%). Secondary glaucoma was observed in 16 eyes (43%). The mean corrected distance visual acuity at the final follow-up was 20/100 (0.7 ± 0.6 logMAR). This study provides relatively long term follow up for rubella cataract surgery, an entity rarely seen in the United States.
Results of late surgical intervention in children with early-onset bilateral cataracts
2014;98:10 1424-1428

This study attempts to investigate visual acuity outcomes after later treatment of early-onset cataracts. 53 children were identified with dense cataracts with an onset with the first 6 months after birth through a survey of over 20,000 rural children in India. All patients had nystagmus and were older than 8 years of age at the time of treatment. They underwent bilateral cataract surgery with intraocular lens implantation and visual acuity was assessed at 6 weeks and 6 months after surgery. 48 of the 53 children showed improvement in visual acuity after surgery. The majority of children demonstrated further improvement from the 6 week to the 6 month assessment. There was not a significant difference between older children and younger ones in the extent of improvement. The authors conclude that significant vision can be acquired until late in childhood and that neural processes underlying basic aspects of vision like resolution acuity remain malleable until at least late adolescence. This study is limited by the small sample size and the limited data on the cataracts during early childhood.

The effects of surgical factors on postoperative astigmatism in patients enrolled in the Infant Aphakia Treatment Study (IATS).

This study utilized handheld keratimeters to assess corneal astigmatism prior to cataract surgery and at 1 year of age. There were 12 clinical sites. 41 of 57 patients in the IOL group had surgical factor data collected. 20/41 received a scleral tunnel or a clear corneal incision and one patient had both types. There was no statistical difference between all surgical factor groups (suture type, incision type, keratome extension, and number of sutures) for mean astigmatism at baseline or at 1 year of age or for the mean change in astigmatism during that interval. When comparing the IOL group and the contact lens (aphakic) group, there was no statistical difference for mean corneal astigmatism at baseline or mean change at 1 year of age. However there was a statistically significant difference in astigmatism at 1 year of age (the contact lens group astigmatism reduced over time but the IOL group did not). There was no difference in the amount of corneal astigmatism pre- or postoperatively based on the age at the time of surgery. This study only measured corneal astigmatism because measurements were obtained with a keratometer. Small sample sizes may have limited the ability of the study to detect differences between the groups. Incision size difference between the two groups may account for the astigmatism difference at 1 year of age. Or it is possible the contact lens used caused this reduction.

A cost analysis of the burden of childhood cataracts at two child eye health tertiary facilities (CEHTF) in Malawi and Zambia was performed. 112 children were treated in Malawi at a cost of 689$ per child and 120 children were treated in Zambia at a cost of 763$ per child. Equipment costs were almost identical. Monthly salaries were slightly higher in Zambia. Consumables and medications cost significantly more in Zambia. Data calculations were affected by some missing data and also the fact that most of the equipment had been donated by charitable organizations, defraying some costs. Only one week of follow-up was included.

Complications in the first 5 years following cataract surgery in infants with and without intraocular lens implantation in the infant aphakia treatment study.

This was a prospective randomized clinical trial to compare rate and severity of complications in infants undergoing cataract extraction with and without lens implantation. 114 infants were enrolled in the IATS. Patients were 7 months of age with IOL or CL treatment. There were more intraoperative complications (28% vs. 11%) and more additional surgeries (72% vs. 16%) in the IOL group. However, adverse events increased in the CL group between years 2-5 while they decreased in the IOL group. Even if only ½ of the CL group goes on to have secondary IOL implantation, then the number of additional surgeries will be equal between the 2 groups. It was suggested to leave the child in CL initially if the family looked like they could cope with CL correction.

Scleral Fixated Capsular Tension Rings and Segments for Ectopia Lentis in Children.

This retrospective observational case series attempted to report the short term outcomes with scleral fixated tension rings in ectopia lentis. 13 patients had in the bag placement of the IOL with a Ciooi capsular tension ring or capsular tension segment with a conventional capsular ring. The mean age was 10.2 years, follow-up was 23.4 months. Posterior capsular opacification occurred in 11 eyes. Other complications included broken suture, conjunctival dehiscence, vitreous strand in paracentesis. These capsular tension rings appear to be safe and effective for ectopia lentis.
Stereopsis Results at 4.5 Years of Age in the Infant Aphakia Treatment Study.

This randomized prospective clinical trial, known as the Infant Aphakia Treatment Trial, assessed stereo at 4.5 years of age by a masked examiner. 28 patients had a positive result to at least 1 stereo test. There was no statistical difference between the two groups. The median age of surgery was younger in the group with stereopsis than for those without stereo. The median visual acuity was better for patients with stereo as well. The type of optical correction did not influence stereo outcomes. Early surgery with vision outcome of 20/40 or better was a stronger predictor for stereo development than optical correction type.

Cost of Intraocular Lens versus Contact Lens Treatment after Unilateral Congenital Cataract Surgery in the Infant Aphakia Treatment Study at Age 5 Years

This is a retrospective cost analysis of a prospective, randomized clinical trial. The Infant Aphakia Treatment Study is a muticenter (n = 12), randomized clinical trial comparing the optical treatment of aphakia with either primary IOL implantation (n = 57) or contact lens correction (n = 57) in 114 infants with unilateral congenital cataract.
Main Outcome Measures: The mean cost of cataract surgery and all additional surgeries, examinations and supplies used up to 5 years of age.
Results: The 5-year treatment cost of an infant with a unilateral congenital cataract corrected optically with intraocular lens was $27,090 versus $25,331 for a patient treated with a contact lens after initial cataract surgery. The total cost of supplies was $3,204 in the IOL group and $7,728 in the contact lens group.
Conclusions: Unilateral cataract surgery in infancy coupled with primary IOL implantation is approximately 7% more expensive than aphakia and contact lens correction. PATIENT COSTS ARE MORE THAN DOUBLE WITH CONTACT LENS VERSUS IOL TREATMENT.

Postoperative Glaucoma Following Infantile Cataract Surgery An Individual Patient Data Meta-analysis

A significant risk of developing glaucoma occurs after infantile cataract surgery. The objective of this study was to determine the effect of primary intraocular lens implantation and timing of cataract surgery on the incidence of glaucoma. This study was comprised of a meta analysis of individual patient data supplied by invited authors of papers culled from a database search of articles on congenital cataract surgery and post-op glaucoma published from 2010 to July 2013. Other
relevant articles whose individual patient data could not studied were reviewed as well. Inclusion criteria were infants with no other ocular anomalies other than congenital cataract, who underwent cataract surgery, with a minimum follow up of one year. Seven centers contributed individual patient data on 470 infants with a median age at surgery of 3.0 months and median follow-up of 6.0 years. Eighty patients (17.0%) developed glaucoma at a median follow-up of 4.3 years. Only 2 of these patients had a pseudophakic eye. The risk for postoperative glaucoma appeared to be lower after primary implantation, higher after surgery at 4 weeks or younger, and higher after additional procedures. In multivariable analysis, additional procedures independently increased the risk for glaucoma, and primary implantation independently reduced it. Results were similar in the aggregate data meta-analysis that included data from 10 published articles.

14. **GLAUCOMA**


This review paper will provide the reader with up to date references addressing the treatment of childhood glaucoma. It should be required reading for all residents who pass through the pedi ophthalmology service.

**Anesthesia considerations in pediatric glaucoma management.**


Current literature suggests the possibility of increased adverse neurodevelopmental outcomes in children with early exposure to general anesthesia. Greater frequency of attention deficit hyperactivity disorder (ADHD), abnormal language processing and cognition has been suggested to occur in children with multiple exposures to anesthetics prior to the age of 3 yo. However, studies are not conclusive. Children with glaucoma have historically required frequent examinations under anesthesia (EUA) to determine their intraocular pressure. The advent of the rebound tonometer has allowed the clinician to obtain IOP measurements more successfully in the office thus reducing the frequency of EUA’s. Ophthalmologists must be prepared to counsel families regarding the potential risks and benefits of general anesthesia associated with the management of potentially vision threatening conditions including glaucoma.

**Optic Disc Torsion Presenting as Unilateral Glaucomatous-Appearing Visual Field Defect in Young Myopic Korean Eyes**


This is a retrospective, cross-sectional study of 39 patients from 20 to 50 years of age with unilateral glaucomatous-appearing visual field defects and nearsightedness. The purpose of the study is to investigate the ocular features
of companion eyes in an attempt to find eye-related factors that are associated with unilateral glaucomatous-appearing visual field defects in young, nearsighted patients.

Main Outcome Measures: Torsion degree, tilt ratio and the severity of the visual field defect.

Results: Optic disc torsion was more prevalent in visual field-affected eyes (66.6%) than in normal contralateral eyes (15.3%). In the multivariate analysis, the degree of optic disc torsion was associated significantly in the presence of a visual field defect. The torsion and the retinal nerve fiber layer thickness were associated significantly with the severity of the visual field defect.

Conclusions: The prevalence and degree of optic disc torsion and the visual field-affected eyes were significantly greater than those of contralateral normal eyes in young, nearsighted patients with unilateral glaucomatous-appearing visual field defect. Optic disc torsion should be considered in the presence of unilateral glaucomatous-appearing visual field defect in young, nearsighted eyes.

The 5-Year Incidence of Bleb-Related Infection and Its Risk Factors after Filtering Surgeries with Adjunctive Mitomycin C: Collaborative Bleb-Related Infection Incidence and Treatment Study 2

T Yamamoto, A Sawada, C Mayama, M Araie, on behalf of The Collaborative Bleb-Related Infection Incidence and Treatment Study Group

Ophthalmology May 2014; 121:1001-1006

This is a prospective, observational cohort study of 1,098 eyes of 1,098 glaucoma patients who had undergone mitomycin C-augmented trabeculectomy or trabeculectomy combined with phacoemulsification and intraocular lens implantation performed at 34 different clinical centers in different Japanese cities.

Methods: The patients were followed at 6 month intervals for 5 years with special attention given to bleb-related infections.

Conclusions: The 5-year cumulative incidence of bleb-related infections in this study was 2.2% in eyes treated with mitomycin C-augmented trabeculectomy combined with phacoemulsification and intraocular lens implantation. Bleb leakages and younger age were the main risk factors for infections.

The use of the Ahmed glaucoma valve in the management of pediatric glaucoma.


The authors assessed IOP control, changes in visual acuity, complications, reoperation rates, and risk factors for failure following implantation of the Ahmed glaucoma valve in consecutive patients under 18 years of age retrospectively. 85 patients underwent the procedure during the study period, but 14 were lost to followup and excluded. Glaucoma type was varied. 62% of patients received the S-2 model and the remainder received the FP-7 model. Of the 71 patients, visual
acuity was measurable in 44. Average visual acuity declined from 0.79 logMAR preop to 1.21 logMAR at final follow-up, mostly because of surgical complications. At final followup IOP was reduced from 35.86 mm Hg to 16.38 mm Hg at final follow-up. Average glaucoma medications needed declined from 2.42 to 1.31. No significant differences were found between implant models except the S-2 implant patients had lower final acuity. However this may have been a reflection of longer follow-up in this group. Most complications were transient but graft failure occurred in 5 of the corneal grafts. Tube-related complications occurred in 13% of patients. Survival analysis showed a success rate of 97% at 12 months and 80% at 24 months. Overall 38% were considered failures. Success was highest and failures were lowest in primary congenital glaucoma, juvenile open angle glaucoma and/or ocular anomalies only not including cataracts. This study provides lots of data but some of the groupings are small and analysis and comparison between groups is problematic.


This study assessed the effect of IOP control on CCT, HCD and AL measurements in PCG and analyzed the correlation among these parameters before surgery and at last visit. This study was a 9.5 years retrospective review. Secondary glaucoma patients were excluded and patients had to have undergone 1 or more trabeculotomies, have a minimum of 6 months follow-up and have an IOP <=12mm Hg with or without medication. 32 eyes of 20 children were included. Mean age at surgery was 12.1 months and there was a mean follow-up of 32.44 months. At final follow-up no patient had corneal edema and ¾ were not on topical medications. Before surgery the mean IOP was 15.69 +/- 5.31 mm Hg (which seems quite low). Preop versus final followup measurements were as follows: Mean CCT 614.38 / 548.56 um; mean HCD 13.45 mm / 13.98mm; mean AL 24.57 mm/ 25.37mm. At final follow-up the % abnormal compared to normal values- 93.8% HCD, 73.9% AL and 60% CCT. The authors found the greater the CCT before surgery, the greater the CCT at final followup. The greater the HCD and AL before surgery, the greater the HCD and AL at final followup. CCD did not correlate with the other two variables.

**Surgical outcomes of Baerveldt implants in pediatric glaucoma patients.** Tai AX and Song JC. J AAPOS 2014;18:550-553.

This study reports the results of Baerveldt glaucoma implant (BGI) in 45 eyes of 36 patients operated on over a 10-year period. This was a retrospective chart review. Patients were aged 5 months to 19 years. 31 eyes had primary glaucoma and 14 had secondary glaucoma. The mean preoperative IOP was 31.6 mm Hg. Post-op mean was 16.3 mm Hg at 3-9 months, 19.5 mm Hg at 12-18 months, and 18.3 mm Hg at 24-30 months. Average glaucoma meds dropped from 3 pre-surgery to 2 post-surgery. 6 eyes failed within 30 months. Cumulative probability of success was 93.3%, 86.7% and 86.7% at the 3 postoperative time periods. There were no intraoperative complications. Two patients had tube
erosions, 1 patient had corneal decompensation, 1 patient had bleb encapsulation and 1 patient suffered cataracts. This was a retrospective, small study not designed or powered to statistically evaluate risk factors for shunt failure.


The authors report outcomes of Ahmed Glaucoma valve (AGV) implantation in a racially homogeneous group of primary congenital glaucoma patients who had undergone prior trabeculotomy. This study was an 8-year retrospective review. Postoperative success was defined as IOP 6-21 mm Hg on a maximum of 3 antiglaucoma medications. 33 eyes of 22 patients were analyzed and there were four different models of the AGV valve used. Mean age at implantation was 2.7 +/- 3.1 years, and mean follow-up was 32.6 +/- 18.3 months. Mean IOP was reduced from 32.8 mm Hg pre-op to 16.8 mm Hg post-op. 70% of eyes had a transient early post-op hypertensive phase. Of these 23 eyes, 5 ended in failure. Mean number of antiglaucoma medications declined from 2.5 to 2.2. Seven of 33 eyes (21%) ended in failure. Success rates were 97.0% at 6 and 12 months, 84.8% at year 2 and 56.3% at year 5. Eight eyes had significant complications (tube-endothelial touch, shunt extrusion, retinal detachment, cataract, or bleb encapsulation), of which 3 ended in failure.

**Cupping Reversal in Pediatric Glaucoma—Evaluation of the Retinal Nerve Fiber Layer and Visual Field.**


This retrospective study tried to identify optic nerve head cupping reversal and looked at OCT and HVF changes as well. Sequential surgical cases of juvenile glaucoma or primary congenital glaucoma were examined. Group 1 had preoperative and postoperative photos and OCT while group 2 had preop clinical optic nerve asessments and post op imaging. 9 eyes were in group 1; 24 eyes were in group 2. 56% of group 1 showed cupping reversal. HVF showed no real change. In group 2, 14 eyes demonstrated cupping reversal. However, some eyes still showed continued nerve fiber layer thinning posteropatively. This suggests that cupping reversal in pediatric glaucoma may not be a predictor of improved optic nerve health.

**Intraocular Pressure in Children: The Effect of Body Position as Assessed by Icare and Tono-pen Tonometers.**


This prospective study evaluated the effects of the body position on IOP results assessed by the Icare and tonopen. 47 children with 94 eyes were assessed. Mean seated IOP was 16.4 for applanation, 17.5 for Icare, and 18.0 for tonopen. Mean supine IOP was 18.4 for the Icare and 18.8 for the tonopen. The Icare
tonometer correlates well with goldmann tonometry in seated children. The Icare correlated well with the tonopen in seated and supine positions.

**Pediatric Glaucoma Surgery: A Report by the American Academy of Ophthalmology**


This is an ophthalmic technology assessment. The American Academy of Ophthalmology prepares Ophthalmic Technology Assessments (OTAs) to evaluate new and existing procedures, drugs and diagnostic and screening tests. The goal of an OTA is to review statically the available research for clinical efficacy and safety. After review of the articles by the Ophthalmic Technology Assessment Committee (OTAC) as well as with input from other academy committees including evaluation by the Academy’s legal counsel and the Academy’s Board of Trustees, the final report is submitted. The purpose of this assessment is to evaluate the success rate with long-term problems associated with differential surgical options using treatment of glaucoma in the pediatric population.

The objective of this study is to review the current public literature to evaluate the success rates in long-term problems associated with surgical pediatric glaucoma. Literature searches of the PubMed and Cochrane Library databases were conducted in May 2012. The search yielded 838 potentially relevant citations and 273 were in non-English languages. The report evaluated the most common surgical techniques including goniotomy, trabeculotomy, trabeculectomy, combined trabeculotomy and trabeculectomy, tube shunt surgery, cyclodestruction and deep sclerectomy.

**Conclusions:** There are many surgical options for the treatment of pediatric glaucomas. The relative efficacy of these various procedures for particular diagnoses should be weighed against the specific risks and complications.

**Addendum:** I very much appreciate the efforts of the Ophthalmic Technology Assessment Committee to review pediatric glaucoma surgeries. A notable absence in this review of literature was trabeculectomy/trabeculotomy with Mitomycin or other anti-proliferative agents. Mitomycin and 5-fluorouracil have been used effectively in a number of difficult pediatric glaucoma cases and there are multiple published articles to support this. This is particularly common prior to the onset of tube shunt surgery, which in itself has its set of complications.

There is also a notable absence in the statistics on the Schei procedure unguarded trabeculectomy which has longstanding efficacy in the treatment of aphakic pediatric glaucoma. The bottom line in the treatment of pediatric glaucoma is even under best conditions it is difficult, parents and family should always be aware of the high probability of repeat operations, the best operation is the operation that the surgeon has the most comfort with in a given situation and tube shunt surgery is not without its complications and reoperation rates.
Corneal Changes in Childhood Glaucoma
Bharat Patil, Radhika Tandon, Namrata Sharma, Meena Verna, Ophthalmology January 2015; 122(1):87-92

This is a cross-sectional, observational study of 58 eyes with childhood glaucoma and 20 eyes of age-matched controls designed to study the clinical features and topography of the cornea in eyes with childhood glaucoma. The mean outcome measures were corneal topographic changes studied with Orbscan Topography System II (Bausch & Lomb, Salt Lake City, UT).

Results: Fifty-eight eyes with childhood glaucoma and 28 eyes of age-matched controls were evaluated. 62.1% were classified as having primary childhood glaucoma and 37.94% as having childhood glaucoma associated with other anomalies.

Conclusion: Childhood glaucoma causes a significant increase in the posterior corneal elevation and irregular astigmatism which contributes to visual disability in glaucomatous eyes in children.

Comment: This study was performed from the All India Institute of Medical Sciences, New Delhi, India. There are a couple of excellent photographs (page 89). The photographs demonstrate Haab’s striae. Orbscans show an increase in posterior elevation on the Orbscan in corneas with large central Haab striae.

15. REFRACTIVE SURGERY


In this study of 97 myopes (ave -5.0 D) undergoing laser refractive surgery the authors measured pre and post operative heterophoria. Preoperatively, 47% had a phoria that was asymptomatic and postoperatively the magnitude changed in up to 20% of these patients, with most improving, especially if they were anisometropic preop. None of the patients were diplopic post op.


The authors evaluated the effects of hyperopic excimer corneal refractive surgery on ocular alignment, uncorrected visual acuity and stereopsis in patients with both accommodative esotropia and amblyopia. This was a prospective study over a 3.5-year period. Patients underwent LASEK or LASIK and were over 14 years of age. Retreatment was allowed during the postoperative period if there was a large residual refractive error, or a large difference between corrected and uncorrected acuity. Thirteen patients ranging in age between 15-34 years (mean 24.3 years) were enrolled (n=9 LASIK and n=4 LASEK). Average follow-up was 15.7 months.
Although there was no significant difference in best-corrected acuity before and after surgery, uncorrected acuity significantly improved (from 0.46 to 0.32). Mean cycloplegic refraction from more than 5.5 diopters of hyperopia to under 1.5 diopters of hyperopia. There was a 0.44 D regression of hyperopia between 1 and 12 months postoperatively. The greater the initial hyperopia the more residual hyperopia was present after surgery. Two patients had glare as a postoperative complication and 1 patient developed a slight corneal haze and a 2-line loss of best-corrected visual acuity.

All 11 patients with a preoperative esotropia converted to orthophoria or esophoria postoperatively. Two patients had preoperative stereopsis and nine patients developed it postoperatively. Mean uncorrected esotropia improved from 37.92 PD to 2.76 prism diopters.

This study is limited by a small number of cases and short follow-up but results were encouraging.

Influence of Ocular Wavefront Aberrations on Axial Length Elongation in Myopic Children Treated with Overnight Orthokeratology

Takahiro Hiraoka, Tetsuhiko Kakita, Fumiki Okamoto, Tetsuro Oshika, Ophthalmology January 2015; 122(1):93-100

This study is from the Faculty of Medicine, University of Tsukuba and the Kakita Eye Clinic, Ibaraki, Japan. This is a prospective, noncomparative study of 59 subjects who met the inclusion criteria determined by axial length and ocular wavefront aberration. This study was designed to determine optical parameters that affect axial length elongation in myopic children undergoing overnight orthokeratology.

Methods: Axial length and ocular wavefront aberrations were assessed before and 1 year after the start of orthokeratology. Corneal topography was performed, and then corneal multifocality was calculated for a 4mm pupil. Optical analysis evaluating simple correlations between axial elongation and optical parameters were taken.

Conclusions: Asymmetric corneal shapes rather than concentric and radially symmetric shapes have a considerable effect on retardation of axial elongation suggesting that the inhibitory effect of orthokeratology on myopia progression is caused by mechanisms other than the reduction in peripheral hyperopic defocus. Comment: This article causes one to look at additional aspects of orthokeratology, glaucoma-like aberrations, spherical-like aberrations and total higher order aberrations with 1 year of treatment. In other words, the orthokeratology, regardless of its mechanism, does not seem to maintain changes in corneal architecture.

16. GENETICS


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.

**Mutation in TMEM98 in a Large White Kindred With Autosomal Dominant Nanophthalmos Linked to 17p12-q12**


The authors identify a mutation in TMEM98 on chromosome 17p12-q12, implicated in autosomal dominant nanophthalmos. This gene is expressed in all ocular tissue tested, including sclera and optic nerve. Nanophthalmos is a congenital disorder characterized by small eyes, severe hyperopia and angle closure glaucoma. Sixteen Caucasian members of a family were studied. Mean axial length was 17.6mm , mean refraction was 11.8 D, and 6/16 family members had angle closure glaucoma. Another unique finding was optic disc drusen. Intraocular surgery was often complicated by macular edema, epiretinal membrane and choroidal effusion. The authors cite that nanophthalmos, in which cornea and lens are normally sized, is along the spectrum of microphthalmos.
The authors cite a report of a gene mutation in the same region of chromosome 17 in a Chinese family with congenital simple microphthalmos.

**Expansion of Ocular Phenotypic Features Associated With Mutations in ADAMTS18**

The authors describe the phenotype of 4 patients with novel homozygous mutations in ADAMTS18 on chromosome 16q23. This gene codes for a zinc dependent protease, which is important in cell migration, coagulation, angiogenesis and extracellular matrix regulation. Clinical features include microcornea, early onset cataracts, ectopia lentis and ectopia pupillae. Funduscopic examination and ERG testing confirmed cone rod dystrophy. The authors cite a similarity to Knobloch syndrome, but the patients in this report had no occipital skull abnormality. Screening for this gene should be considered in patients with microcornea and cone rod dystrophy.

**Nonpenetrance of the Most Frequent Autosomal Recessive Leber Congenital Amaurosis Mutation in NMNAT1**

The NMNAT1 gene was found to be mutated in a subset of patients with Leber’s congenital amaurosis (LCA) and macular atrophy. The most prevalent variant, p.Glu257Lys, was observed in 35.8% of alleles. It was deemed a severe variant based on functional assays. However this variant is 80 fold less frequent in a homozygous state in patients with LCA than predicted based on the frequency of heterozygotes in a European American population. The authors also describe patients with homozygosity for this variant with no ocular abnormalities. They caution genetic counselors in how they interpret this variant to patients and parents.

**Retinal Morphology of Patients With Achromatopsia During Early Childhood Implications for Gene Therapy**

This study is a comparative case series of 9 affected patients and 9 healthy controls which seeks to characterize the macular and foveal architecture of patients with achromatopsia during early childhood with handheld spectral-domain optical coherence tomographic imaging and to make phenotype-genotype correlations. Patients underwent complete ocular examination, full-field electroretinography, handheld spectral-domain optical coherence tomographic imaging, and screening for genetic mutations. The mean age of the patients with achromatopsia was 4.2 years, and the mean age of the control participants was 4.0 years. Cone-driven responses to photopic single-flash or 30-Hz stimuli were nonrecordable in 7 patients and severely attenuated in 2. Six patients (67%) had foveal ellipsoid zone disruption. Four patients (44%) had foveal hypoplasia. The
average total retinal thicknesses of the macula and fovea in the patients with achromatopsia were 14% and 17% thinner than in the control participants (P < .001 and P = .001), which was mostly due to the outer retina that was 18% and 26% thinner than in control participants (both P < .001), respectively. Genetic testing revealed a common homozygous mutation in CNGB3 in 5 patients with complete achromatopsia and heterozygous mutations in CNGA3 in 2 patients with incomplete achromatopsia. The authors emphasize that with the advent of gene therapy early diagnosis of macular abnormalities with OCT may be useful in identifying eligible patients and monitoring treatment response.

Optic Atrophy and a Leigh-Like Syndrome Due to Mutations in the C12orf65 Gene: Report of a Novel Mutation and Review of the Literature.


Two siblings with compound oxidative phosphorylation deficiency type 7 (COXPD7) caused by a compound heterozygous mutation in the C12orf65 gene are presented. Both had optic atrophy and developmentally delays at initial evaluation and imaging demonstrated symmetric lesions in the brainstem similar to those typically described in Leigh syndrome. One went on to improve neurologically but the other maintained persistent neurological deficits and developed a fatal associated cardiomyopathy. This report describes the phenotypic disparity and compares finding with the five other patients in three previously described families with mutations in the C12orf65 gene whose clinical course was consistent with COXPD7 deficiency. It is notable that early in their course these siblings did not demonstrate elevation in plasma or CSF lactate, and that the absence of this finding should not prevent consideration of the diagnosis of COXPD7.

Novel Splice-site and missense mutations in the ALDH1A3 gene underlying autosomal recessive anophthalmia/microophthalmia

C. Semerci, E. Kalay, C. Yildirim, T. Dincer, et al. BJO 2014; 98: 832-840. Two turkish families with 9 affected individuals were reviewed in this study. When looking at these families, the causitive genetic defect was mapped to 15q26.3. This discovery showed the importance of this genetic region in eye development.

Ophthalmic features of PLA2G6-related paediatric neurodegeneration with brain


Pediatric neurodegeneration with brain iron accumulation (NBIA) is a genetically heterogenous disorder. There tends to be excessive iron accumulation in the basal ganglia on MRI scanning. One cause of this condition is recessive mutation in the PLA2G6. In this study they attempted to qualify the ophthalmic phenotype of PLA2G6-related NBIA in 8 patients. Upgaze palsy was found in all cases. Therefore, this should be considered part of the phenotype of this condition. In addition, abnormal convergence, saccadic
pursuits, and saccadic intrusions. Optic nerve head pallor and strabismus have been previously reported and were found in 100% and 50% of all cases.

**Diagnostic Distinctions and Genetic Analysis of Patients Diagnosed with Moebius Syndrome**


This is a prospective, observational study of 112 participants from 107 families enrolled in the study. Participants underwent standardized ophthalmologic exam for Moebius syndrome. Minimal diagnostic criteria included congenital, nonprogressive facial palsy, abduction deficit and genetic testing for the HOXA1, HOXB1, and TUBB3 mutations. The purpose of this study was to improve the diagnostic assessment in Moebius syndrome by creating more selective diagnostic subgroups and conducting a genetic evaluation in a large patient cohort. Patients included in this study came from ophthalmology departments in Boston, Massachusetts, Riyadh, Saudi Arabia and Tygerberg, South Africa.

Conclusions: Moebius syndrome is a complex, rare developmental anomaly of the hind brain that has been described historically as a combination of congenital palsies of abducens and facial nerves, frequently with additional features including oral facial malformations, limb defects and musculoskeletal, behavioral and cognitive abnormalities.

This study attempts to further subdivide Moebius syndrome by the analysis of new candidate genes, which are currently in the process of development. The HOXA1, HOXB1 and TUBB3 mutations are commonly felt to be associated with Moebius syndrome. The authors recommend a full ocular motility evaluation to fulfill the minimal diagnostic criteria for Moebius syndrome. Their recommendations for minimal diagnostic criteria include congenital, nonprogressive facial palsy, abduction deficit, genetic testing and vertical motility assessment.

Reviewers’ Comment: There are excellent photographs of adult and pediatric patients with different types of Moebius syndrome. Volitional Bell’s phenomenon that occurs in up gaze is shown in figure 5 and figure 4 shows eye alignment in a horizontal ocular motility pattern in 2 participants with classic Moebius syndrome. Figure 2 shows an eye alignment and ocular motility pattern in participants not meeting the minimum diagnostic criteria for Moebius syndrome.

**Retinal gene therapy in patients with choroideremia: initial findings from a phase 1/2 clinical trial.**


Background; Choroideremia is an X-linked recessive disease that leads to blindness due to mutations in the *CHM* gene, which encodes the Rab escort protein 1 (REP1). We assessed the effects of retinal gene therapy with an adeno-associated viral (AAV) vector encoding REP1 (AAV.REP1) in patients with this disease.
Methods: In a multicentre clinical trial, six male patients (aged 35—63 years) with choroideremia were administered AAV.REP1 (0·6—1·0×10¹⁰ genome particles, subfoveal injection). Visual function tests included best corrected visual acuity, microperimetry, and retinal sensitivity tests for comparison of baseline values with 6 months after surgery. This study is registered with ClinicalTrials.gov, number NCT01461213.

Findings: Despite undergoing retinal detachment, which normally reduces vision, two patients with advanced choroideremia who had low baseline best corrected visual acuity gained 21 letters and 11 letters (more than two and four lines of vision). Four other patients with near normal best corrected visual acuity at baseline recovered to within one to three letters. Mean gain in visual acuity overall was 3·8 letters (SE 4·1). Maximal sensitivity measured with dark-adapted microperimetry increased in the treated eyes from 23·0 dB (SE 1·1) at baseline to 25·3 dB (1·3) after treatment (increase 2·3 dB [95% CI 0·8—3·8]). In all patients, over the 6 months, the increase in retinal sensitivity in the treated eyes (mean 1·7 [SE 1·0]) was correlated with the vector dose administered per mm² of surviving retina (r=0·82, p=0·04). By contrast, small non-significant reductions (p>0·05) were noted in the control eyes in both maximal sensitivity (—0·8 dB [1·5]) and mean sensitivity (—1·6 dB [0·9]). One patient in whom the vector was not administered to the fovea re-established variable eccentric fixation that included the ectopic island of surviving retinal pigment epithelium that had been exposed to vector.

Interpretation: The initial results of this retinal gene therapy trial are consistent with improved rod and cone function that overcome any negative effects of retinal detachment. These findings lend support to further assessment of gene therapy in the treatment of choroideremia and other diseases, such as age-related macular degeneration, for which intervention should ideally be applied before the onset of retinal thinning.

Genome-wide association studies of refractive error and myopia, lessons learned, and implications for the future.


The investigation of the genetic basis of refractive error and myopia entered a new stage with the introduction of genome-wide association studies (GWAS). Multiple GWAS on many ethnic groups have been published over the years, providing new insight into the genetic architecture and pathophysiology of refractive error. This is a review of the GWAS published to date, the main lessons learned, and future possible directions of genetic studies of myopia and refractive error.
Trans-ethnic Replication of Association of CTG18.1 Repeat Expansion of TCF4 Gene with Fuchs Corneal Dystrophy in Chinese Implies Common Causal Variant.


Purpose: To test the association between the CTG18.1 trinucleotide repeat expansion of TCF4 gene and Fuchs' endothelial corneal dystrophy (FECD) in a Chinese population.

Methods: The CTG18.1 trinucleotide repeat polymorphism was genotyped using short tandem repeat (STR) and triplet repeat primed polymerase chain reaction (TP-PCR) assays in 57 Chinese subjects with FECD and 121 controls. Statistical association of the expanded CTG18.1 allele and 18 single nucleotide polymorphisms (SNPs) across TCF4 with FECD was evaluated. To investigate the linkage disequilibrium structure of the TCF4 region, haplotype analysis was performed on our study subjects and compared to genotyping data of 97 Han Chinese and 85 Caucasians in the 1000 Genomes Project.

Results: The expanded CTG18.1 allele was associated with FECD (P = 4.7 X 10^-14) with the odds ratio of each copy of the expanded allele estimated to be 66.5 (95% confidence interval: 12.6-350.1). Five TCF4 SNPs showed association with FECD at a nominal level (P < 5.0 X 10^-2); however, conditional on the expanded CTG18.1 polymorphism, none of the SNPs showed association with FECD. The only haplotype associated with the disease was the one with the expansion at the CTG18.1 locus.

Conclusions: Trans-ethnic replication of the association between the CTG18.1 repeat expansion in the TCF4 gene and FECD suggests it a common, causal variant shared in Eurasian populations conferring significant risk for the development of FECD. Our data suggests that the expanded CTG18.1 allele is the main, if not sole, causal variant at this gene locus in Chinese.

Nature of the visual loss in observers with Leber's congenital amaurosis caused by mutations in RPE65.


Purpose: To characterize visual losses associated with genetic mutations in the RPE65 gene that cause defects in the retinal pigment epithelium-specific isomerase, RPE65. RPE65 is an important component of the retinoid cycle that restores 11-cis-retinal after its photoisomerization to its all-trans form. The defects investigated here cause Leber's congenital amaurosis (LCA2), an autosomal, recessively-inherited, severe, congenital-onset rod-cone dystrophy.

Methods: Vision was assessed in 9 patients and 10 normal controls by measuring: (1) L-cone temporal acuity (critical flicker fusion frequency or cff) as a function of target illuminance, and (2) L-cone temporal contrast sensitivity as a
function of temporal frequency at a fixed target illuminance. Measurements were made by modulating either a 650-nm light superimposed on a 480-nm background or the red phosphor of a color monitor on a background produced by the monitor's blue phosphor.

Results: RPE65-mutant observers have severely reduced cffs with shallower cff versus log illuminance functions that rise with a mean slope of 4.53 Hz per decade of illuminance compared with 8.69 Hz in normal controls. Consistent with the cff differences, RPE65-mutant observers show losses in temporal contrast sensitivity that increase rapidly with temporal frequency.

Conclusions: All RPE65-mutant observers have consistent and substantial losses in temporal acuity and sensitivity compared with normal observers. The losses can be characterized by the addition of two sluggish filters within the mutant visual pathway, both filters with a time constant of 29.5 ms (i.e., low-pass filters with cut-off frequencies of 5.40 Hz).

Should patients with ocular genetic disorders have genetic testing?

Genetic testing may include analysis of single genes (sequencing), multiple genes simultaneously (microarray chips), chromosomal microarrays to detect copy number variations or regions of homozygosity, whole exome or genome sequencing or karyotype identification of large chromosomal aberrations. Genetic testing has 5 parts: clinical identification of a genetic disease, the genetic test, comparing results to established databases/literature, interpretation of test results in the context of clinical findings and counseling. Genetic testing should not be done if counseling is not available. Direct-to-consumer testing is an example of testing in the absence of proper counseling. Pre-symptomatic testing of children for untreatable conditions with adult onset is controversial. Benefits of genetic testing include identification of a definite diagnosis, access to support and possible treatment. Risks of genetic testing include discrimination by insurance companies and discovery of non-paternity, unknown family relationships such as adoption or incest resulting in psychological and social consequences. Little has been written about the economics of genetic testing for ophthalmic diseases.

This article is important because it reviews important issues that should considered prior to recommending genetic testing.

The ECEL1-related strabismus phenotype is consistent with congenital cranial dysinnervation disorder. Khan AO, Shaheen R and Alkuraya FS. J AAPOS 2014;18:362-367
The authors document ophthalmic findings in multiple affected siblings with recessive ECEL1 mutations from a consanguineous family. 10 family members underwent clinical assessment and genetic testing. Four children were affected with distal arthrogryposis and three had ophthalmic findings (strabismus with abnormal synkinesis and ptosis). None of the individuals without arthrogryposis had ophthalmic findings and the one affected individual without ophthalmic findings had the mildest form. The four affected children had the homozygous recessive ECEL1 mutation whereas no other individuals were homozygous for this mutation.

**Novel Recessive Cone-Rod Dystrophy caused by **POC1B** Mutation.**

Cone-rod dystrophy (CORD), which is caused by the progressive degeneration of cones and rods, usually presents with decreased central visual acuity, photophobia, color vision defects, and/or nystagmus in the first decade of life. Nyctalopia, or night blindness, tends to develop later in the disease. This prospective observational case series studied thirteen members of a consanguineous family and 113 unrelated control individuals. Nine of the family members were clinically evaluated, four of which had CORD while the remaining five acted as control relatives. The patients with CORD displayed photophobia, decreased central vision, and dyschromatopsia. On spectral-domain optical coherence tomography (SD-OCT), all the CORD patients exhibited a disrupted inner segment/outer segment (IS/OS) line as well as a blurry external limiting membrane within the central fovea. The cone outer segment line was also noted to be absent in this region. In the midperipheral retina, the rod IS/OS line was disrupted and blurry, and the rod outer segment tip line was absent. Cone response was nonrecordable in all patients. The rod response was nonrecordable in the eldest patient, but subnormal in the others. The Arden Index was abnormal in the youngest patient and flat in the rest of the patients. Linkage mapping was performed using single-nucleotide polymorphism genotype data. Candidate genes were analyzed for mutations via Sanger sequencing. The disease-causing gene mapped to a less than 2-megabase recessive locus at 12q21.33 with a logarithm of odds score of 3.92. A homozygous missense **POC1B** p.R106P mutation was identified at the locus. This mutation was predicted to be damaging to protein function by two online tools. This study reported a novel CORD gene. Interestingly, none of the patients reported nyctalopia, though rod dysfunction was present in all of them. Furthermore, SD-OCT and ERG findings correlated well with clinical observations. The form of CORD seen in this report was assessed as severe and slowly progressive compared with most other CORDs. Overall, this study supports the screening for **POC1B** mutation in patients with CORD, especially those with a more severe phenotype.
Identification of an \textit{HMGB3} Frameshift Mutation in a Family with an X-linked Colobomatous Microphthalmia Syndrome using Whole-Genome and X-Exome Sequencing.


Microphthalmia is a rare heterogeneous condition that may be sporadic or inherited. There are at least six X-linked loci in the Online Mendelian Inheritance in Man database (http://omim.org) that include microphthalmia in the phenotype description. This study identified the causative gene, \textit{HMGB3}, in a pedigree with an X-linked colobomatous microphthalmos phenotype. Four male family members, including the proband, exhibited colobomatous microphthalmia, blepharoptosis, microcephaly, intellectual disability, and short stature. The proband’s mother had left esotropia and a prominent limbal dermoid in the left eye. Whole-genome sequencing and chromosome X-exome-targeted sequencing were performed on the proband and his mother. Polymerase chain reaction and Sanger sequencing were used to confirm the findings. Thirteen unrelated male patients with a similar phenotype were also screened. A two-base pair frameshift insertion in the \textit{HMGB3} gene was found in the proband and his carrier mother but not in any of the unrelated patients. The mutation, confirmed by three orthogonal methods, alters an evolutionarily conserved region of the HMGB3 protein and likely interferes with normal protein function. This study supports \textit{HMGB3} as a new causal gene of microphthalmia. Therefore, an individual with a similar phenotype, particularly if he is a male patient, should be screened for this mutation.

A Novel Test for Recessive Contributions to Complex Diseases Implicates Bardet-Biedl Syndrome Gene \textit{BBS10} in Idiopathic Type 2 Diabetes and Obesity.


When testing for disease association in common, complex diseases most widely used tests assume an additive risk model. One hypothesis is that variants may influence disease susceptibility in a nonadditive, recessive fashion. The power of the additive model to detect recessive alleles is greatly diminished at lower frequencies. Therefore, conventional association tests may miss rare variants associated with common, complex diseases. The authors describe a statistical methodology, termed recessive-allele-frequency-based test (RAFT), designed to detect rare recessive variants in complex diseases. RAFT does not directly compare homozygous counts in case and control subjects. Instead, it evaluates the likelihood of observing the number of homozygotes in the cases ($N_{\text{case}}$) compared to the expected number of homozygotes and normalizes this by the same statistic for observing $N_{\text{controls}}$, the number of homozygotes in the controls compared to the expected number of homozygotes. RAFT was applied to 1,791 Finnish individuals with type 2 diabetes (T2D) and 2,657 matched control subjects. A rare variant (c.1189A>G) in Bardet-Biedl syndrome 10 (\textit{BBS10}) was detected that confers significant risk of T2D in a recessive manner. It was
determined that this rare variant would be missed by Fisher’s exact test, a conventional method. The variant was tested in an in vivo zebrafish model and confirmed to be pathogenic. When compared to standard additive tests, RAFT provides significantly more power to detect lower-frequency recessive variants (allele frequency ≤ 5%). The evidence provided in this study suggests that targeted methods, such as RAFT, may prove to be crucial in identifying rare recessive variants associated with complex diseases.

Phenotypic Overlap Between Familial Exudative Vitreoretinopathy and Microcephaly, Lymphedema, and Chorioretinal Dysplasia Caused by KIF11 Mutations.


Mutations in the KIF11 gene have been associated with microcephaly, lymphedema, and chorioretinal dysplasia (MLCRD), as well as chorioretinal dysplasia, microcephaly, and mental retardation (CDMMR). None of these patients had retinal folds or microphthalmia and only one individual had a unilateral retinal detachment. KIF11 mutations, however, have not been previously associated with familial exudative vitreoretinopathy (FEVR), a hereditary development disorder characterized by failure of peripheral retinal vascularization at birth. To date, five genes have been identified that account for about 50% of FEVR cases: NDP, FZD4, LRP5, TSPAN12, and ZNF408. This study included 72 FEVR probands, 28 (5.6%) of which were found not to have a known FEVR gene mutation. At least one patient in each pedigree manifested ≥1 of the following: macular dragging, partial retinal detachment, falciform folds, or total retinal detachment. Whole-exome sequencing was conducted on affected members in multiplex pedigrees, while Sanger sequencing of the 22 exons of the KIF11 gene was performed on singletons. A mutation in the KIF11 gene was discovered in 4 of 28 probands (14.2%), with a phenotype mimicking FEVR. Two of these four probands were not reported to have microcephaly at the time of recruitment. Three of the six probands with microcephaly associated with chorioretinopathy and/or retinal folds or detachment had a KIF11 mutation. Four novel heterozygous KIF11 mutations (p.A218Gfs*15, p.E470X, p.R221G, and c.790-1G>T) and one previously described heterozygous mutation (p.R47X) were identified in the probands. Documentation of peripheral avascular areas on intravenous fluorescein angiography (IVFA) was possible in two probands with fibrovascular proliferation demonstrating phenotypic overlap with FEVR. This study reveals that the KIF11 gene likely plays a role in retinal vascular development and mutations in this gene can lead to clinical overlap with FEVR. As a result, the spectrum of ocular disease associated with KIF11 mutations has been broadened. Cases of FEVR warrant careful inspection for microcephaly, which could serve as a marker for KIF11-related disease. Additionally, the findings suggest that newly diagnosed cases and newborns at risk for MLCRD should receive IVFA in order to identify peripheral avascular areas that have the potential to be treated.
Frequency and Clinical Pattern of Vitelliform Macular Dystrophy Caused by Mutations of Interphotoreceptor Matrix IMPG1 and IMPG2 Genes.


Vitelliform macular dystrophies, which are the second most common cause of inherited maculopathy after Stargardt disease, have previously been linked to only two genes, BEST1 and PRPH2. A recent paper by the authors associated IMPG1 with autosomal dominant and recessive vitelliform macular dystrophies. Another report implicated IMPG2 in autosomal recessive retinitis pigmentosa with a frequent macular involvement. In this retrospective study the authors assessed the frequency and the clinical findings of vitelliform macular dystrophy linked to IMPG1 and IMPG2. The database of a national referral center specialized in genetic sensory disease was screened for patients with a macular vitelliform dystrophy without an identified mutation, small deletion, or large arrangement in the BEST1 and PRPH2 genes. Forty-nine families were included. IMPG1 was the causal gene in three families (11 patients) and IMPG2 was in a fourth family (2 patients). With autosomal dominant transmission, families 1 and 2 had the c.713T\(\rightarrow\)G (p.Leu238Arg) mutation in IMPG1 and family 4 had c.3230G\(\rightarrow\)T (p.Cys1077Phe) mutation in IMPG2. Patients with IMPG1 or IMPG2 mutations had a late onset and moderate visual impairment (mean visual acuity, 20/40; mean age of onset, 42 years), even in the sporadic case of family 3 with a presumed recessive transmission (mean visual acuity, 20/50; age at onset, 38 years). Drusen-like lesions adjacent to the vitelliform deposits were observed in nine of thirteen patients. The vitelliform material was above the retinal pigment epithelium (RPE) at any stage of the macular dystrophy, and this epithelium was well preserved and maintained its classical reflectivity on spectral-domain optical coherence tomography (SD-OCT). Electro-oculogram results were normal or borderline in nine cases. IMPG1 (6%) and IMPG2 (2%) are new causal genes in 8% of families negative for BEST1 and PRPH2 mutations. These genes should be screened in adult-onset vitelliform dystrophy with moderate visual impairment, drusen-like lesions, normal RPE reflectivity on SD-OCT, and vitelliform deposits located between ellipsoid and interdigitation lines on SD-OCT. These clinical characteristics are not observed in the classical forms of BEST1 and PRPH2 vitelliform dystrophies.

OTX2 Mutations Cause Autosomal Dominant Pattern Dystrophy of the Retinal Pigment Epithelium.


Pattern dystrophy (PD) of the retinal pigment epithelium (RPE), which is typically inherited in an autosomal dominant fashion, is a heterogeneous group of disorders. Some types of PD have been associated with mutations in PRPH2 or BEST1. Many cases of PD, however, have yet to be genetically accounted for. This study identified two families of Caucasian background with autosomal dominant PD at The Hospital for Sick Children (HSC), Toronto. Eight members of
family 1, five of whom were affected, underwent whole-genome SNP genotyping. Multipoint genome-wide linkage analysis was utilized to identify seven regions of potential linkage. Four additional members from family 1 were genotyped, resulting in a maximum logarithm of odds score of 2.09 observed across four chromosomal regions. Fifteen shared nonsynonymous rare coding sequence variants within the linked regions were established by exome sequencing two affected family 1 members. Candidate genes were then prioritized and further analyzed. Sanger sequencing confirmed a novel heterozygous missense variant (E79K) in orthodenticle homeobox 2 (OTX2) that segregated with the disease phenotype. A shared haplotype of 19.68 cM encompassing OTX2 was isolated in affected members of both families. Previously, heterozygous mutations in OTX2 have been associated with anophthalmia, microphthalmia, optic nerve hypoplasia/aplasia, microcephaly, structural pituitary anomalies, and pituitary hormone deficiencies in humans. All of the affected family members, except one individual, demonstrated a distinct macular pattern dystrophy. SD-OCT showed discrete areas of RPE-photoreceptor separation within the macula in all cases. Three individuals displayed generalized photoreceptor degeneration on ERG. All affected individuals were myopic. In addition, mild developmental anomalies, including optic nerve head dysplasia (four cases), microcornea (one case), and Rathke’s cleft cyst (one case), were observed. Pituitary hormone levels were found to be normal. This is the first report implicating OTX2 as a cause of PD. The OTX2-related PD phenotype exhibited interfamilial and intrafamilial variability, similar to what has been observed in PRPH2-related PD. This report broadens the phenotypical spectrum of OTX2-related disease.

Whole Exome Sequencing Identifies CRB1 Defect in an Unusual Maculopathy Phenotype
Stephen H. Tsang, Tomas Burke, Maris Oll, Suzanne Yzer,
Ophthalmology September 2014; 121(9):1773-1782

This is a very detailed article describing the findings of two affected siblings and three unaffected family members of Irish heritage. This study was performed at the Department of Ophthalmology, Columbia University, New York, with input from the Department of Ophthalmology, Stoke Mandeville Hospital, Buckinghamshire, Unite Kingdom, and University Eye Clinic, Tartu, Estonia. Objective of this study is to report a new phenotype caused by mutations in the CRB1 gene in a family with 2 affected siblings.

Design: Molecular genetics and observational case studies.

Methods: Each subject received a complete ophthalmic examination including color fundus photographs, fundus autofluorescence, spectral-domain optical coherence tomography (SD-OCT), electroretinography and other studies.

Conclusions: This report illustrates a novel presentation of a macular dystrophy caused by CRB1 gene mutation. Both affected siblings exhibited a relatively well-developed retinal structure and preservation of generalized retinal function. An unusual 5-year progression of macular atrophy was observed that has not been described previously with CRB1-associated phenotypes.

Comment: Mutations of CRB1 gene have been associated with a variety of generalized retinal dystrophies ranging from retinitis pigmentosa to Leber congenital amaurosis (LCA). Retinitis pigmentosa refers to a group of clinically
and genetically heterogenous disorders affecting one and half million people worldwide. Reported cases of retinitis pigmentosa associated with CRB1 mutation (RP12 phenotype) present with an early disease onset including nystagmus, farsightedness, optic nerve head drusen, attenuation of arterioles, maculopathy and nummular type pigmentation of the periphery. CRB1 mutations have also been correlated to retinal vascular sheathing, preserved para-arteriolar retinal pigment epithelium and development of a Coats-like exudative vasculopathy (condition of a normal appearing blood vessel leading to exudative retinal detachment). Mutations in the CRB1 gene have been detected in 10-13% of the patients with Leber congenital amaurosis. Typical patients with Leber congenital amaurosis with CRB1 usually show a described RP12 characteristics including early onset maculopathy/macular dysplasia, nystagmus, hyperopic, optic nerve head drusen, vascular attenuation and nummular changes in the retinal periphery. CRB1 is the human homologue of the gene encoding the crumbs (Crb) protein in Drosophila melanogaster. This gene is expressed in the fetal brain and inner segments of photoreceptors in humans as well as expression in the brain, kidney, colon, stomach, lung and testis. CRB1 maps to chromosome 1q31.3 and is composed of 12 exons that are translated into 2 protein isoforms (FERM and PDZ that enable adherin junction formation and actin skeleton association. More than 150 disease-associated variants have been described to date in the CRB1 gene, the most common of which is the p.C948Y variant in exon 9. This study describes the clinical appearance of a combination of novel CRB1 variants that were associated with an unusual and previously not described phenotype in 2 affected siblings of Irish descent.

There are some extraordinary photographs, OCT and electroretinogram findings on page 1776, which show a lot of the fine “non-bull’s eye maculopathy” with peripheral retinal changes. The figures also show schisis type changes. The OCT shows cystoid macular edema and schisis type changes of the macula in the right eye. (Please see photographs pages 1776-1779.)

**Single Nucleotide Polymorphisms at the PRR3, ABCF1, and GNL1 Genes in the HLA Class I Region Are Associated with Graves’ Ophthalmopathy in a Gender-Dependent Manner**


This article comes from the Department of Medical Genetics and Medical Research, China Medical University Hospital, Taichung, Taiwan. This is a case-control study of 468 Taiwan-Chinese patients with Graves’ disease; 200 of these patients had Graves’ ophthalmopathy and 268 patients did not have Graves' ophthalmopathy. The purpose is to investigate whether a conserved HLA class I region influenced the development of Graves’ ophthalmopathy in patients with Graves' disease in a Taiwan-Chinese population.

Methods: Five single nucleotide polymorphisms (SNPs) between the HLA-A and HLA-C loci were genotyped. The Mann-Whitney U test and chi-square test were used for statistical analysis. The odds ratio was estimated by applying unconditional logistic regression analysis with 95% confidence intervals.
Conclusions: The results suggested that single nucleotide polymorphisms at the PRR3 and ABCF1 genes and the haplotype composed by SNPs at GNL1 and PRR3 tended to predict Graves' ophthalmopathy in a gender-dependent manner in patients with Graves' disease in Taiwan.

Comment: This study is very important in a sense that it correlates single nucleotide polymorphisms in patients with established thyroid disease (Graves' disease) but who do not have Graves' ophthalmopathy. This study suggests that SNPs at PRR3 and ABCF1 genes between HLA-A and HLA-C genes tended to predict Graves' ophthalmopathy. Graves' disease is a complex disorder that develops through interaction between susceptibility genes and environmental agents such as infection and stress. Grave's disease affects women 5-10 times more frequently than men. Graves' disease is characterized by hyperthyroidism, diffuse goiter and the presence of auto-antibodies targeting the thyroid stimulating hormone receptor (TSHr) and hyperthyroid features, such as weight loss, fatigue, weakness, rapid heartbeat and hand tremors. Some Graves' disease patients also experience extrathyroidal manifestations, such as Graves' ophthalmopathy and thyroid dermatopathy.

Graves' ophthalmopathy is the most common organ specific endocrine disease. It affects 25-50% of patients with Graves' disease. The etiologic factor of Graves' ophthalmopathy remains unknown; however, Graves' ophthalmopathy is generally believed to be associated with genetic predisposition and environmental factors including exposure to cigarette smoke, high dietary iodine intake and stressful lifestyle. Many genetic loci influencing Graves' ophthalmopathy have been identified using genome-wide linkage and candidate gene-association studies. The human leukocyte antigen (HLA) was the first Graves' ophthalmopathy susceptibility gene region to be identified in different ethnic groups; however, this region does not account for all the genetic information associated with Graves' ophthalmopathy. Other genetic loci associated with Graves' disease and Graves' ophthalmopathy primarily in genes involved in immune regulation have been identified cytotoxic T-lymphocyte associated protein 4 (CTLA4), intracellular adhesion molecule 1 (ICAM1), integrin AE (ITGAE) and tumor necrosis factor (TNF).

Using whole-genome sequencing was identified in the HLA region on chromosome 6 as containing susceptibility loci for Graves' disease and also Graves' ophthalmopathy. This is new information regarding the genetics of thyroid eye disease and its associated autoimmune based inflammation.

Identification of CNGA3 Mutations in 46 Families: Common Cause of Achromatopsia and Cone-Rod Dystrophies in Chinese Patients.


Mutations in CNGA3 are the most common cause of achromatopsis and cone-rod dystrophies (CORDs). This study identified CNGA3 mutations in patients with cone dystrophies of Leber congenital amaurosis (LCA). Clinical data and genomic DNA in 267 Chinese probands from 138 families with cone dystrophies.
and 129 families with Leber congenital amaurosis were collected. Variants in CNGA3 were assessed by Sanger sequencing. Homozygous or compound heterozygous mutations in CNGA3, including 26 novel and 13 known mutations, were identified in 46 probands from 138 families with cone dystrophies, but none were found in the families with LCA. The 46 probands with CNGA3 mutations were further classified as having achromatopsia (18 probands) and CRDs (28 probands) based on electoretinographic recordings. Analysis of family members in 17 of 46 families demonstrated good segregation of the disease with the CNGA3 mutations. This is the first large-scale analysis of CNGA3 in Chinese patients. This study reveals that CNGA3 mutations may be the most common cause of CORDs among Chinese patients. In addition, when comparing genes associated with retinal diseases, the large number of mutations in CNGA3 suggests that CNGA3 mutations may be the most common cause of hereditary retinal degeneration in the Chinese population. Therefore, CNGA3-associated cone dystrophies could represent a large proportion of early-onset severe retinal dystrophy. This implies that treatment, such as gene therapy, may benefit some children with early-onset severe retinal dystrophies.

Mutations in MFSD8, Encoding a Lysosomal Membrane Protein, Are Associated with Nonsyndromic Autosomal Recessive Macular Dystrophy.
This case series identified the genetic defect in two families with autosomal recessive macular dystrophy and central cone involvement. Genome-wide linkage analysis and exome sequencing was used in one large nonconsanguineous Dutch family with five affected individuals. The proband of the second Dutch family underwent exome sequencing. An additional cohort of 244 individuals with inherited maculopathies and cone disorders, the majority of whom represented isolated cases, underwent subsequent analysis by Sanger sequencing or restriction enzyme digestion. Compound heterozygous variants in MFSD8, which encodes a lysosomal transmembrane protein, were identified in the two families with macular dystrophy. MFSD8 mutations have been previously associated with variant late-infantile neuronal ceroid lipofuscinosis (vLINCL), a severe multisystem lysosomal storage disease. A heterozygous missense variant p.Glu336Gln, which was predicted to have a mild effect on protein function, was identified in both families. In the first family, a protein-truncating variant (p.Glu381*) on the other allele was found. A variant (c.1102G>C) that causes a splicing defect leading to skipping of exon 11 (p.Lys333Lysfs*3) was isolated in the second family. The affected family members exhibited a normal or subnormal ERF response, but notably a reduced mERG response. Furthermore, they did not display any neurological features consistent with vLINCL. The frequency of the p.Glu336Gln allele in affected individuals with inherited maculopathies and cone disorders (6/488; 1.2%) was significantly higher than in ethnically matched controls (0.18%; P < 0.0001). Though MFSD8 mutations have been associated with vLINCL, the affected individuals in this study have a nonsyndromic macular dystrophy with central cone involvement due to MFSD8 variants. The milder phenotype observed in this study is thought to be due to the combination of a
severe heterozygous mutation and a heterozygous missense variant (p.Glu336Gln), rather than two severe mutations as seen in vLINCL. This paper highlights the genetic overlap between lysosomal storage disorders and nonsyndromic retinal dystrophies, opening new avenues for treatment by targeting lysosomal dysfunction.

Quantitative Fundus Autofluorescence Distinguishes ABCA4-Associated and Non-ABCA4-Associated Bull's-Eye Maculopathy.

Bull's-eye maculopathy (BEM), a common phenotype in some retinal dystrophies, has been linked to various causal genes and is not specific to ABCA4. Concentric parafoveal rings of increased and decreased fundus autofluorescence (AF) are seen with the classic BEM phenotype. This typical AF pattern, however, may not always be present or easy to discern. These factors contribute to the challenges in elucidating the underlying cause of BEM. Through this prospective cross-sectional study, the authors investigate whether quantitative fundus autofluorescence (qAF) and spectral-domain optical coherence tomography (SD OCT) can assist in differentiating ABCA4-associated from non-ABCA4-associated disease in BEM. Thirty-seven BEM patients (age range, 8-60 years) were recruited by the Department of Ophthalmology at Columbia University on the basis of fundus AF. The patients displayed a localized macular lesion with a smooth contour and a qualitatively normal surrounding retina devoid of flecks. A confocal laser ophthalmoscope, with an internal fluorescent reference to account for variations in laser power and detector sensitivity, was used to obtain fundus AF images. Image analysis software written in IGOR (WaveMetrics Lake Oswego, OR) was used to yield qAF. Mean grey levels (GLs) of the internal reference and of eight circularly arranged segments positioned at an eccentricity of about 7º to 9º were recorded. The qAF for each segment was calculated after the GLs were calibrated to the reference (0 GL), magnification, and normative optical media density. The average qAF from the 8 segments (qAF8) for each eye was then generated. This data was compared to control values in a previously published study of 277 healthy subjects with no family history of retinal dystrophy. ABCA4 mutations were identified in 22 patients (60%), who were on average younger than their ABCA4-negative counterparts. Similar qualitative AF features were seen in ABCA4-positive and ABCA4-negative patients. Despite this similarity, ABCA4-positive eyes exhibited significantly higher qAF levels than ABCA4-negative eyes. The majority of eyes (90%) in the ABCA4-positive group had qAF8 of more than the 95% confidence interval (CI) for age. On the contrary, 85% of ABCA4-negative eyes had qAF8 within the normal range. The sensitivity and specificity of qAF measurements in this study were 86.4% and 86.67%, respectively. This qAF data indicates that ABCA4-positive patients have increased lipofuscin levels throughout the posterior pole. Phenotypic differences between the two groups were not apparent on SD OCT. This study demonstrated that although qualitative fundus AF and SD OCT findings are indistinguishable between ABCA4-positive and ABCA4-negative BEM eyes, the two groups could be distinguished by qAF.
Quantitative AF, therefore, proves to be an important tool in guiding clinical diagnosis and genetic testing.

Clinical Aspects of Usher Syndrome and the USH2A Gene in a Cohort of 433 Patients

Usher syndrome, an autosomal recessive disorder, is the most common form of genetic deafness and blindness, afflicting 3.2 to 6.2 out of 100,000 people. It is characterized by sensorineural hearing loss, retinitis pigmentosa (RP), and variable vestibular dysfunction. Type I Usher syndrome is the most severe form and is characterized by severe to profound congenital deafness, vestibular areflexia, and prepubertal onset of retinitis pigmentosa (RP); type II Usher syndrome manifests as moderate to severe hearing loss, absence of vestibular dysfunction, and subsequent onset of RP; and type III Usher syndrome is characterized by progressive postlingual hearing loss, variable onset of RP, and variable vestibular response. Ten genes responsible for Usher syndrome have been identified: 6 genes responsible for type I Usher syndrome (MYO7A, USH1C, CDH23, PCDH15, USH1G, and CIB2); 3 genes responsible for type II Usher syndrome (USH2A, GPR98), and DFNB31; and 1 gene responsible for type III Usher syndrome (USH3A or CLRN1). Auditory and vestibular functions are the distinguishing features of the different types of Usher syndrome. RP is the main ophthalmic manifestation shared by all the types of Usher syndrome.

In this study, the authors evaluated 433 patients who received a diagnosis of Usher syndrome. Three hundred four patients underwent molecular analysis. The study’s aim was to quantitatively describe the primary phenotypic characteristics and differences between type I and type II Usher syndrome in this cohort and to establish a phenotype-genotype correlation for the most frequent mutations in the USH2A gene. This information would be useful in determining the prognosis for affected patients and would assist in genetic counseling and in assigning phenotypes for molecular study.

Results of clinical data, including age at diagnosis of disease, age at onset of night blindness, age at onset of visual field loss and age at diagnosis of hearing loss were significantly younger in Usher I patients compared with Usher II patients. (p<.001) Age of onset of cataracts was not significantly different between the Usher I and II patients.

Usher II patients with the p.Glu767Serfs*21 USH2A gene mutation were diagnosed with hearing loss at an earlier age than other USH2A mutations.
Vitritis in Pediatric Genetic Retinal Disorders
Maria Stunkel, Sajag Bhattarai, Andrew Kemerley, Edwin M. Stone,
Ophthalmology January 2015; 122(1):192-199

This is a retrospective, observational study in humans designed to determine which types of pediatric retinal degeneration are associated with inflammatory cells in the anterior vitreous.

Main Outcome Measures: Cell counts in slit lamp examination of anterior vitreous (SLAV) and clinical and molecular genetic diagnoses were documented. Anterior vitreous cells were graded clinically with SLAV from rare cells 1+ 5-9, 2+ 10-30 and 3+ greater than 30 cells.

Results: The most frequent diagnosis of cells included Bardet-Biedl syndrome (BBS), Leber’s congenital amaurosis (LCA) and retinitis pigmentosa. The most frequent diagnosis without cells included congenital stationary nightblindness, Stargardt’s disease and blue cone monochromacy.

Discussion: A nonrandom subset of pediatric retinal degenerations exhibit vitritis. Cells were present in 5 of 5 Bardet-Biedl patients, whereas cells were not detected in any of the 12 patients with congenital stationary nightblindness.

Conclusions: Studying vitritis in pediatric retinal degenerations may reveal whether inflammation accompanies progressive vision loss in certain subtypes. Potentially, inflammation could be treated. In addition, slit-lamp examination of anterior vitreous may aid in a clinical diagnosis.

Clinical and Molecular Characteristics of Childhood-Onset Stargardt Disease.

Stargardt disease (STGD), the most common juvenile macular degeneration, displays a large amount of phenotypic and genotypic variability. This retrospective case series describes characteristics of childhood-onset STGD and compares them to that of adult-onset STGD. Forty-two patients < 17 years of age with molecularly confirmed STGD were examined at Moorfields Eye Hospital. The median age of onset was 8.5 years, whereas the median age of baseline examination was 12.0 years. The median baseline logMAR VA was 0.74. Thirty-nine patients had baseline color fundus photos. The most common fundus appearance was macular atrophy with macular/ peripheral flecks (67%), followed by macular atrophy without flecks (28%), and numerous flecks without macular atrophy (2.5%). A normal fundus appearance was observed in 2.5% of patients. At baseline, central atrophy was present in 95% of patients and flecks were not observed in 31% of patients. Thirty-two patients obtained baseline fundus autofluorescence (FAF). The most common fundus FAF pattern (69%) was described as a localized low macular AF signal surrounded by a heterogeneous background with widespread high or low AF foci extending anterior to the vascular arcades. Foveal outer retinal disruption was detected in all patients who received a baseline SD-OCT. Twenty-five patients underwent electrophysiological testing at baseline. Macular and generalized cone and rod dysfunction, the most prevalent ERG phenotype observed, occurred in 60%. Retinal dysfunction confined to the macula was seen in 36%. Forty-six ABCA4
variants were identified, of which 13 were novel variants. In 90% of patients at least one disease-causing \textit{ABCA4} variant was identified. Two or more variants were confirmed in 81% of patients. The childhood-onset STGD group was compared to 64 adult-onset STGD patients harboring \geq 2 disease-causing \textit{ABCA4} variants. The childhood-onset group had less retinal pigmentation, more deleterious variants, and thinner central fovea thickness compared to the adult-onset group. Two deleterious variants were identified in 18% patients with childhood-onset STGD, while only 5% of adult-onset STGD patients harbored this amount. This study supports that childhood-onset STGD is associated with foveal structural changes and severe vision loss early in the disease process. Though most children in the study displayed the classic fundus appearance of STGD, one-third in fact did not have visible flecks at presentation. When compared to the adult-onset disease, childhood-onset STGD is more likely to be associated with generalized retinal dysfunction. The higher proportion of deleterious \textit{ABCA4} variants in childhood-onset STGD suggests that the earlier disease onset and more severe phenotype in this patient population may be attributed to more severe variants in \textit{ABCA4}.

\textbf{Early-Onset Stargardt Disease: Phenotypic and Genotypic Characteristics.}

Early-onset Stargardt disease lies within a spectrum of retinal phenotypes associated with mutations in the \textit{ABCA4} gene. Due to its wide clinical variability, Stargardt disease can be challenging to diagnose at a young age. This retrospective cohort study described the phenotype and genotype of 51 early-onset Stargardt patients (defined by \leq 10 years). Genetic screening of 44 patients revealed \geq 2 \textit{ABCA4} mutations in 37 patients (84\%) and single heterozygous mutations in seven (16\%). The mean age at onset was 7.2 years (range, 1-10). The median times to develop BCVA of 20/32, 20/80, 20/200, and 20/500 were 3, 5, 12, and 23 years, respectively. Initial ophthalmoscopy revealed no abnormalities in 24.4\% of patients (10/41). Foveal retinal pigment epithelium (RPE) changes were observed in 22\% (9/41). The remaining 53.7\% (22/41) of patients had foveal atrophy, atrophic RPE lesions, and/or irregular yellow-white fundus flecks. Foveal atrophy occurred before flecks developed in 28\% of patients (14/50). A “dark choroid” was seen in 21 out of 29 patients (72.4\%) on fluorescein angiography (FA). On fundus autofluorescence (FAF), disseminated atrophic spots underwent centrifugal expansion with progression to eventual profound chorioretinal atrophy. Spectral-domain optical coherence tomography (SD-OCT) revealed early photoreceptor damage followed by atrophy of the outer retina, RPE, and choroid. On full-field electroretinography (ffERG), 57.7\% (15/26) of patients had normal amplitudes, while 42.3\% (11/26) had reduced photopic and/or scotopic amplitudes at their first visit. Thirteen out of 25 (52\%) patients had progressive ffERG abnormalities. However, no correlation between ffERG abnormalities and the rate of vision loss was found. The findings in this study indicate that early-onset Stargardt disease can be considered a distinct severe subtype characterized by early foveal abnormalities and rapid loss of visual function. In contrast, foveal sparing is common and visual acuity is often
preserved to a relatively advanced age in late-onset Stargardt disease. The study also advocates for the utilization of FAF and SD-OCT in patients suspected of having early-onset Stargardt disease, particularly when no or mild foveal abnormalities are present in a child with unexplained central vision loss.

**Macular Function and Morphologic Features in Juvenile Stargardt Disease: Longitudinal Study.**


Autosomal recessive Stargardt disease (STGD1) is caused by mutations in the photoreceptor-specific ATP-binding cassette transporter (ABCA4) gene. This longitudinal cohort study evaluated disease progression in patients with a clinical and genetic diagnosis of STGD1. The study was designed to incorporate patients who satisfy the inclusions criteria required in gene therapy clinical trials, such as the StarGen study (clinicaltrials.gov; identifier NCT01367444), which enrolled patients with at least two mutations in ABCA4. A total of 56 patients with early-onset STGD1 were followed for a median length of two years. The patients had a mean age at disease onset of 15.3 years (range, 3-28 years), mean disease duration of 12.1 years, and mean age at baseline of 27.4 years. The median BCVA was 20/200 in both eyes. Optical coherence tomography (OCT), which was not obtained in seven patients due to poor signal quality, revealed a mean retinal pigment epithelium (RPE) lesion area of 2.6 mm², preserved foveal inner segment/outer segment (IS/OS) junction in 4.1% of patients, foveal IS/OS junction loss in 59.2% of patients, and extensive macular IS/OS junction loss in 36.7% of patients. Microperimetry (MP) showed reduced macular sensitivity (mean, 10 decibels [dB]) and an unstable fixation in half of the patients. The longitudinal analysis showed a significant progressive reduction in BCVA and macular sensitivity (at an estimated rate of 0.04 decimals and 1.19 dB/year, respectively) with a significant associated RPE lesion area enlargement (0.282 mm²/year). There were no significant changes in ophthalmoscopic findings and electroretinographic responses detected. The literature supports that visual acuity data alone were not able to detect Stargardt disease progression, particularly in the short-term (< 5 years). This highlights the importance of monitoring retinal function by MP and OCT in order to accurately define disease progression in STGD1 during a short-term follow-up. Previous studies investigated MP parameters in heterogeneous cohorts of patients with macular diseases including only small subgroups of STGD1. In addition, few data regarding OCT lesion area have previously been available since the algorithm was only recently introduced. This study suggests that MP and OCT should be included as outcome measures in the design of future gene therapy clinical trials.
17. TRAUMA

Ocular Safety of Recreational Lasers

The authors bring to attention potential for severe retinal injury with significant visual loss with the improper use of recreational lasers. It can be difficult to distinguish high powered handheld lasers from laser pointers. Because light is focused by the ocular structures the radiance the retina is exposed to is 5-6 times more than the laser’s output. Types of injury include retinal hemorrhage, disruption of Bruch’s membrane and injury to photoreceptors. Vision loss is immediate and may be preceded by an audible pop. Enhanced safety awareness and consumer regulation of lasers are essential to decreasing the incidence of injury and vision loss from recreational lasers.

Ocular Trauma Scores in paediatric open globe injuries

This study assesses the predictive value and applicability of the Ocular Trauma Score (OTS) for pediatric eye injuries. The authors performed a retrospective case series of 71 open globe injuries. Patients were less than 18 years of age with a minimum follow-up of 1 year. They found that initial visual acuities, retinal detachments, wound locations, lens injuries, posterior segment injuries, traumatic cataracts, hyphema, and vitreous hemorrhages had significant impacts on visual outcome. Application of OTS proved difficult as the presence of a subtle relative afferent pupillary defect could not accurately be evaluated in these patients. They found that calculating the OTS without the relative afferent pupillary defect was easily applicable to their initial examinations and remained significantly prognostic (P<0.001). The predications of the Pediatric Penetrating OTS (POTS) correlated with the actual final visual acuities (p<0.001). The authors conclude that OTS has a high predictive value for visual outcome after open globe injuries in children, even without evaluation of a relative afferent pupillary defect.

Epidemiology of blunt head trauma in children in U.S. emergency departments.

This was a large, prospective, observational study conducted in United States emergency rooms examining the characteristics of blunt head trauma among children. Among more than 43,000 children treated in 25 emergency departments for blunt head trauma, traumatic brain injury was identified on CT scan in 7% of the patients. An additional 500 (3%) had skull fractures without intracranial findings. Of all the children who were evaluated, 78 (0.2%) died. Falls were the most frequent injury mechanism for children under the age of 12.
years. Injuries among adolescents were more frequently caused by assaults, sports activities, and motor vehicle crashes.

18. RETINA

Spectral-Domain Optical Coherence Tomography Staging and Autofluorescence Imaging in Achromatopsia

Achromatopsia, a congenital cone photoreceptor disorder, is being recognized as a progressive disease and treatments are on the horizon. This fact underscores the need for a staging system to determine treatment eligibility and to evaluate treatment response. This was a prospective study of 17 patients (age 10-62 years) with full-field ERG-confirmed achromatopsia. Achromatopsia was categorized into 5 stages based on spectral-domain optical coherence tomography findings: stage 1 (2 patients [12%]), intact outer retina; stage 2 (2 patients [12%]), inner segment ellipsoid line disruption; stage 3 (5 patients [29%]), presence of an optically empty space; stage 4 (5 patients [29%]), optically empty space with partial retinal pigment epithelium disruption; and stage 5 (3 patients [18%]), complete retinal pigment epithelium disruption and/or loss of the outer nuclear layer. All patients demonstrated autofluorescence abnormalities in the fovea and/or parafovea. Five novel mutations were identified (4 in the CNGA3 gene and 1 in the CNGB3 gene).

Four-Year Placebo-Controlled Trial of Docosahexaenoic Acid in X-Linked Retinitis Pigmentosa (DHAX Trial) A Randomized Clinical Trial

No cure exists for X-linked retinitis pigmentosa (XLRP) a rare severe degeneration of photoreceptors leading to nyctalopia, tunnel vision and eventual legal blindness. This condition afflicts about 3000 people in the United States. Vitamin A (15000 iu/day) slows rate of cone ERG loss. Docosahexaenoic acid (DHA) is an omega 3 fatty acid found in cold water fish. DHA accounts for 30% to 40% of fatty acids in phospholipids of the retina and is concentrated in the outer segments of rod and cone photoreceptors. Levels of red blood cell DHA are reduced in some patients with XLRP. This study sought to determine the effect of DHA supplementation on ERG measured cone function. In this placebo controlled trial, no effect was found on the annual rate of decline in the primary outcome measure, cone ERG amplitude, by 30mg/kg/d of DHA supplementation during the 4-yearDHAX trial (p = .30) despite greater than a 3-fold elevation in the RBC DHA level. Elevated DHA levels did not effectively slow disease progression as measured by cone and rod ERG function. However, the event rate for this trial was unexpectedly less than predicted from previous studies in XLRP.
Chorioretinal coloboma in a paediatric population
OM Uhumwangho and S Jalali  Eye (2014) 28, 728–733;

In this large observational study, 335 eyes with chorioretinal coloboma in patients younger than 15 were studied. Some patients received prophylactic laser treatment to the edge of the coloboma. The incidence of retinal detachment in the two groups was analyzed – follow up was similar for the two groups (1.5 years in laser group vs 0.8 years in non laser group). The incidence of retinal detachment in the laser group was 3% in the laser group vs 24% in the non laser group. The study was not randomized and selection criteria for laser was not standardized, but the authors state that since the visual outcome of RD in these patients is so poor and the risk of laser in this eyes is low, prophylactic laser should be considered in these patients.

Retinal Segmentation Using Multicolor Laser Imaging.

Multicolor technology utilizing 3 simultaneous lasers- red, green and blue- now permit OCT images to separately display three layers or zones of the retina. (infrared 815 nm, green 518 nm and blue 486 nm). Infrared penetrates deeper layers imaging the choroid, RPE and photoreceptors. The green laser enhances imaging of blood vessels, hemorrhages, and exudates in the mid retina. The blue best captures RNFL, ganglion cell layer, macular pigment, and surface structures like epi-retinal membranes. Artifacts remain an issue typically caused by the presence of corneal or lenticular opacities, poor pupillary dilatation, and high myopia.


This is a retrospective analysis of Spectral Domain OCTs in pediatric (age 0.3 – 16.5 years) and adult (age 40 – 88 years) patients with epiretinal membranes (ERMs). They identified morphologic differences between pediatric and adult patients with ERMs. Pediatric ERMs were more conflually attached to the retina than adult ERMs and had a less fibrillary appearance of the inner retina when separation was present. Pediatric ERMs were associated with more vessel dragging and less external limiting membrane and inner segment band visibility, with a trend toward foveal sparing by the ERM and “taco” retinal folds compared with adult eyes. In both groups intact photoreceptors were predictive of better visual acuity after surgical removal.

CHOROIDAL THICKNESS MEASUREMENT IN CHILDREN USING OPTICAL COHERENCE TOMOGRAPHY  Bidaut-Garnier, M et al Retina April 2014 Vol 34(4) p. 768-774
This is a prospective study of spectral domain OCT measurements of the choroid in healthy children. 348 eyes in 174 children aged 3.5-14.9 years with no known ocular disease and less than 2D of myopia were imaged. The mean subfoveal choroidal thickness (CT) was 341.96 microns +/- 74.7 microns. CT increased with age, height, and weight but was not associated with gender. It was also inversely correlated with axial length as in adults. The nasal choroid appeared thinner than the temporal area. There was significant variation of CT between children of the same age.


This study compared a cohort of young Finnish patients (<25 years of age) with choroidal and ciliary body melanoma with case series from areas of mostly lower risk for uveal melanoma (UM). Forty-seven years of medical records were retrospectively reviewed. During the first 34 years, surgery was performed (Gp 1), and during the last 28 years (overlapped with Gp 1) irradiation was performed (Gp 2). Eight patients underwent surgery (6- enucleation, 2- local resection), and 10 patients were treated with brachytherapy. 13/18 were female. None had a lesion predisposing to UM. Median follow-up time was 11.6 years. Survival in the series was 76% at 5 and 10 years and 68% at 15 years. Based on age, mortality at 15-year follow-up was 0% (age <18 years), 20% (age 18-20 years), and 42% (age 21-24 years). Mortality was not associated with tumor thickness or largest basal diameter. Mortality was higher if the ciliary body was involved. Mortality at 5 years was 0% for stage I tumors, 8% for stage II tumors, and 50% for stage III tumors. Iris melanomas were not included in this study and all patients were >=13 years of age. All patients who died of metastasis in this study and in a number of prior studies were female.


This study identified the prevalence of retinal hemorrhages in intubated patients <4 years of age at our facility and identified associated diagnoses and risk factors. This was a prospective, observational study. Eighty-five patients were examined with an average age of 8.2 months. The in-hospital mortality rate was 17.6%. 6 patients (7%) had retinal hemorrhages. 4 of the 6 had abusive head trauma (AHT), of whom 3 had bilateral severe retinal hemorrhages extending past the posterior pole into the retinal periphery. AHT was significantly associated with retinal hemorrhages. The other two patients had: SIDS (with mild retinal hemorrhages), and accidental head trauma (with diffuse hemorrhages). Coagulopathy (present in 21 patients), was not found to be associated with retinal hemorrhages. Emergent intubation (n=15), was also not associated with retinal hemorrhages. Eight patients had undergone CPR; only one of these had retinal hemorrhages and they were confined to the posterior pole. This study had few patients with accidental head trauma, so retinal
hemorrhage prevalence in this group cannot be commented on. Many families declined participation in the study.

The Spectrum of Ocular Alterations in Patients with β-Thalassemia Syndromes Suggests a Pathology Similar to Pseudoxanthoma Elasticum


This is a cross-sectional observational study of 255 patients with β-thalassemia major (TM) and β-thalassemia intermedia (TI). These groups were investigated and recruited in consecutive fashion.

Methods: The patients underwent best corrected visual acuity, indirect ophthalmoscopy, fundus photography, fundus autofluorescence (FAF) and near-infrared reflectance imaging using a confocal scanning laser ophthalmoscope (cSLO). Hematologic parameters were determined in factors of association with ocular phenotype using logistic regression analysis.

Main Outcome Measures: Ocular phenotype as determined by clinical examination and multimodal imaging.

Conclusions: Pseudoxanthoma elasticum-like fundus changes are a frequent finding in patients with β-thalassemia. In β-thalassemia intermedia (TI), these changes increase in proportion to duration or severity of the illness. The TI phenotype suggested ocular pathologies similar to pseudoxanthoma elasticum (PXE). Retinal vascular tortuosity is felt to be an additional disease manifestation independent of PXE-like syndrome.

Recommendations: Patients with longstanding β-thalassemia major (TM) or β-thalassemia intermedia (TI) who have received multiple iron-chelating treatment and also have a history of splenectomy need regular ophthalmic checkups because they are at risk of developing subsequent choroidal neovascularization similar to that seen in pseudoxanthoma elasticum.

Proton Beam Therapy for Uveal Melanoma in 43 Juvenile Patients: Long-Term Results

A Petrovic, C Bergin, A Schalenbourg, G Goitein, *Ophthalmology* April 2014; 121:898-904

This is a retrospective case-factor match control study of 43 patients younger than 21 years treated with proton beam radiotherapy (PBRT) for uveal melanoma. This study was performed at the Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Lausanne, Switzerland.

Purpose: Examine the metastatic and survival rate, eye retention probability and the visual outcomes of juvenile patients after proton beam radiotherapy for uveal melanoma.

Results: 43 juvenile and 129 controlled cases were reviewed. The metastatic rate at 10 years was significantly lower in juvenile melanoma patients than in adult controls. In the adult control group, 27% matched patients demonstrated metastases; there were 2 cases of local recurrence and 16% underwent enucleation because of complications. A visual acuity more than 0.10 was
maintained in most cases without any significant differences before or after treatment observed between both groups.

Conclusions: After proton beam radiotherapy, the metastatic and survival rates were significantly better for juveniles than for adult patients with uveal melanoma. Clinically, juvenile and adult eyes react similarly to proton beam radiotherapy, with patients having a comparable eye retention probability and maintaining a useful level of vision in most cases. This study validates the proton beam radiotherapy as an appropriate conservative treatment of uveal melanoma in patients younger than 21 years of age.

**Planned Preterm Delivery and Treatment of Retinal Neovascularization in Norrie Disease**


This study is from the Cincinnati Children’s Hospital Medical Center in Cincinnati, Ohio. This report describes the anatomic and functional outcomes of planned pre-termed delivery and treatment for Norrie disease and the first reported use of intravitreal bevacizumab in the vascularly active stage.

The study reports on a 1 month old boy born with leukocoria, microphthalmia and closed funnel retinal detachments in both eyes. The family history was suggestive of X-link inheritance pattern and genetic diagnosis was established by Sanger sequencing. Genetic counseling was offered to the patient’s mother and genetic testing of the fetus by amniocentesis was performed when the subsequent pregnancy was male, confirming NDP mutation.

High risk obstetrics and maternal-fetal medicine specialists determined 34 weeks was the earliest gestational age that they could minimize complications for planned pre-term delivery. No evidence of retinal detachment was present by pre-natal ultrasound. Corticosteroids were used to accelerate fetal lung maturity and vaginal delivery was induced at 34 weeks gestation.

Two days after birth, an examination under anesthesia was performed with laser ablation of the avascular retina in both eyes as well as the intravitreal bevacizumab was injected in the left eye with the hope that additional macular vascularization would proceed.

Ten months after initial treatment, the retina remained completely attached in both eyes and the fovea remained avascular in both eyes. Pendular nystagmus developed at 3 months of age. Teller visual acuities were 20/540 in both eyes. Cycloplegic retinoscopy revealed high myopia and high astigmatism in each eye. Spectral domain optical coherence tomography failed to demonstrate the foveal differentiation. The right eye had a posterior staphyloma. The child was meeting all major developmental milestones. There was no auditory deficit. There have been no long-term complications with pre-term delivery and specifically no respiratory issues.

Summary: Long-term outcomes after early laser treatment for Norrie disease remains unknown although high myopia, high astigmatism and posterior staphyloma formation was observed in this case. The authors suggest that
visual acuity in future patients with Norrie disease largely depends on the degree of foveal vascularization and differentiation, which also drives the degree for the possibility of deprivational and/or refractive amblyopia.

**Stellate Nonhereditary Idiopathic Foveomacular Retinoschisis**

This is a retrospective case series and literature review involving 17 patients from 5 different institutions in the United States. The purpose of the study is to describe a new classification of stellate nonhereditary idiopathic foveomacular retinoschisis (SNIFR). Stellate foveal retinoschisis is most commonly associated with congenital juvenile X-linked retinoschisis (CXLR) due to a defect in the RS1 gene. Foveal retinoschisis is found in nearly all cases of CXLR. Some of these cases also develop peripheral retinoschisis. CXLR accounts for nearly all cases of congenital foveal retinoschisis. The entity is almost exclusively found bilaterally in males.

Methods: Detailed case history, multimodal imaging and genetic testing were reviewed for patients with macular schisis without a known predisposing condition.

Main Outcome Measures: Clinical features, anatomic characteristics and visual acuity were measured in 22 eyes from 16 female patients and 1 male patient with foveomacular schisis.

Conclusion: This is the largest known series of patients with stellate, nonhereditary idiopathic foveomacular retinoschisis (SNIFR). All patients demonstrated splitting of the outer plexiform layer in the macula with relatively preserved visual acuity (20/40 or better) except in 1 patient in whom subretinal fluid developed under the fovea.

Reviewers’ Comment: This is a rare clinical condition that tends to occur in females more than males. The article has excellent photographs and OCT images characterizing the condition.

**Prevention of Retinal Detachment in Stickler Syndrome: The Cambridge Prophylactic Cryotherapy Protocol**
G S Fincham, L Pasea, C Caroll, A M. McNinch, *Ophthalmology* August 2014; 121:1588-1597

This is a retrospective, comparative case series of 487 patients with type 1 Stickler syndrome. Type 1 Stickler syndrome carries a lifelong risk of retinal detachment and prophylaxis is offered to patients of any age. Historically, prophylaxis was only given after the age of 5 when children were considered cooperative enough to accurately phenotype the vitreous on slit lamp biomicroscopic exam.

Methods: Time to retinal detachment was compared between the patients who received bilateral prophylaxis and untreated controls with and without individual patient matching.
Conclusion: In the largest global cohort of type 1 Stickler syndrome patients published, all analyses indicate that the Cambridge prophylactic cryotherapy protocol is safe and markedly reduces the risk of retinal detachment. Stickler syndrome is the most common cause of inherited in childhood retinal detachment. However, there is no consensus regarding effectiveness of prophylactic intervention. This study evaluated the long-term safety and efficacy of the Cambridge Prophylactic Cryotherapy Protocol. This was developed with the specific rationale of preventing retinal detachment arising from giant retinal tears. This protocol was established 37 years ago. Prophylaxis has been offered to all type 1 Stickler syndrome patients and deployed in a standardized fashion.

Reviewers’ Comment: This study was carried out by the Vitreoretinal Service at Cambridge University, Cambridge, United Kingdom, School of Research, University of Sheffield, Sheffield, United Kingdom.

**Terson’s Syndrome---Rate and Surgical Approach in Patients with Subarachnoid Hemorrhage: A Prospective Interdisciplinary Study**


This is a prospective, uncontrolled, interdisciplinary study of 102 patients with subarachnoid hemorrhage over a period of 24 months. The purpose of the study was to analyze the need for surgical intervention and Terson’s syndrome and the rate of Terson’s syndrome as well as the effect of pars plana vitrectomy with or without internal limiting membrane peeling.

Participants: A total of 102 patients with subarachnoid hemorrhage over a period of 24 months. Patients were examined on days 1 and 14. A pars plana vitrectomy was indicated in cases of nonresorbing vitreous hemorrhage. Peeling of the internal limiting membrane was performed using end-gripping internal limiting membrane forceps and BLUE contrast dye.

Conclusions: Pars plana vitrectomy and internal limiting membrane peeling have beneficial effects on the visual rehabilitation of patients with nonclearing vitreous hemorrhage after Terson’s syndrome. The authors did not identify any safety concerns for these procedures that persisted for more than 3 months.

Reviewers’ Comment: Terson’s syndrome was named after the French ophthalmologist Albert Terson in 1900. His original publication was in French. Today Terson’s syndrome is commonly defined as the occurrence of intraocular hemorrhage associated with subarachnoid hemorrhage (SAH). Clinically, intraocular hemorrhage may be subretinal, intraretinal, pre-retinal, subhyaloid or intravitreal and are present in any type of intracranial hemorrhage accompanied by vitreous or retinal hemorrhages known as Terson’s syndrome. According to the current literature, Terson’s syndrome may be caused by intracerebral hemorrhage, subdural and epidural hematoma, severe brain injury or intraventricular hemorrhage. The mechanism causing intraocular bleeding remains unclear but the prevailing hypothesis is that Terson’s syndrome is the result of retinal venous hypertension caused by displaced blood that is forced into the liquer spaces of the optic nerve and causes obstruction of the central retinal vein and choroidal anastomoses under high intracranial pressure.
This study was performed by the Department of Ophthalmology in Department of Ophthalmology, University Medical Center, Hamburg-Eppendorf, Hamburg, Germany.

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**Vigabatrin retinal toxicity in children with infantile spasms**


This is an observational cohort study to evaluate risk factors for, and time to induce retinal damage from vigabatrin (VGB) in children with infantile spasms. The authors included 146 patients who had baseline electroretinogram (ERG) before, or within 4 weeks of initiating VGB therapy, and defined VGB induced retinal damage as a significant reduction in amplitude on 30-Hz ERG flicker. Follow-up ERG was performed every three months. They found that 30 (21%) of patients developed VGB induced retinal damage (5.3% within six months, and 13.3% within 12 months). ERG amplitude was significantly correlated with duration of therapy. They found no recovery following cessation of therapy. Age, sex and cumulative dosage were not associated with the development of VGB induced retinal damage. The authors recommend limiting exposure to VGB to six months to decrease the prevalence of VGB induced retinal damage.


The authors characterize the prevalence and features of fovea plana in normal children, using OCT. Data from a previous study with 286 normal children were included. 9/286 (3%) showed the absence of a defined foveal pit in both eyes. Two of these children had strabismus and 1 had a history of unilateral amblyopia. Fundus exams were all normal, and all obtained a final acuity of 20/20 in each eye with normal stereoacuity. These patients had a significantly thicker fovea on OCT, but there was no difference in total macular volume. There was a continuation of the inner retinal layers over the fovea with a minimally present or absent pit at the foveal center. Patients with high refractive errors were excluded. The original study used Stratus-OCT, which may have missed fine macular details.

**Grading system for retinal hemorrhages in abusive head trauma:**


The main purpose of grading retinal hemorrhages (RH) in abusive head trauma (AHT) is to describe the severity and distribution. The authors devised and clinically evaluated a grading system and descriptive nomenclature for RH in AHT. They categorized:

1. Extent (Region 1 was centered on the fovea and with a radius of 2x disk to fovea; Region 2 represented the rest of the retina)
2. Spread (Mild, moderate, severe)
3. Morphology (intra- or extra-retinal)
There was a high level of intraobserver and interobserver reliability. Obscuration of the fovea by hemorrhages can make grading difficult. Timing can affect grading because hemorrhages resolve. Dense vitreous hemorrhages prevent accurate grading.


The authors attempted to determine whether the mean area of retinal hemorrhages in the posterior pole of children suspected of being victims of abuse is associated with specific clinical findings. This was a 10-year retrospective review of children under 3 years of age. Widefield retinal photography was performed within 36 hours of admission. 149 patients were classified as either definite or possible abuse. Of the 139 patients who had eye exams, 82 had retinal hemorrhages. A total of 96 eyes had adequate photographs. Definite abuse was associated with increased hemorrhage-covered fraction (HCP). HCP was not associated with death, length of hospital stay or skull fracture. It was significantly associated with axial skeletal fracture, and severe neurological injury. One limitation of this study is that patients who died may not have received eye examinations before demise, which could have altered or masked any association.

**Clinicopathological Findings in Abusive Head Trauma: Analysis of 110 Infant Autopsy Eyes.**
Breazzano M, Unkrich K, Barker-Griffith A. Am J Ophthal; Dec. 2015; vol 158(6); pg 1146.

This retrospective case control series looked at 110 eyes from 55 autopsies over 21 years. 60 eyes were identified as abusive head trauma, 46 as alternative cause, and 4 as abusive head trauma survivor. All ocular histopathologic observations were similar in infants younger than 16 months. When present, cherry hemorrhage and perimacular ridge were most often found together. Survivor abusive head trauma demonstrates irreversible macular and optic nerve damage.

**Heidelberg Spectralis Ultra-Widefield Fundus Fluorescein Angiography in Infants**

Retrospective observational case series using a modified Heidelberg Spectralis to perform wide field fundus fluorescein angiography in infants undergoing sedated exam. 22 eyes of 11 infants were examined. The procedure was successfully performed in all children. This permitted capture of the posterior pole as well as the peripheral retina in a single shot.

This is a case report of a 4 year old with a juxtapapillary choroidal osteoma that was treated with proton beam radiotherapy. The patient presented with a subretinal tumour of unknown origin in the left eye found on retinoscopy. At the first examination, the VA in both eyes was 20/20. The tumour increased progressively in size, approaching the fovea. Proton beam radiation was performed with a total dose of 20 cobalt gray equivalent (CGE) in 4 fractions of 5 CGE on 4 consecutive days, using a technique that led to sparing of the cornea, the anterior chamber, and the orbit. Two years after proton beam radiotherapy, her vision dropped to 20/50 and she was found to have CNV. After 3 intravitreal injections of bevacizumab, the CNV was regressed, without any hemorrhages on the fundus exam.

Vitrectomy with Inner Retinal Fenestration for Optic Disc Pit Maculopathy

This article comes from the Manhattan Eye Ear and Throat Hospital, New York, New York, and Vitreoretinal Surgery, Minneapolis, Minnesota. This is a retrospective interventional case series designed to evaluate clinical outcomes after vitrectomy with inner retinal fenestration making a partial thickness retinal hole radial to the optic pit for treatment of optic disc pit maculopathy. Eighteen eyes with optic disc pit maculopathy were studied. All eyes received a pars plana vitrectomy with creation of an inner retinal fenestration.

Conclusions: The introduction of a partial thickness fenestration, radial to the optic pit was associated with retinal anatomic and functional improvement without additional treatments. These results are consistent with the hypothesis that reduction of flow to allow egress of fluid into the vitreous cavity instead of into the retina can achieve long-lasting amelioration of findings associated with pit maculopathy.

Proposed Classification of Posterior Staphylomas Based on Analyses of Eye Shape by Three-Dimensional Magnetic Resonance Imaging and Wide-Field Fundus Imaging
Kyoko Ohno-Matsui, *Ophthalmology* September 2014; 121(9):1798-1809

This is an observational case series of 105 patients with pathologic myopia (-8.0 diopters of myopia or greater than 26.5mm axial length). The patients were examined by 3D MRI and Optos imaging. Staphyloma was defined as an outpouching of the wall of the eye that had a radius of curvature less than the surrounding curvature of the wall of the eye. The presence and types of staphylomas were determined by the entire eye shape in 3D MRI scans. Fundus abnormalities suggesting the staphyloma border were analyzed in the fundus images.
The figure on page 1799 shows the 3 different types of staphylomas that were evaluated. MRI images on page 1802 were compared with fundus photographs. There is a very interesting correlation between fundus findings and the associated MRI findings. The author describes 5 types of staphylomas (page 1800).

Conclusion: Three-dimensional MRI was very useful in analyzing the shape of eyes with and without staphylomata. Even in healthy individuals with severe myopia approximately one-half of the patients did not show clear outpouching or other findings suggestive of staphyloma. The author suggests the correlating MRI data to Optos images provided useful information on the relationship between the eye shape and fundus appearance found with standard fundus photography.

Comment: This article appears to be a professional thesis by Dr. Ohno-Matsui. He proposes a classification of posterior staphylomas. He has some very extensive fundus photographs (both in color and black/white) and specific MRI images, which correspond with the fundus images. The most important finding is that one-half of the patients with high myopia did not show clear findings supportive of staphyloma by MRI criteria.

**Diversity of Retinal Vascular Anomalies in Patients with Familial Exudative Vitreoretinopathy**


This article comes from William Beaumont Hospital, Department of Ophthalmology, Royal Oak, Michigan. A total of 174 eyes of 87 subjects were studied. A retrospective chart review was conducted of patients with a diagnosis of FEVR between January 2011 and January 2013. Data was collected from patient charts including sex, gestational age, age at presentation and referring diagnosis. Clinical and angiographic findings were assessed/evaluated. Results: A total of 87 subjects were studied. A broad spectrum of clinical and angiographic findings was associated with familial exudative vitreoretinopathy (FEVR) on wide-field angiography study. Anatomic and functional changes were evaluated. Conclusions: Familial exudative vitreoretinopathy has a wide range of under-recognized clinical and angiographic findings that are easily identified using wide-field fluorescein angiogram technique. These findings have led to an update of the original FEVR classification scheme. These new findings were more completely characterized of early stages of familial exudative vitreoretinopathy.

Comment: The William Beaumont group has published a familial exudative vitreoretinopathy on a regular basis for the past 10 years. This latest study looks at the familial exudative vitreoretinopathy classification scheme and modifies it according to the findings of the wide-field fluorescein angiography. This can best be seen on Table 3 where the authors describe a revised familial exudative vitreoretinopathy clinical staging system based on the angiographic findings. Stage 1 is defined with and without exudative stages. Stage 2 is defined with and without exudative leakage; likewise, stage 3, stage 4 and stage 5.
Concentric Macular Rings Sign in Patients With Foveal Hypoplasia

The appearance of foveal hypoplasia has never been documented with infrared reflectance (IRR). Foveal hypoplasia has been described in patients with oculocutaneous albinism, ocular albinism, and aniridia. Idiopathic cases of foveal hypoplasia are also found in the literature. The advantage of detecting this characteristic foveal macular reflex on IRR is the ease of the test, which differentiates it from optical coherence tomography (OCT) which may be difficult to obtain in children with high amplitude nystagmus. Concentric macular rings were unique to the study patients and was absent in the healthy control.

Massive Retinal Gliosis in Neurofibromatosis Type 1

The authors describe the first case of extensive retinal gliosis and neurofibromatosis Type 1 (NF-1). They review the typical extraocular features of this autosomal dominant condition, including bilateral ptosis, diffuse and plexiform neurofibromas, optic nerve gliomas, and dysplasia of the sphenoid bone. Intraocular findings in NF-1 include enlarged corneal nerves, Lisch iris nodules, dysplasia of the anterior chamber angle causing glaucoma, multiple choroidal nevi, diffuse uveal hamartomatous thickening, enlarged nerves, uveal peripheral nerve tumors, and retinal astrocytic hamartomas. The 6 year old boy described in this report eventually had his left eye enucleated which had become blind and painful. Histopathology confirmed massive retinal gliosis (MRG) among other more typical findings of intraocular NF-1. Massive retinal gliosis is typically a reactive, nonneoplastic, unilateral condition that develops in adults. The hallmark of MRG is a proliferation of fibrillated eosinophilic spindle cells that replace the vitreous. Glial fibrillary acidic protein positivity confirms the diagnosis. Massive retinal gliosis is typically encountered in phthisical eyes after trauma, surgery, or inflammation and has been described in other conditions such as phthisis associated with advanced retinopathy of prematurity or Coats disease.

MYELINATED NERVE-FIBER ASSOCIATED LOCAL SCLERAL EXCAVATION AND INDUCED AXIAL MYOPIA
Baek-Lok Oh, Jeong-Min Hwang, Se Joon Woo, Retina, October 2014, 34(11)2202-2207

In this study the association of local scleral excavation and myelinated nerve fibers (MNF) was looked at with spectral domain OCT (SDOCT) to determine a pathogenic mechanism for axial myopia in eyes with MNF. Previous studies have shown that eyes with MNF have increased axial lengths and myopia in proportion to the amount of MNF. The degree of myopia is one of the visual prognostic factors in eyes with MNF. The mechanism by which MNF is associated with axial myopia is unknown. This study is a retrospective chart
review of six eyes in six pediatric patients with MNF. All patients had extensive MNF originating at the disc and extending to the retinal mid-periphery. MNF was associated with underlying local scleral excavation as demonstrated by SD-OCT. All eyes also had axial myopia and the authors theorize that MNF causes local visual deprivation which then induces the scleral excavation and thereby the development of myopia.

OUTCOMES OF TREATMENT OF PEDIATRIC CHOROIDAL NEOVASCULARIZATION WITH INTRAVITREAL ANTIANGIOGENIC AGENTS: THE RESULTS OF THE KKESH INTERNATIONAL COLLABORATIVE RETINA STUDY GROUP
Kozak, Igor et al Retina, October 2014, 34(10)2044-2052

This was a retrospective, interventional, case series. A total of 45 eyes of 39 pediatric patients with choroidal neovascularization (CNV) of various etiologies were treated with intravitreal injection of antiangiogenic agents (1.25 mg per 0.05 mL of bevacizumab or 0.5 mg per 0.05 mL of ranibizumab). There were 24 girls and 15 boys with a median age of 13 years (range 3-17 years). Mean follow-up period was 12.8 months. Median visual at presentation and last follow-up was 0.87 logMAR and 0.7 logMAR respectively. Mean and median number of injections received over the follow-up period was 2.2 and 1 respectively. At the last follow-up, 22 eyes (48%) gained more than 3 lines of vision and 27 eyes (60%) had final visual acuity 20/50 or better. Nine eyes (20%) did not improve and had severe vision loss (20/200 or worse). It appears that intravitreal antiangiogenic therapy for CNV in pediatric patients is safe and effective in the short term in the majority of treated eyes. The rarity of pediatric CNV makes it difficult to design and conduct clinical trials to study this further.


The purpose of this study was to assess combined hamartoma of the retina and retinal pigment epithelium with enhanced depth imaging optical coherence tomography (EDI-OCT). This is a retrospective, observational cases series in eight eyes of eight patients, with comparison between affected and unaffected eyes regarding EDI-OCT features of tumor, fovea, and choroid. The mean age at presentation was 7 years. The tumor was macular (n = 5) or extramacular (n = 3). EDI-OCT revealed irregularities in inner retina (n = 8) and/or all retinal layers (n = 3), with epiretinal membrane (n = 8), causing an inner retinal sawtooth (mini-peak) pattern (n = 2), full thickness retinal folds (maxi-peak) (n = 3), or both (n = 3). In the 5 macular tumors, foveal retinal thickness measured mean 608 mm compared with 244 mm in the unaffected eye. Mean tumor epicenter retinal thickness in 8 tumors measured 650 mm compared with 327 mm in a corresponding area in the unaffected eye. In all cases, choroidal thickness beneath the tumor epicenter was decreased at mean 210 mm compared with
Neutralization of Vascular Endothelial Growth Factor Slows Progression of Retinal Nonperfusion in Patients with Diabetic Macular Edema

Peter A. Campochiaro, Charles C. Wykoff, Howard Shapiro, Roman G. Rubio, *Ophthalmology* September 2014; 121(9):1783-1789

This is an unplanned retrospective analysis of prospectively collected data from 2 randomized, sham injection-controlled, double-masked, multicenter clinical trials. The objective of the study was to determine the affect of suppression of the vascular endothelial growth factor (VEGF) by monthly injection of ranibizumab (Lucentis) on posterior retinal nonperfusion in patients with diabetic macular edema.

VEGF contributes to the progression of retinal nonperfusion and retinal vein occlusion as well as diabetic macular edema. This suggests that regardless of the underlying disease process (such as what we also see in retinopathy of prematurity) high levels of VEGF can cause closure of retinal vessels. The authors in this study noted that monthly injections of ranibizumab slow but not completely prevent, retinal capillary closure in patients with DME.

Comment: The most important part of this article is on page 1787 where the authors have demonstrated a schematic representation of the events leading to closure of retinal capillaries in patients with diabetes showing that hyperglycemia causes elevated glucose in the retina. It also mentions a VEGF positive feedback loop and shows where ranibizumab plays in the area of nonperfusion in retinal ischemia. This schematic representation has applications to all types of proliferative retinopathy and the VEGF positive feedback loop is APPLICABLE TO RETINOBLASTOMA. For this reason, this article is presented in articles pertinent to pediatric ophthalmology.

19. RETINOBLASTOMA

Combined Intravitreal Melphalan and Topotecan for Refractory or Recurrent Vitreous Seeding From Retinoblastoma


The purpose of this retrospective study was to determine the efficacy and complications of combined intravitreal chemotherapy for viable vitreous seeding from retinoblastoma. Nine eyes with group D or E retinoblastoma (International Classification of Retinoblastoma) were treated with intravenous chemotherapy and /or intraarterial chemotherapy. Yet these patients developed vitreous seeds. Trans–pars plana intravitreal injection of melphalan hydrochloride combined with topotecan hydrochloride was performed, followed by injection site cryotherapy.
Outcome measure was complete regression of vitreous seeds. Administration of combined intravitreal melphalan and topotecan in eyes not subsequently enucleated appears to be safe and effective for resistant or recurrent vitreous seeds from retinoblastoma. Complete control of vitreous seeds was achieved in 3/9 patients with one injection. However, another 3/9 patients, an eye needed to be enucleated because of recurrent tumor or anterior chamber involvement.

Intravitreal Melphalan for Persistent or Recurrent Retinoblastoma Vitreous Seeds Preliminary Results

Recurrent or persistent vitreous seeds following treatment of retinoblastoma poses difficult management and often leads to enucleation. The purpose of this study is to describe the technique and evaluate the efficacy and complications of intravitreal melphalan for vitreous seeding from retinoblastoma. The study included 11 consecutive eyes of 11 patients with viable persistent or recurrent vitreous seeds following treatment of retinoblastoma. All eyes received intravitreal melphalan injection (20-30 μg) by transconjunctival pars plana route with concomitant triple-freeze cryotherapy at the injection site during needle withdrawal for prevention of extraocular seeding. Outcome measure was control of vitreous seeds and adverse events. At a mean of 9 months of follow-up all patients had complete vitreous seed regression. Complications included focal retinal pigment epithelial mottling near the site of chemotherapy injection (2 eyes) and nonaxial posterior lens opacity (2 eyes). There was no case of extraocular tumor extension, hypotony, or phthisis bulbi.

Tethered Vitreous Seeds Following Intravitreal Melphalan for Retinoblastoma

The authors describe 2 patients with retinoblastoma and vitreous seeds who were injected with Melphalan. They cite the historical admonition against entering an eye with active tumor, lest active cancer cells be drawn out leading to extraocular extension of the tumor. A 33 gauge was used to inject Melphalan at the pars plana and the injection site was closed and sterilized with cryotherapy, the eye submerged in sterile water and antibiotic applied. Post injection scleral depression revealed a vitreous seed drawn toward the injection site. The vitreous seed was eventually obliterated with repeat injections of Melphalan and in one case, repeat cryotherapy. The authors raise awareness of the real possibility of drawing cancer cells toward a point of egress from the eye.
Retinoblastoma Incidence Patterns in the US Surveillance, Epidemiology, and End Results Program

The purpose of this study was to examine updated US retinoblastoma incidence patterns by sex, age at diagnosis, laterality, race/ethnicity, and year of diagnosis. The Surveillance, Epidemiology, and End Results (SEER) databases were examined for retinoblastoma incidence patterns by demographic and tumor characteristics. The number after SEER refers to the city/region in the United States which participated in the registry. Hence, 18 cities/regions participated in SEER 18 and so on. During 2000-2009 in SEER 18, the total retinoblastoma incidence rate (per 1,000,000 person-years) was 13.2 among boys and 11.2 among girls, giving a significantly elevated male/female incidence rate ratio (IRR) of 1.18. Incidence rates for unilateral cases were more than twice those for bilateral cases among boys and girls. Retinoblastoma incidence was uniformly lowest among white non-Hispanics, and only the male incidence of bilateral retinoblastoma among white Hispanics was significantly higher than among white non-Hispanics (IRR 1.81). The incidence rates for unilateral and bilateral retinoblastoma diagnosed at 1 to 4 years of age were significantly lower than those at younger than 1 year among both boys and girls.

Retinoblastoma: The Zimmerman Family Story

Mary Louise Z. Collins shares her family's amazing story of the intersection of the professional and personal. Her father, Lorenz Zimmerman, a preeminent ocular pathologist, conducted seminal work in retinoblastoma and is the father of a child with bilateral retinoblastoma and a granddaughter with trilateral retinoblastoma. An inspiration to all in our field, the Zimmerman’s family journey is a tale of courage, perseverance and commitment to medical discovery and innovation.

Ocular side effects following intravitreal injection therapy for retinoblastoma: a systematic review
S J Smith, B D Smith, B G Mohney

This study reviewed the ocular side effects in patient receiving intravitreal injection therapy (IViT) for retinoblastoma. For decades the use of IViT in retinoblastoma patients has been limited due to concerns for the risk of tumor seeding into the orbit. In Japan IViT has been incorporated more widely over the past two decades as cultural differences drive a more aggressive approach to globe salvage. Recent reports have suggested the risk of tumor dissemination may be quite small with only one case of confirmed tumor spread in over 300 patients treated with IViT. The authors searched PubMed, Scopus, Science Citation Index, and Conference Proceedings Citation Index – Science to identify all published reports of therapeutic intravitreal injections for retinoblastoma in humans. They found 10 studies that totaled 1287 intravitreal injections in 306 eyes. The mean follow-up was 74.1 months. Ocular side effects occurred in 38 patients. The proportion of patients experiencing potentially significant ocular side
effects following standard melphalan IViT regimens was 0.031 (8/261; 95% CI 0.013 to 0.06). The side effects in these eight patients included iris atrophy, chorioretinal atrophy and vitreous hemorrhage, and one retinal detachment. Of the other 9 patients with significant complications, 5 experienced sight-threatening complications following dramatic dose escalations (4 with melphalan, one with thiotepa), 3 experienced complications that are commonly associated with concurrent therapies given to these patients, and one had a retinal detachment. Of the 61 patients receiving IViT via safety-enhancing injection techniques, all of the significant side effects were either attributed to the therapeutic dose or confounded by concurrent treatments. The authors conclude that significant ocular complications following IViT for retinoblastoma are uncommon, and the risk may be reduced further by the use of careful injection technique and standard dosing regimens.


This study was a prospective interventional study looking at 6 patients who were going to undergo enucleation due to retinoblastoma. The patients were divided into 3 groups. Each group was given a retrobulbar injection of nanoparticle carboplatin. Two eyes were enucleated at 6 hours, 24 hours and 72 hours after injection. IV blood was collected at the same time of enucleation. The eyes were examined to see the intraocular concentration of carboplatin. In results, the retina had the highest concentration up to 24 hours post injection. The vitreous level increased up to the 72 hours level. The choroid and lens showed very little concentration. No signs of tissue damage. IV concentrations were undetectable. Retrobulbar injection of carboplatin may be a useful adjunctive therapy for patients with advanced retinoblastoma and vitreous seeds.

OCULAR PHARMACOLOGY OF TOPOTECAN AND ITS ACTIVITY IN RETINOBLASTOMA Schaiquevich, P et al Retina September 2014 Vol.34(9) p. 1719-1727

This is a literature review of Topotecan and its efficacy in the treatment of retinoblastoma. Forty two available studies from PubMed were reviewed. Topotecan alone or in combination with other agents is active against retinoblastoma showing favorable vitreous penetration and a safe toxicity profile. The activity of topotecan against retinoblastoma is evident from in vitro and in vivo models, patient cohorts with intraocular disease and a limited cohort of extraocular disease. However, its exact role in the clinical management of retinoblastoma remains to be determined. The intravitreal route is very promising, but is still in the preclinical phase, and additional studies may provide more information on schedule, efficacy, and toxicity with the final aim of adding another drug to the limited armamentarium for intravitreal chemotherapy in clinical use.
Clinical Pharmacokinetics of Intra-arterial Melphalan and Topotecan Combination in Patients with Retinoblastoma
P Taich, A Ceciliano, E Buitrago, B C Sampor, *Ophthalmology* April 2014; 121:889-897

This is a single-center, prospective, clinical pharmacokinetic study performed in private services and National Cancer Institute in Argentina, Brazil and Venezuela.

Participants: 26 patients/27 eyes with intraocular retinoblastoma.

The purpose is to assess the antitumor activity, toxicity and plasma pharmacokinetics of the combination of melphalan and topotecan for superselective ophthalmic artery infusion (SSOAI) treatment of children with retinoblastoma.

Conclusions: A regimen combining melphalan and topotecan for superselective ophthalmic artery infusion for the treatment of retinoblastoma is active and well tolerated. This combination of chemotherapy previously showed synergistic pharmacologic activity. This study was carried out and showed no evidence of increasing the hematologic toxicity compared with single agent melphalan.

Diagnostic Performance of Magnetic Resonance Imaging and Computed Tomography for Advanced Retinoblastoma: A Systematic Review and Meta-analysis
M C. de Jong, P de Graaf, D P. Noij, S Goricke, *Ophthalmology* May 2014; 121:1109-1118

This is a systematic review and meta-analysis of patients with advanced retinoblastoma who underwent MRI, CT or both for the detection of tumor extent from published diagnostic accuracy studies.

Purpose: To determine and compare the diagnostic performance of magnetic resonance imaging and computed tomography for the diagnosis of tumor extent in advanced retinoblastoma, using histopathologic analysis as the reference standard.

Main Outcome Measures: Sensitivity and specificity of MRI versus CT in detecting tumor extent.

Conclusions: Magnetic resonance imaging showed no superiority over CT scan diagnosing retinoblastoma. This diagnostic accuracy is less than optimal in regard to sensitivity. There is very little evidence in literature on the diagnostic accuracy of CT. Generally these studies show low diagnostic accuracy. Future studies assessing the role of MRI and clinical decision making in terms of prognostic value for advanced retinoblastoma are needed.

Intra-arterial chemotherapy for retinoblastoma in 70 eyes: Outcomes based on international classification of retinoblastoma.
This is a retrospective interventional case series of 70 eyes in 67 patients. The purpose of the study is to analyze a 5-year experience of intra-arterial chemotherapy (IAC) for retinoblastoma as primary or secondary therapy. Intervention: Ophthalmic artery chemotherapy infusion under fluoroscopic guidance was performed using melphalan in every case. Additional topotecan was administered as necessary.

Main Outcome Measures: Tumor control and treatment complications.

Results: The mean patient age for intra-arterial chemotherapy was 30 months. The treatment was primary in 36 eyes and secondary therapy in 34 eyes.

Conclusion: 5-year experience with intra-arterial chemotherapy indicates that this technique is remarkably effective for the management of retinoblastoma as both a primary and a secondary treatment.

Reviewers’ Comment: There are excellent photographs on page 1455 showing resolution of primary (figure 1) and secondary (figure 2) retinoblastomas. Some complications include forehead hyperemia, slight ptosis of the upper eyelid, sector choroidal atrophy in the nasal quadrant after intra-arterial chemotherapy, branch retinal artery obstruction and intraretinal hemorrhages after several treatments of intra-arterial chemotherapy.


The authors emphasize the importance of accurately diagnosing retinoblastoma (RB) as over 25 conditions can simulate RB. Treatment of RB is complex and may include chemotherapy, enucleation, laser photocoagulation, thermotherapy and cryotherapy. Chemotherapy administration is based on the type of mutation present (germline or nongermline), laterality and stage of disease. Chemotherapy delivery may be intravenous (IV), intra-arterial, periocular and intravitreal. IV chemotherapy is the first line of therapy for bilateral (germline) RB to control intraocular disease, prevent metastasis, and reduce the prevalence of pineoblastoma and second malignant neoplasms. Bilateral groups D and E receive additional periocular chemotherapy with carboplatin or topotecan boost for improved local control. Treatment with intra-arterial chemotherapy for unilateral (nongermline) RB or for salvage after chemoreduction failure should be considered. Intravitreal chemotherapy is reserved for recurrent vitreous seeds following other therapies.

This article is important because it reviews ocular conditions that can be misdiagnosed as retinoblastoma, RB classification, and indications for enucleation and chemotherapy. The treatment strategy for RB is complex but this article helps to break down the decision making process.
Retcam fluorescein angiography findings in eyes with advanced retinoblastoma
Jonathan W Kim, Lynn K Ngai, Srinivas Sadda, Yohko Murakami, Diana K Lee, A Linn Murphree

This is a retrospective case series to characterize the fluorescein angiogram (FA) findings of eyes with advanced retinoblastoma evaluated with Retcam contact fundus camera. Inclusion criteria included (1) patients with advanced retinoblastoma (group D or E), (2) eyes studied with early, mid-phase and late-phase Retcam FA photographs and (3) no prior treatment. A total of 100 eyes were identified. For the 47 eyes in group D the FA findings included iris neovascularization (10/47), large retinal vessel dilatation (46/47), small retinal vessel changes (35/47) and retinal venous leakage (20/47). Among the 53 eyes in group E, FA findings included iris neovascularization (45/53), large retinal vessel dilatation (43/53), small retinal vessel changes (37/53), and vascular abnormalities at multiple levels (11/53). The authors conclude that advanced intraocular retinoblastoma is associated with multiple retinal vascular abnormalities on Retcam FA. These findings may be helpful in defining the extent of disease or distinguishing it from other pediatric ocular conditions.


Incidence of retinoblastoma and the long-term survival rate of retinoblastoma patients in South Korea born between 1993 and 2010. The overall incidence was 11.2 for children aged 0 to 4 years and 5.3 for children aged 0 to 9 years per 1,000,000 person-years, 5.9 per 100,000 live births, and 5.3 per 100,000 live births. The all-cause mortality rate was 7.9% at 5 years and 8.4% at 10 years. The rate improved from 12.5% for patients diagnosed in 1993 to 2000 to 4.5% for those diagnosed in 2001 to 2010. The incidence of retinoblastoma in Korea was found to be similar to that in the United States, Europe, and Asia. The survival rate of retinoblastoma patients in Korea was significantly better during 2001 to 2010 than during 1993 to 2000.

Local and Systemic Toxicity of Intravitreal Melphalan for Vitreous Seeding in Retinoblastoma
A Preclinical and Clinical Study
Jasmine H. Francis, Paula Schaiquevich, Emiliano Buitrago, María José Del Sole, Ophthalmology September 2014; 121(9):1810-1817

This is a clinical prospective cohort study that studies the intravitreal melphalan as an emerging and effective treatment for refractory vitreous seeding in retinoblastoma. This study evaluates the retinal and systemic toxicity of intravitreal melphalan in retinoblastoma patients. Preclinical validation studies were performed in a rabbit model. Sixteen patients received 107 intravitreal injections of 30 micrograms of melphalan given weekly for a median of 6.5 times
(range, 5-8). In the animal study, 12 New Zealand/Dutch Belt pigmented rabbits were given 3 weekly injections of 15 micrograms of intravitreal melphalan to the right eye. Weekly injections of intravitreal melphalan showed a reduction in the amplitude ERG by approximately 5.8 microvolts after each injection. The ERG remained stable once the treatment course was completed. In retinoblastoma patients there was no grade 3 or 4 hematologic event. One week after the second injection in the rabbits, the A and B wave declined significantly in the melphalan treated eyes. Conclusions: Weekly injections of 30 micrograms of melphalan resulted in a decreased ERG response which is indicative of retinal toxicity. These findings are confirmed on equivalent dosage in rabbit eyes by ERG measurements and by histopathologic evidence of severe retinal damage.

Comment: Please see figure 1, page 1812 where there is a very impressive case of salt-and-pepper retinopathy after intravitreal melphalan. These findings were suggestive of melphalan toxicity. On page 1815, hematoxylin and eosin stained representative rabbit eyes demonstrated “severe atrophic retina with loss of photoreceptors, outer nuclear layers, vitreous cells and pigment migration from the retinal pigment epithelium. This is an excellent clinical and preclinical study using human and animal data to help describe the toxic effects of intravitreal melphalan. This treatment is now being considered for fresh onset vitreous seeding because it appears to be a safer procedure than intra-arterial melphalan injection in young children.

**Randomized, Controlled trial in Groups C and D Retinoblastoma**


This study comes from the Oculoplastics & Ocular Oncology Service of the All India Institute of Medical Sciences, New Delhi, India. This is a prospective randomized control trial performed in India. All new retinoblastoma cases are presented between April 2009 and May 2011 and were evaluated prospectively using magnetic resonance imaging, contrast enhanced computed tomography orbit, ultrasonography and examinations under anesthesia. The purpose of this study is to determine the effect of an increased dose of intravenous Carboplatin improves the globe salvage rate in groups C and D retinoblastoma. Results: Treatment responses were analyzed for retinal tumor, vitreous and subretinal seeds. Conclusions: Pilot data suggested of this study showed that increasing the dose of intravenous Carboplatin may not be an effective strategy to improve the outcomes of groups C and D retinoblastoma patients.
Enophthalmos and Choroidal Atrophy after Intraophthalmic Artery Chemotherapy for Retinoblastoma
Brian C. Tse, Sue C. Kaste, Rachel Brennan, Brent Orr, Ophthalmology
February 2015; 122(2):435-437

This comes from the Department of Ophthalmology, Hamilton Eye Institute, University of Tennessee Health Science Center, Memphis, Tennessee. Superselective intraophthalmic artery chemotherapy (SSIOAC) has come to the forefront in the treatment of retinoblastoma. The authors have presented the histopathologic findings of retinoblastoma patients who subsequently developed enophthalmos, choroidal ischemia, iris atrophy and scleritis as delayed toxicitiets of superselective intraophthalmic artery chemotherapy. The authors report a 5 month old, identical twin born at 34 weeks with a right esotropia who was diagnosed with retinoblastoma. The authors hypothesize that chronic damage to orbital vasculature by this method of treatment lead to poor orbital and globe perfusion ischemia and impaired ocular growth and orbital fat atrophy. The authors findings underscore the need for further preclinical modeling and close clinical follow-up with specific sensitivity for ocular and orbital toxicity to assess the long-term consequences of superselective intraophthalmic artery chemotherapy (SSIOAC).

20. ORBIT

Angiolympoid Hyperplasia With Eosinophilia of the Orbit and Ocular Adnexa Report of 5 Cases

The authors present the largest case series of angiolympoid hyperplasia with eosinophilia (ALHE). This rare benign disorder is characterized by marked vascular proliferation and inflammation and affects the head and neck, usually in middle-aged patients. Two of the five patients in this study were children, aged 11 and 12. Presenting signs included blurred vision, proptosis, diplopia, and lid swelling. Differential diagnosis includes lymphoma, hemangioma or lacrimal gland involvement with sarcoidosis. The authors note that mildly elevated ACE levels can be seen in younger pateints without sarcoidosis. Thus, a definitive diagnosis of ALHE can only be made by histopathologic analysis of a biopsy specimen. It has been proposed that ALHE may represent a benign proliferation of the endothelial cells in response to trauma or inflammation. Since most lesions regress spontaneously, it is reasonable to observe the lesion waiting for spontaneous regression after an incisional biopsy. If regression does not occur, treatment could include surgical excision, irradiation, oral and intralesional steroids, and cytotoxic agents.
Pingyangmycin as First-Line Treatment for Low-Flow Orbital or Periorbital Venous Malformations: Evaluation of 33 Consecutive Patients

R Jia, SXu, X Huang, X Song, et al.

The authors conduct a retrospective non-comparative interventional study of intralesional pingamycin injection for the treatment of 33 patients with low flow orbital or periorbital venous malformations. Vascular malformations may be arterial, venous or lymphatic or a combination. Orbital or periorbital venous malformations (OVM) are among the most common and while congenital, may clinically become apparent in childhood when the lesion internally hemorrhages or thrombosis resulting in pain or disfigurement. Treatment has included excision, sclerotherapy, electrocautery and laser treatment. Pingamycin is a chemotherapeutic agent which destroys endothelium and causes inflammation leading to thrombus formation and involution of the lesion. Outcome measures included reduction in volume of lesion as determined by ultrasound and overall appearance. The mean pretreatment volume was 4.4 cm cubed and posttreatment was 1.0 cm cubed (p<0.001). No recurrences were noted after a median of 2 injections per lesion and an average follow up of 7.9 months. Adverse events were limited to conjunctival swelling and subcutaneous atrophy.

Epstein-Barr Virus–Positive Polymorphous Lymphoplasmacytic Infiltrate of the Lacrimal Glands in a Patient With Acute Lymphoblastic Leukemia


The authors highlight a clinical dilemma of determining if acute onset of periorbital swelling is indicative of leukemia relapse in a teenager who was receiving maintenance chemotherapy for high risk acute lymphocytic leukemia (ALL). Extensive evaluation included blood cultures, CT scan of the orbits, and lacrimal gland biopsy with immunohistochemical staining and PCR. Results confirmed Epstein barr virus as the etiology of the preseptal cellulitis and dacryoadenitis and not a recurrence of this patient’s leukemia.

Clinical Features and Treatment of Pediatric Orbit Fractures


In the US, approximately 850,000 pediatric ER visits per year are the result of craniofacial injuries. This investigative case series looked retrospectively at 312 pediatric patients with orbit fractures diagnosed by CT. Fractures were most commonly due to falls in the toddler years and from sports related injury in patients older than 5. Roof fractures occured more commonly in younger patients. They tended to be associated with skull fractures and neurological injuries. They were less likely to require surgical intervention. Floor fractures occurred more frequently in older children and were more likely to require
surgical repair. They were associated with other midface fractures. Neurologic injuries were more common (23%) than associated ophthalmic injuries (20%).


The authors evaluated whether or not the classification system, including CT imaging findings, helps predict which patients require subsequent surgical intervention. This was a retrospective review of cases seen over an 11-year period. 101 cases were included. The mean patient age was 7.2 years. 71/101 were managed medically while the rest were managed surgically. Bony destruction on CT was significantly correlated with surgical intervention. 1 case of bony destruction affected the orbital floor, the rest affected the lamina papyracea. The presence of a subperiosteal abscess was higher in the surgical group (86%) than in the medically treated group (65%). Volume of the abscess was correlated with management outcome (larger size meant greater likelihood of surgery) as well as duration of antibiotic therapy. The surgical group had longer duration of intravenous antibiotic therapy and total duration of antibiotic therapy, as well as length of hospital stay. Residual ophthalmoplegia and/or diplopia was uncommon and had similar rates in the two groups (10% surgical group, 8% antibiotic only group). Age was not a factor in the need for surgical intervention in this study. The Chandler classification system was not found to predict the risk of surgical intervention well. The authors propose a modified classification system, adding volume of the abscess to enhance predictive value.

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Surgical Timing and Postoperative Ocular Motility in Type B Orbital Blowout Fractures

Indications and optimal timing for surgical repair of orbital blowout fractures have been debated for decades. This study aims to evaluate whether patients with Type B orbital blowout fractures have greater postoperative vertical binocular fusion if repaired within 7 days of injury than similar patients who undergo later surgery. Typ B fractures have soft-tissue distortion disproportionate to bone-fragment displacement. This includes pediatric trapdoor ("white-eyed blowout") fractures but is not limited to that specific syndrome. The study was a prospective and retrospective case series. Group 1 (surgery within 7 days) had postoperative vertical binocular fusion averaging 100 degrees, while group 2 averaged 70 degrees. Group 1 also yielded statistically better motility. The authors recommend that all Type B fractures be considered for repair within a few days of injury to minimize ongoing soft-tissue compromise.
Oral Propranolol as an Alternative Therapy for Orbital Angiolymphoid Hyperplasia with Eosinophilia
McClintic EA, Ting A, Yeatts RP. Ophthal Plast Reconstr Surg 2014; 30(6);e1-2

This is a case report of an 8 year old female with left upper eyelid swelling and erythema. An orbital mass was revealed and incisional biopsy lead to the diagnosis of angiolymphoid hyperplasia with eosinophilia (ALHE). Oral propranolol (2mg/kg/day) was initiated after unwanted side effects of steroid therapy. Interval decrease in lesion size was observed on subsequent imaging with complete resolution of subjective symptoms. ALHE is a benign reactive process presenting with lesions in head and neck. Traditional treatment includes excision or steroid therapy. This case lends evidence that propranolol may be considered a noninvasive treatment option for ALHE.


Causes of motility disturbance in patients with orbitofacial NF1 (OFNF) with neurofibromas of the lids, brow, face and orbit were evaluated. Thirty years of medical records were retrospectively reviewed. 84 patients were identified, of whom 49 had adequate motility information. 4/49 had bilateral involvement. No patient had a significant motility disturbance or diplopia, except for one patient who developed a superior oblique palsy after orbital decompression. Anatomic abnormalities in the fourteen patients without strabismus, in order of occurrence included a large globe ipsilateral to the OFNF (n=14), sphenoid dysplasia (n=5), and orbital or cavernous sinus neurofibromas (n=4). Eight patients had comitant strabismus and 27 had incomitant strabismus. Of the 31 patients with sphenoid dysplasia, 20 had some duction limitation causing incomitant strabismus. The nine patients who also had pulsatile exophthalmos all manifest strabismus. 2/3 of the 27 patients with tumor infiltrating the orbit or cavernous sinus, and 2.3 of the patients with optic pathway glioma had mild ductional defects. Globe displacement was often associated with strabismus. This study was based at a tertiary center which may have introduced selection bias.


Surgical outcomes of DCR at a single tertiary eye care center in Nepal in a pediatric population in Nepal were assessed. This was a retrospective review of patients with a minimum follow-up of 3 months operated on over an 18-month period. 38 patients were included with a mean age of 10.2 years. Exam follow-up was 11.5 months. Overall success was 37/38 (97%). Complications included punctual laceration (n=1), epistaxis (n=3), wound infection (n=1), and pyogenic granuloma (n=1).
Clinically Recognizing Enlarged Extraocular Muscles from Lymphoid Origin

This is from the Department of Ophthalmology, University Hospitals Leuven, Belgium. This article involves a retrospective review of clinical charts and orbital MRI and computed CT scans of patients with extraocular tumors seen between 1998 and 2012. The final analysis included 11 patients with a mean age of 58 years (range 21 to 84 years). The initial presenting symptom in 91% of the patients was double vision, 45% presented with proptosis and 36% eyelid swelling and tearing. None of the patients presented with orbital pain. On MRI or CT the belly of the muscle was diffusely, smoothly enlarged and contrast enhanced with anterior tendon enlargement in 43% of the lymphoid and 25% of the metastatic patients.

In conclusion, the finding of weakening without restriction in a painless enlarged extraocular muscle can be considered a useful clinical finding favoring the diagnosis of lymphoid tumor. It underscores the importance of obtaining biopsies and systemic oncologic screening when the clinicoradiologic pattern deviates from the classic thyroid eye disease or Graves’ orbitopathy pattern.

21. OCULOPLASTICS


This is a retrospective study looking at the prevalence of strabismus in children with ptosis. They evaluated 107 records of patients with ptosis over a 40 year period in Minnesota. Twenty of 107 patients were found to have strabismus (18.7%). All cases of strabismus happened in unilateral ptosis patients except for 3 cases. 1 patient with bilateral ptosis had strabismus due to congenital fibrosis of the EOM, the other patient ad Noonan Syndrome, and the other had Myasthenia gravis.

There were 81 patients with simple congenital ptosis, 8 of which were diagnosed with strabismus (9.9%). Half had esotropia and half had exotropia. There were no cases of isolated vertical muscle deviations.

General population incidence of strabismus is 1-5%.

Surgical Treatment of Severe Congenital Ptosis in Patients Younger than Two Years of Age Using Preserved Fascia Lata. K. Woo. Y. Kim, Y. Kim. Am J Ophthal June 2014; 157(6); pg 1221.

This is a retrospective study that looked at the outcome of frontalis sling using preserved fascia lata in children less than 2 years of age. The mean age of surgery was 15 months. 82 patients were found with visual axis obscuring congenital ptosis. 64 patients showed good to fair outcome. Reoperation was needed in 16 of the patients. The study ascertains that preserved fascia lata is an acceptable alternative in the young age group and may provide permanent solution to ptosis. Mean follow up was 54 months.

This study was a prospective case control study. 88 children with chalazia were divided into 2 groups (one group was under 6 years, the other over 6 years). The control group was normal. Both groups had their serum vitamin A, D3, and immunoglobulin E tested. Average serum vitamin A was lower in the case group than in the control. No differences were found in the D3 or Ig E level. Low vitamin A level may account for chalazion, especially multiple chalazion in young age group.

Supramaximal Levator Resection for Unilateral Congenital Ptosis: Cosmetic and Functional Results

This retrospective review of 35 children with unilateral congenital ptosis who underwent supramaximal levator resection looked to analyze its cosmetic and functional results. The surgery was performed in children with poor function of the levator palpebrae superioris muscle and no clinical evidence of ipsilateral compensatory frontalis hyperaction. The supramaximal resection did effectively raise the lid and reduce the asymmetry between the eyelids. However when large sections of the levator palpebrae muscle are resected the elastic properties of the eyelid are severely impaired. Thus, side effects included a reduction in spontaneous blinks and downward saccades. This surgery should therefore only be considered in patients with normal Bells signs.

Frontalis Suspension with Supramid Suture: Longevity Results in Very Young Patients with Congenital Ptosis

The purpose of this study was to evaluate the longevity of Supramid suture for frontalis suspension. Supramid suture is a polyfilament, cable-type 3-0 suture. Previous reports had cited high recurrence rates within the first 18 months postoperatively. Criticisms have also cited a high risk of infection and granuloma formation. 44 patients, aged 4 years or less, were retrospectively reviewed who underwent frontalis suspension with Supramid suture. Average duration of the sling was 3.4 years (ranging 19 days to 13 years). Survival rate was 87.5% at 1 year, 74.5% at 3 years, 58.2% at 4 years and 53.7% at 5 years. 5 cases (11%) developed granulomas. The authors believe that Supramid suture is a viable option in the treatment of early congenital ptosis with the risk of amblyopia.

PEDIG performed a multi-center study of office-based probings in infants aged 6 to <15 months. There were two large prospective studies. Study A was a nonrandomized prospective study and 193 subjects (243 eyes) are included. Study B was a randomized trial and 111 subjects are included here. Of Study A patients, 96% completed the 1-month outcome visit. Treatment success was 72%, subject-level treatment success (both eyes needed to have resolution of the NLDO) was 70%, and in subjects <10 months old treatment success was seen in 75% of eyes. Study B had 89% of patients complete the 6-month outcome visit. 80% of eyes were treated successfully and 79% of subjects achieved successful surgery. Overall success was 75%. Success was lower in bilateral cases and in eyes with 2 or 3 clinical signs of NLDO compared to one clinical sign.


The authors analyzed the clinical characteristics and treatment outcomes of patients with congenital membranous punctual obstruction. Medical records of patients <30 years of age over a 12-year period were reviewed retrospectively. During the first 10 years, simultaneous punctoplasty and bicanalicular silicone intubation was performed in the OR. After this, the procedure was modified (Children: one-snip punctoplasty and punctual dilation +/- three-snip procedure +/- probing and bicanalicular silicone tube intubation. Adults: three-snip punctoplasty +/- additional surgery). 51 puncta of 31 eyes of 23 patients (18 <10 years of age) with congenital membranous punctual obstruction were analyzed. 2/3 were unilateral. 20/31 had both upper and lower obstructions. Regardless of surgical technique, all patients improved postoperatively. One adult patient required silicone tube intubation at a later date. Nasolacrimal duct obstructions were found in 7 of the 13 patients who were evaluated for lacrimal patency. This study enrolled adults as well as children and is limited by the small number of cases in each surgical group.


Down syndrome children (DS) who had persistent epiphora following NLD probing with stent placement were studied with CT imaging and histopathological studies of the nasal mucosa. The study consisted of a 4-year retrospective review. Nine children were included. They had failed 1-3 NLD probings with or without stent placement. At initial probing, 8 of the 9 had no encountered resistance along the NLD and one was felt to have a membranous obstruction. Seven underwent CT imaging, 6 underwent biopsy, and 4 underwent both procedures. CT scan showed the bony portion of the NLD in children with DS was well below age-matched controls <6 years of age. With increasing age,
maxillary sinus height growth occurred in the DS group but was 50% of that in the control group. Overall DS patients who failed surgery had reduced NLD dimensions and postductal mucosal obstructions. The lower volume affects hydrostatic pressure and reduced maxilla growth rates also contribute to the problem. Histopathologic findings in most patients showed abnormal lymphoplasmacytic inflammation of the nasal mucosa consistent with chronic infection, allergic disease or immune dysregulation. The authors provide an excellent summary of proposed mechanisms for NLDO. The authors now recommend a trial of intranasal or topical ocular corticosteroids if nasal endoscopy confirms engorgement of the nasal mucosa. High-resolution facial CT scan is also felt to be helpful.

“PUSHED” STENT INTUBATION FOR TREATMENT OF COMPLEX CONGENITAL NASOLACRIMAL DUCT OBSTRUCTION


A prospective study on 44 eyes with complex congenital nasolacrimal duct obstruction (CNLDO) to assess the success rate of pushed stent intubation in children with complex congenital nasolacrimal duct obstruction (CNLDO).

Results: Complete resolution was achieved in 26 of 44 eyes (59.1%) after a mean follow-up of 9.0 months. Pushed stent has the advantage of reduced operating time and easy placement.

Long-Term Outcomes of Monocanalicular Repair of Canalicular Lacerations

H R. Chowdhury, G E. Rose, D G. Ezra, Ophthalmology August 2014; 121:1665-1666

This study was performed at the Lacrimal Clinic at Moorfields Eye Hospital, London, United Kingdom, and other institutions in the United Kingdom. This is a case review of 61 patients, 46 male and 15 females, who underwent repair of canalicular lacerations using the mini-Monoko stents. The median age of presentation was 27 years (ranges 1 year to 89 years).

Results: 75% of canalicular repairs were conducted within 24 hours of injury, 15% were within 2 days, 3% within 3 days and 5% on day 4. 13% of the repairs were performed by consulting surgeons and the remainders by fellows. The stents were removed at an average of 8.8 weeks. Nine patients failed to attend for follow-up and it has been necessary to presume spontaneous extrusion of their silicone stents.

Conclusions: The outcome of surgery did not seem to be affected by delays in repair. Likewise, owing to typical presentation times for such cases, most repairs were performed by fellows with similar outcomes to consultant staff.
Under-Through Levator Complex Plication for Correction of Mild to Moderate Congenital Ptosis
Hong SP, Song SY, Cho IC. Ophthal Plast Reconstr Surg 2014; 30(6):468-472

Levator plication for congenital ptosis has a high rate of ptosis recurrence due to weak adhesion of the levator complex to the tarsal plate. In this study the authors report an alternative technique which can produce permanent adhesions between the folded levator complex and the tarsal plate. The posterior part of the levator complex is advanced to the tarsal plate to produce strong adhesions. The study looked retrospectively at the results of five hundred and ten eyelids of 255 patients who underwent the "under-through levator complex plication" method. 3 mm of plication was planned for every 1mm of ptosis. Outcomes were assessed at 5 months after surgery. Overall surgery success rate was 94.5% with recurrent ptosis not observed. This method also preserves the advantages of levator plication methods including simplicity, reduced edema formation and easy adjustment of eyelid height intraoperatively.

A prospective, randomised comparison of probing versus bicanalicular silastic intubation for congenital nasolacrimal duct obstruction

This is a prospective randomized study to compare success rates of probing versus bicanalicular silastic intubation as the primary treatment for congenital nasolacrimal duct obstruction (CNLDO) in children ≥1 year old. The procedure was considered successful when all preoperative manifestations disappeared with normal dye disappearance test and positive Jones primary dye test at least 6 months postoperatively. 207 eyes of 181 children ages 1-8 years were included in the study. 88 eyes underwent probing with an 84.1% success rate and 93 eyes underwent bicanalicular silastic intubation with an 89.2% success rate (p=0.429). For simple CNLDO, there was a 94.2% success rate with probing and a 90.0% success rate with bicanalicular silastic intubation. In complex CNLDO, there was a 47.4% success rate with probing and an 85.2% success rate with silastic intubation (p=0.016). The authors conclude that probing for simple CNLDO is adequate. Bicanalicular silastic intubation seems to have a role in achieving successful outcomes in complex CNLDO.

Superior rectus underaction following botulinum toxin injection to induce protective upper eyelid ptosis – a comparative study of two techniques
Sadiq SA, Dharmasena A. Strabismus. September 2014;22(3):111-114

Purpose: To compare the incidence of reduced upgaze in transcutaneous versus transconjunctival administration of botulinum toxin A (BTXA) (Dysport) to induce protective ptosis in patients with exposure keratopathy due to facial nerve palsy. 
Methods/Results: Retrospective review. Fifteen consecutive patients who
received a mean of 54.8 units (range 6–125 units) BTXA transconjunctivally via the central portion of the upper lid skin crease with an insulin syringe perpendicular to the skin (Group B) were compared to 20 patients from a previous publication who received 10 units BTXA transcutaneously at the superior border of the tarsal plate along the central 75% of the eyelid (Group A) to induce a protective ptosis. In group A, reduced upgaze occurred in 9 patients (45%). Although half of these resolved completely, the remainder required treatment with a Fresnel prism or by ocular occlusion. In Group B, only 2 patients developed post-treatment superior rectus underaction. The difference in incidence of reduced upgaze between the 2 techniques was statistically significant.

**Conclusion:** Injecting BTXA to induce protective ptosis via a transconjunctival supratarsal route was significantly less likely to induce superior rectus underaction than when given via the transcutaneous route.


This is a case report of an infant with congenital nasolacrimal duct obstruction and fungal dacryoliths. This is an interesting case because congenital nasolacrimal duct obstruction is very common, while dacryoliths are uncommon in infants. In this case, there was no improvement with probing, and the patient was examined with a lacrimal endoscope, which was useful to both diagnose and remove the dacryoliths. A culture and histopathologic examination of the dacryoliths successfully identified an organism. To the author’s knowledge, there have been previously published reports about CNLDO with dacryoliths.

**Comparison Of Intralesional Corticosteroid And Propranolol Treatment Of Periorbital Infantile Hemangiomas: An Outcome Study Of 61 Cases**
Marije J. Hoornweg, Peerooz Saeed, Michael W.T. Tanck, J. Joris Hage

This is a study that compared intralesional steroid injections with oral propranolol in a group of 45 children, 29 of whom were treated with steroid injections and 14 treated with propranolol. In children undergoing steroid injections, there was prolonged duration of therapy (16 months vs. 6.5 months of propranolol), more complications (bleeding 9, ulceration & vs. no complications in the propranolol group). The outcome of amblyopia prevention was equal in both groups. The authors recommend the use of propranolol because of its quick effect and lack of complications compared to steroid injections.
22. INFECTIONS

**Efficacy and safety of azithromycin 1.5% eye drops in paediatric population with purulent bacterial conjunctivitis**

This study was a multi-center, international, randomized, investigator masked study involving 286 children with purulent conjunctivitis. Patients were randomized to either 1.5% azithromycin bid for 3 days or tobramycin 0.3% q2hours for 2 days and then qid for 5 days. Cultures were taken at the first day and again at day 7. 203 of the patients had a positive culture. On day 3, Azithromycin was superior to tobramycin. It appears that azithromycin had a more rapid cure rate than tobramycin and a more convenient dosing regimen.

**Pediatric Microbial Keratitis in Taiwan: Clinical and Microbiological Profiles, 1998-2002 vs. 2008-2012.**

Contact lens related microbial infections increased in Taiwanese children especially because of overnight orthokeratology. Orthokeratology increased from 9.9% to 19.1%. Infections increased from 40% to 52.9%. Pseudomonas remained the most common infectious agent.

**Recurrence Rates of Ocular Toxoplasmosis During Pregnancy.**

This is a retrospective longitudinal cohort study where all women seen during childbearing age that experienced a recurrence of their toxoplasmosis was questioned. 50 of the 86 questionnaires were returned. 34 women had 69 pregnancies during this time period. There were 128 episodes of ocular toxo during the study period, 6 during pregnancy. By evaluating these numbers, it was felt that ocular toxo was not more common during pregnancy and was not significant from the null point.

**C-Reactive Protein as a Marker for Initiating Steroid Treatment in Children with Orbital Cellulitis**

The purpose of this study was to determine the benefit of systemic steroids in pediatric patients with orbital cellulitis and to evaluate the usefulness of C-reactive protein (CRP) levels as a marker for starting steroids. Most infections are accompanied by an acute phase response resulting in elevation of inflammatory markers including CRP. This was a prospective, comparative interventional study. All patients were treated with IV antibiotics. Those with subperiosteal abscess that met published criteria underwent surgical decompression. CRP was measured daily and when it dropped below 4 mg/dl
the patient was started on oral prednisone 1mg/kg for 7 days. Children whose parents did not give consent for steroid treatment served as the control group. 31 patients were included in the study of which 24 received steroids (77%) and 7 did not (23%). Patients who received steroids were admitted for an average of 3.96 days, 1.1 days after initiating the steroid treatment. Patients who did not receive steroids had an average admission of 7.17 days (p<0.05). There was no cases of vision loss or permanent ocular disability in either group. The authors believe that this study shows the benefit of steroids in children with orbital cellulities. The clinician must carefully balance the anti-inflammatory effect of steroids with the immune-modulating effect. The goal of this project was to divise an initial starting point for timing and dosing of oral steroids in children with orbital cellulitis. Future studies can help elucidate if steroid treatment can be initiated earlier without increased risk to the patient.

23. PEDIATRICS/INFANTILE DISEASE/ SYNDROMES


Perinatal asphyxia is a common cause of cerebral visual impairment. In this randomized controlled trial, newborns with asphyxia were assigned to either cooling therapy vs standard therapy; their neurocognitive function was then assessed at age 6-7 years. 325 newborns with asphyxial encephalopathy who were born at a gestational age of 36 weeks or later were randomized to receive standard care alone (control) or standard care with hypothermia to a rectal temperature of 33 to 34°C for 72 hours within 6 hours after birth. The primary outcome of this analysis was the frequency of survival with an IQ score of 85 or higher. A total of 75 of 145 children (52%) in the hypothermia group versus 52 of 132 (39%) in the control group survived with an IQ score of 85 or more (relative risk, 1.31; P=0.04). The proportions of children who died were similar in the hypothermia group and the control group (29% and 30%, respectively). More children in the hypothermia group than in the control group survived without neurologic abnormalities (65 of 145 [45%] vs. 37 of 132 [28%]; relative risk, 1.60; 95% confidence interval, 1.15 to 2.22). Among survivors, children in the hypothermia group, as compared with those in the control group, had significant reductions in the risk of cerebral palsy (21% vs. 36%, P=0.03) and the risk of moderate or severe disability (22% vs. 37%, P=0.03); they also had significantly better motor-function scores. The rate of visual impairment not improved by glasses (7% in hypothermia group vs 12% in control group) and blindness (1% in both groups), however, did not differ the two groups. Moderate hypothermia after perinatal asphyxia resulted in improved neurocognitive outcomes in middle childhood but not in a difference in visual outcomes.
The orthoptics of Down syndrome
Emily A. Miyazaki, *Am Orthopt J* Sept 2014;64:17-20

This review article describes some of the common ocular disorders among individuals with Down syndrome. Although no original data is presented but the author highlights refractive errors, accommodative insufficiency, strabismus, amblyopia and nystagmus. A description of the technique of dynamic retinoscopy is given.

Strabismus in cerebral palsy: When and why to operate

This review article provides a historical tour of ophthalmologists’ approach to strabismus in patients with CP from 1953 to today. The author’s conclusions are to that the incidence of CP is increasing, there is a relatively high incidence of strabismus in the CP population (especially those with spastic diplegia), mild CP does not preclude potential for binocular vision and that medical/surgical treatment provides functional and/or psychosocial benefits. There is a need for prospective study of strabismus natural history and management in individuals with CP.

Visual surveillance in craniosynostoses

This review article highlights several current aspects of craniosynostoses. The type of craniosynostosis is now described by which suture has closed. Gain of function mutation in FGFR2 (fibroblast growth factor receptor type 2) causes Crouzon, Pfeiffer and Apert syndromes. Vision outcomes are commonly 20/40 or worse in the better seeing eye and this may be due to amblyopia and/or elevated ICP. However the correlation of disc swelling with elevated ICP due to craniocerebral disproportion is not straightforward in that cranial volumes may be normal or even larger than normal in some patients with Apert and Crouzon syndrome. The presence of obstructive sleep apnea and absence of intracranial venous sinuses may contribute to elevated ICP without craniocerebral disproportion. The also author discusses the hypothesis of FGFR2 mutation also causing extra fibrous-like tissues in the lamina cribrosa that prevents swelling of the optic disc despite elevated ICP. The author recommend cycloplegic refraction q6 months in patients less than 8 years of age, optical treatment, amblyopia treatment, inspection of the optic nerve head and use of VEP for longitudinal evaluation of the visual pathway function.


The authors quantitatively tested 18 subjects with this syndrome. They wanted to determine which ophthalmic findings were altered in the early stages of Wolfram syndrome and which correlate with overall disease severity. Mean patient age was 14.2 years. Mean best-corrected visual acuity was 20/60 with 16/18 20/40 or
worse. 17/18 had detectable color vision deficits. 12 subjects had testable visual fields and showed visual fields deficits. 17/18 subjects had optic nerve pallor, and all had thinned RNFL on OCT. 11 had sluggish pupils and 4 had cataracts. Both nystagmus and strabismus were noted in 7/18. Worse severity of disease was seen in the presence of an afferent papillary defect (bilateral so this means sluggish pupils), strabismus, or nystagmus. Overall severity of disease correlated with thinning of the RNFL.

**Ocular Manifestations of Hypoxia-Inducible Factor-2x Paraganglioma-Somatostatinoma-Polycythemia Syndrome**


This is a report that describes a 9 year old girl referred for evaluation of an abdominal paraganglioma with polycythemia, a 32-year-old woman with a Marfanoid habitus and paraganglioma-somatostatinoma-polycythemia previously reported and a 15-year-old boy with a Marfanoid habitus was evaluated for right adrenal and pelvic paraganglioma. 

Comment: All of these patients were felt to have neural crestoma type tumors. All patients had gain-of-function mutations of the HIF2-alpha gene (encoding HIF-2 alpha peptide) detected in tumors but not in leukocyte DNA. This report shows a picture of a 9 year old girl (page 2292) with impressive disc edema with peripapillary exudates. At the time of the report, greater than 20 patients have been described in literature with HIF-2 alpha mutations associated with paraganglioma polycythemia. This series represents 4 cases with the same condition.

The authors bring to our attention the presence of disc edema and retinal findings in patients with this condition. This study was performed at The National Institute of Health, Eunice Kennedy Shriver National Institute of Child Health.


Enhanced S cone syndrome was first described in 1990 and is characterized by nyctalopia, with an onset in the first decade of life, hyperopia (mean of +4.4.D in this study), and pathognomonic findings on ERG testing of short wavelength sensitive cones such that the ERG responses is high amplitude, delayed and simplified. Mutations in the nuclear receptor gene NR2E3 help explain the pathophysiology of this syndrome. This gene encodes a transcription factor which is important in determining photoreceptor cell fate. Mutations in this gene lead to abnormal differentiation of postmitotic photoreceptor precursor cells, altering their cell fate from rod to S-cone. In this study of 9 children from 5 families, new genetic mutations were found in the NR2E3 gene and the fundus was found to initially appear normal, but later developed mottled retinal pigment epithelium change along the arcades, followed by the appearance of white dots in the same distribution. Some children had macular schisis cavities. Fundus autofluorescence imaging is abnormal even in children with a normal fundus appearance.
Adalimumumab for Pediatric Sympathetic Ophthalmia

The authors describe a child with refractory inflammation secondary to sympathetic ophthalmia who responded with complete resolution of inflammation to adalimumab (Humira). Corticosteroids are the first line of treatment for sympathetic ophthalmia, a bilateral granulomatous uveitis that may occur after trauma. Sympathetic ophthalmia is presumed to be an autoimmune, T-cell–mediated response to melanocyte self antigens exposed during surgery or trauma. An animal model resembling SO showed upregulation of tumor necrosis factor-α (TNF-α) levels associated with photoreceptor damage. Biological response modifiers, such as the class of medicines which target mediators of inflammation, like TNF-α, can be effective in corticosteroid dependent or refractory cases of uveitis. Adalimumab is a human monoclonal recombinant anti TNF-α antibody given subcutaneously.


This study investigates the long-term efficacy and tolerability of tumor necrosis factor α (TNFα) inhibitors in the therapy of children with refractor antinuclear antibody (ANA) – associated chronic anterior uveitis. The study is a retrospective review of 31 children with ANA-associated uveitis treated with TNFα inhibitors with a minimum follow-up period of 2 years. The indication for treatment had to be anterior uveitis and not control of arthritis to be included in the study. The authors evaluated control of inflammation, corticosteroid-sparing potential, and side effects. 74% were treated with adalimumab, 16% with infliximab, and 10% with etanercept. Control of uveitis was defined as 0 anterior chamber cells while on ≤ 2 drops/day of topical corticosteroids. This was achieved in 22 of 31 patients (71%) after 1 year and 22 of 31 patients after 2 years of treatment. Control was observed in 78% of children treated with adalimumab and 40% of those treated with infliximab. Control of uveitis was not observed in any of the children treated with etanercept. 71% of children were able to discontinue systemic corticosteroids and 55% were able to stop topical corticosteroids. The authors conclude that adalimumab and infliximab have beneficial effects in the therapy of severe ANA-associated anterior uveitis in children. They do note that the results should be interpreted cautiously given the small number of patients receiving infliximab and etanercept.
**Dexamethasone intravitreal implant (Ozurdex) for the treatment of pediatric uveitis.** Bratton ML He Y-G, and Weakley DR. J AAPOS 18:110-113

Ozurdex is a biodegradable polymer that provides anti-inflammatory effect over six months, with a peak intravitreal concentration over the first two months. The authors report its use in the treatment of pediatric uveitis. This was a retrospective review of all patients who were unresponsive to standard uveitis modalities over a 24-month period. Fourteen eyes of 11 patients with noninfectious uveitis were included. Mean age at diagnosis was 7 years and at time of implantation was 10.1 years. Six of the fourteen eyes received more than one implant. Average follow-up time was 11.3 months. Eight eyes experienced visual acuity improvement of one or more Snellen lines (6 eyes were excluded from this evaluation because of concomitant surgery or inability to test acuity). Intraocular inflammation was improved at 1-3 months in 17 of 22 insertions. After 18 of the 22 insertions, topical steroids were reduced or discontinued. Inflammation recurred in over half of the patients at an average of 4.3 months after insertion. Complications included a marked elevation of IOP (>10mm Hg) in 5 eyes, cataract progression requiring surgery in 1 eye and anterior chamber implant migration in 4 eyes. The patients in this study were from a tertiary center and data was gathered from multiple physicians.

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This retrospective cohort study analyzed the predictors for development of uveitis in JRA patients. 147 patients were diagnosed with chronic anterior uveitis (41%). Young age of onset, +ANA, increased ESR were predictive factors. After adjusting for other relevant factors, elevated ESR appears to be a predictor of uveitis in patients with JIA.

**A Randomized Clinical Trial Comparing Methotrexate and Mycophenolate Mofetil for Noninfectious Uveitis**


This is a multicenter, block-randomized, observer-masked clinical trial of 80 patients with noninfectious intermediate posterior uveitis or panuveitis requiring corticosteroid sparing therapy at Aravind Eye Hospital in Madurai and Coimbatore, India. The purpose of this study was to compare the relative effectiveness of Methotrexate and Mycophenolate Mofetil for treatment of noninfectious intermediate posterior and panuveitis. The patients were randomized to receive 25 mg weekly oral Methotrexate or 1 g twice daily of oral Mycophenolate Mofetil (MPM) and were monitored for 6 months. Oral Prednisone and topical corticosteroids were tapered. Masked examiners were used to assess the primary outcome of treatment success.
Conclusions: There was no statistically significant difference in corticosteroid-sparing control of inflammation between patients receiving Methotrexate and Mycophenolate. However, there was a 20% difference in treatment success favoring Methotrexate.

Comment: In total, 39 patients (58%) had corticosteroid-sparing controlled inflammation at 5 and 6 months (15 with Mycophenolate Mofetil (47%) and 24 with Methotrexate (69%)). The Methotrexate was 22% more effective in controlling inflammation in noninfectious intermediate posterior and panuveitis. In addition 5 patients (8%) were declared treatment failures because of intolerability of the side effects (3 taking Methotrexate and 2 taking Mycophenolate). One patient was declared a failure because of safety concerns after developing chicken pox while taking Methotrexate.

IT APPEARS IN THIS STUDY THAT MYCOPHENOLATE MOFETIL AND METHOTREXATE ARE EFFECTIVE IN TREATING STEROID REFRACTORY NONINFECTIONOUS INTERMEDIATE POSTERIOR AND PANUVEITIS WITH ORAL METHOTREXATE 25 MG PER WEEK AND MYCOPHENOLATE 1 G TWICE DAILY FOR 6 MONTHS.

Rituximab Therapy for Refractory Scleritis
Results of a Phase I/II Dose-Ranging, Randomized, Clinical Trial
Eric B. Suhler, Lyndell L. Lim, Robert M. Beardsley, Tracy R. Giles, Ophthalmology October 2014; 121(10):1885-1891

This study comes from the Portland Veterans Administration Medical Center, Portland, Oregon; Oregon Health & Science University; Casey Eye Institute, Portland, Oregon; Centre for Eye Research Australia, University of Melbourne, Australia. This is a prospective, dose-ranging, randomized, double-masked phase I/II clinical trial involving 12 patients with noninfectious scleritis refractory to systemic corticosteroid and greater than 1 additional systemic immunosuppressive agent between January 2007 and March 2010. The objective was to determine whether Rituximab, a monoclonal antibody against the beta-lymphocyte antigen CD20 is effective in the treatment of refractory noninfectious scleritis. The main outcome measures included reduction in inflammation with a validated scleritis disease grading scale (SGS) and reduction in corticosteroid dose by greater than 50%. Patients were characterized as responders to study therapy if greater than one of these endpoints showed improvement and neither showed evidence of worsening. Of the 12 enrolled patients, 9 met the scleritis disease grading scale endpoint at or about 24 weeks. 4 additional patients were able to reduce corticosteroid dose by greater than 50%. 11 of the 19 patients showed improvement in global health scores. Conclusions: Rituximab was effective treatment for 9 of 12 enrolled patients with refractory noninfectious scleritis at 24 weeks. 7 patients required reinfusion of Rituximab to maintain inflammatory control. The treatment was well tolerated. Peri-infusional inflammatory exacerbations were managed with oral corticosteroids.

Comment: Scleritis is an inflammatory disease of the sclera that is often painful and in many cases may cause loss of vision or even loss of the eye. In most
instances, it is presumed secondary to vasculitis of scleral vessels. The inflammation may be caused by a heterogenous collection of diseases including severe or life threatening inflammatory disease, such as severe rheumatoid arthritis, granulomatosis with polyangiitis (GPA), microscopic polyangiitis, inflammatory bowel disease, relapsing polychondritis, systemic lupus erythematosus and other systemic vasculitides.

Rituximab is a human-mouse chimeric monoclonal antibody that recognizes CD20, an antigen expressed on the surface of mature B lymphocytes. Rituximab is approved for the treatment of B-cell lymphomas and chronic lymphocytic leukemia and for moderate to severe rheumatoid arthritis. The medication has shown efficacy in patients with refractory systemic lupus erythematosus. Most recently, Rituximab has been shown to be “noninferior” to cyclophosphamide in the treatment of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis.

Based on this study, it appears that the medication is also helpful in the treatment of severe scleritis in patients who are refractory to currently available treatments. Scleritis is associated with or may have similar pathogenesis to many of these autoimmune or inflammatory diseases that also respond to Rituximab.

**The Value of Measuring Urinary β2-Microglobulin and Serum Creatinine for Detecting Tubulointerstitial Nephritis and Uveitis Syndrome in Young Patients With Uveitis**

Ymkje M. Hettinga, Laura M. E. Scheerlinck, Marc R. Lilien, Aniki Rothova, et al.


The authors wanted to determine the utility of non-invasive testing, specifically measuring urinary β2 microglobulin and serum creatinine, in diagnosing tubulointerstitial nephritis associated uveitis (TINU). Tubulointerstitial nephritis and uveitis syndrome is a condition first described in 1975 by Dobrin and coworkers, which mainly affects young patients; the prevalence of TINU syndrome peaks at 14 years of age. TINU syndrome accounts for only 1% to 2% of all patients at specialized uveitis centers, which likely is a gross underestimation since the nephritis is often self-limiting. Usually a renal biopsy is needed to definitively diagnose TINU syndrome, but this is a highly invasive procedure.

An increased level of β2-microglobulin (β2M) in the urine has been proposed as a potential screening tool for detecting acute tubulointerstitial nephritis in TINU syndrome. β2-microglobulin is a small (12-kDa) protein that is excreted by the glomeruli into the ultrafiltrate and then resorbed by the tubules. In tubulointerstitial nephritis, β2M is excreted but not resorbed, leading to elevated levels of β2M in the urine.

Forty five patients under age 22 with a new diagnosis of uveitis were enrolled in this prospective cohort study. Intervention was to prospectively measure urinary β2M, urinary protein, and serum creatinine and calculate estimated glomerular filtration rate. The study sought to determine whether urinary β2M, urinary protein, serum creatinine, estimated glomerular filtration rate, and/or pyuria were correlated with definitive and probable cases of TINU syndrome. Eight out of 45
patients with definitive or probable TINU syndrome had higher urinary β2M levels than patients with normal renal function. The study revealed that the positive predictive value of increased β2M combined with increased serum creatinine was 100% for detecting definitive and/or probable TINU syndrome.

25. PRACTICE MANAGEMENT/HEALTH CARE SYSTEM

A Proposal to Improve Ophthalmic Education in Medical Schools
D M. Albert, G B. Bartley, *Ophthalmology* June 2014; 121:1157-1159

This editorial is written by Dr. Daniel Albert and Dr. George Bartley. Both of these gentlemen are established professors of ophthalmology who are concerned about the paucity of ophthalmic education in the medical school curriculum. The authors feel: “It is essential to establish competency-based standards that can be tested, measured and used to generate scientific data indicative of the students’ level of knowledge and adequacy of training.” They felt that not only should there be a universal curriculum available in all medical schools, but there should also be included in “year end professional skills assessment of the medical student.” These criteria would parallel similar skills assessment for treatment of patients with migraine headaches, appendicitis and other common medical problems.

The authors suggest a curriculum to prepare students to be examined in 1) how to perform an eye examination, 2) detection of visual field defects, 3) use of the direct ophthalmoscope and 4) matching the patients’ optic nerves to one of a series of fundus photographs. Students should be prepared for this short course taught at a level appropriate for the primary care provider. The authors feel that there is a “crisis in ophthalmic medical education that must be overcome.”

They recommended collaboration between the American Academy of Ophthalmology, the American Board of Ophthalmology, National Eye Institute, the Association for Research in Vision and Ophthalmology, the Association of University Professors of Ophthalmology and the American Ophthalmologic Society.

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The study provides detailed analysis of a prior publication of EHR. Productivity, efficiency, and work hours are evaluated in an academic pediatric ophthalmology practice. Data from four providers with varied volume of patients were evaluated. Overall patient volume declined by 11% when comparing pre-EHR to post-EHR (allowing for the assumed slow ramp up time for a few months during transition). However data was widely distributed with one provider actually seeing more patients and one provider unchanged. Chart completion also varied widely and seemed most affected by the practice style of the specific clinician. Overall 56%
of charts were completed during normal business hours. The authors comment that the volume decrease in patients seen was greater than that of the ophthalmology department as a whole, and that Pediatric Ophthalmologists may be more burdened and negatively affected by currently available EHR systems. The volume of patients seen by each provider was dramatically different and the study was too small to determine if a provider’s patient volume impacts the effect of EHR on productivity and efficiency.

Meaningful Use: How Did We Do, Where Are We Now, Where Do We Go from Here? Michele C. Lim, Michael F. Chiang, Michael V. Boland, K. David Epley, *Ophthalmology* September 2014; 121(9):1667-1669

This is an editorial that represented members from the American Academy of Ophthalmology, West Coast and East Coast Academic Groups and private practitioners. Seven of the nine authors are from the West Coast and two are from the East Coast. There are no authors from the Midwest or the Heartland of the United States.

The term “meaningful use” (MU) describes the program created as part of the 2009 Health Information Technology for Economic and Clinical Health Act (HITECHA). This act was designed to promote adoption of the electronic health record (EHR). Meaningful use criteria for electronic health records are organized in stages. Moving from a less to a more complex task that the EHR and its users must be able to accomplish. Not all, but most meaningful use objectives are relevant to ophthalmology. The American Academy of Ophthalmology (AAO) continues to try to ensure that criteria appropriate for the specialty of ophthalmology are developed and implemented. “ALL IN ALL, MEANINGFUL USE IS A WAY TO MAKE THE USE OF AN ELECTRONIC HEALTH RECORD BENEFICIAL TO BOTH PHYSICIAN AND PATIENT.”

This initiative is an answer to President George W. Bush’s 2004 State of the Union Address in which he called for “most Americans to have interoperable EHRs within ten years.” The ensuing strategy had four goals: 1) Bring electronic health records to clinical practice, 2) Inter connect physicians through interoperable electronic health records, 3) To use health information technology to get patient’s access to their own health records and 4) To improve population health.

The center for Medicare and Medicaid services (CMS) developed three stages of implementation: 1) Establish a baseline for electronic data capture, 2) Focus on information exchange and 3) (which is in the process of being developed) Focus on quality improvement with measures yet to be defined.

**HOW DID WE DO?** Between 2011 and 2013, 7,119 ophthalmologists received $167 million (average $23,458 per ophthalmologist) to implement EHRs in the practices and institutions. Ophthalmologists ranked eighth among the medical and surgical specialties in total number of payments received. This represents 36% of the practicing ophthalmologists in the United States. This is approximately 5% higher than primary care physicians who also received incentive payments. The top 5 EHRs vendors for ophthalmology are: 1) NextGen
Stage 1: Implementation (baseline for electronic data capture). Ophthalmologists were exempt from the information regarding immunizations and vital signs. The American Academy of Ophthalmology worked with ophthalmologists to lobby the Office of the National Coordinator for Health Information Technology (ONCHIT) which is part of the Department of Health and Human Services to keep Meaningful Use relevant to ophthalmologic practices.

Stage 2: The American Academy of Ophthalmology advocated for continuation of exemption regarding recording the vital signs, inclusion of reporting of a specialty registry as an alternative to reporting immunizations and inclusions of an option to report on viewing images in practice electronic health records.

WHERE ARE WE NOW? On December 4, 2012, the Center for Medicare and Medicaid services published the final rules that specified the stage 2 criteria that eligible professionals must meet to continue to participate in Medicare Electronic Health Records Incentive Program (MEHRIP). Stage 2 is in the process of being implemented (problem with 2014 EHR certification delays).

Once the process is completed, all providers must meet Meaningful Use stage 1 criteria before becoming eligible to report on stage 2. For eligible professionals, the difference between stage 1 and stage 2 are: 1) Increase from 13 to 17 core objectives stage 2 and 2) Selection of 3 and 6 menu objectives in stage 2 (as opposed to 5 to 10 objectives in stage 1). THE AAO RECOMMENDS OPHTHALMOLOGISTS BE ABLE TO REPORT THE FOLLOWING OBJECTIVE MENUS: 1) ELECTRONIC NOTES, 2) IMAGING RESULTS, 3) FAMILY HEALTH HISTORY, 4) SPECIFIC CASES TO A SPECIALIZED REGISTRY (FOR EXAMPLE, INTELLIGENT RESEARCH IN SIGHT (IRIS) REGISTRY). The IRIS Registry (sponsored by AAO) is the nation’s first comprehensive eye disease clinical registry and is key to quality improvement in eye care. It is a passive platform to which ophthalmologists can contribute clinical data. In return, the IRIS registry will allow them to benchmark their outcomes. It will also allow ophthalmologists to report on the 2014 Clinical Quality Measures for Meaningful Use. On a larger scale it will allow our profession to demonstrate the value of our services.

WHERE DO WE GO FROM HERE? Stage 3 is currently in the process of being implemented (once stage 2 is fully implemented). The contents of stage 3 have been proposed by the Health Information Technology Policy Committee (HITPC), which is a Federal Advisory Committee that weighs in on how to define Meaningful Use for electronic health records. Stage 3 measures have not been finalized. The goal of stage 3 is to “transition from a setting-specific focus to a collaborative patient- and family-centric approach.” For example, the patient centered medical home.

The American Academy of Ophthalmology has recommended to the Health Information Technology Policy Committee to adopt the "Digital Imaging and Communication in Medicine standards and other quality measures align
ophthalmology with other quality reporting systems such as PQRS (Physician Quality Reporting System).

The American Academy of Ophthalmology has the following recommendations for continuing to improve Meaningful Use.
1) Continue working on national registry (IRIS registry)
2) Achieve standardization in patient information by completing Clinical Document Architecture (CDA) for the eye examination. The CDA is a specification for the way data is stored, recorded and exchanged in ophthalmology. This allegedly will allow for the seamless transfer of patient data from one EHR to another.
3) Work with vendors to make Meaningful Use easier for ophthalmologists.
   a) Work with vendors to improve automated Meaningful Use reports.
   b) Standardized integration of ophthalmic images.
   c) Electronic sharing of information with patients.
   d) Patient portals and secure messaging.
   e) using ophthalmology Clinical Document Architecture (CDAs) to exchange information across EHRs with IRIS registries.

Comment: Meaningful Use has been a burden for pediatric ophthalmologists. It puts a significant increase in the time of completion of a health record both with the patient in the room during real time and afterwards. If, indeed, this information is truly meaningful, we need to find a quicker way to obtain and record it.

Factors Related to Online Patient Satisfaction with Ophthalmologists
Robert M. Kinast, Gordon T. Barker, Susan H. Day, Stuart K. Gardiner,
Ophthalmology September 2014; 121(9):1843-1845

(Comment: This is a very important report for all ophthalmologists/pediatric ophthalmologists to read.)
Patient satisfaction is an increasingly important factor in evaluating physician performance and now affects Medicare reimbursement rates under the Affordable Care Act. Online patient reviews of physicians have a growing presence on the internet because they are free, easily accessible and largely anonymous. Patients are increasingly using the internet to seek information on health care providers. The purpose of this study was to identify the reason why patients write positive/negative online reviews of ophthalmologists. The authors searched Yelp.com (Yelp Incorporated, San Francisco, California) to review products and services. The Yelp.com was used for all patient reviews of San Francisco ophthalmologists over an 8 year period from October 2004 to August 2012. This information was entered on an Excel spreadsheet. Various statistical methods were used to compile the data.
Results: The authors collected 595 online reviews from 60 ophthalmologists in the San Francisco area. The results of this survey were broken into A) All Patient Review Comments,
B) Positive Patient Review Comments and C) Negative Patient Review Comments. 1,675 reviews were collected and 1,211 were felt to be positive patient reviews and 464 were found to be negative patient reviews. All 3 categories are more than 50% of the review comments were confined to the staff, appointment time wait, access/availability, office environment, cost/finance and location.

“Despite their limitations, online reviews still influence patients and provider customer feedback. Online reviews may provide useful information and are likely to become more common in the future.” In all 3 studies, comments were shown to significantly predict review score. Office and other factors unrelated to the quality of opthalmic care are important components of a patient/consumer evaluation of the ophthalmology experience. IT IS ESSENTIAL THAT OPHTHALMOLOGISTS RECOGNIZE THAT PATIENTS HAVE CHOICES AND THAT ALL FACTORS THAT CONTRIBUTE TO A PATIENT’S EXPERIENCE MUST BE CONSIDERED FOR EFFECTIVE PRACTICE MANAGEMENT.

This study was presented to the American Academy of Ophthalmology Annual Meeting in November 2013 in New Orleans, Louisiana.

The Care of the Patient: Field Notes from a Veteran

Dr. Kushner shares with us 10 points of wisdom, which he gained from his 40 years of practice as an academic pediatric ophthalmologist. During this time, he taught many medical students, fellows and ophthalmology residents. Dr. Kushner delivered the keynote address at the graduation of the Wisconsin Department of Ophthalmology 2014 graduation.

The theme of Dr. Kushner’s presentation was “What would be meaningful to these about-to-become colleagues who were just beginning their careers.”

Recommendation #1: On talking to patients with wisdom derived from Mark Twain. “The difference between the almost right word and the right word is really a large matter---“tis the difference between the lightning-bug and the lightning.” Dr. Kushner recommended using the words “relax” rather than “paralyze” for their pupil. “Relaxation” has good energy; “paralysis” sounds ominous. After dilation, tell patients they may “sensitive to light, rather than bothered by light.”

Recommendation #2: Listening to patients with words from a Zen Master. 1) Listen for the facts, 2) Listen to the emotions, 3) the body language, 4) how the conversation is affecting you and 5) what is not being said.

Recommendation #3: Talking in front of patients with advice from a former mentor. Every word we utter in the patients’ presence will be chewed upon, mulled over and repeated. When doctors talk to one another in front of patients, the patient may not understand the meaning and importance of what we are discussing. Physicians need to recognize that we speak a different language than patients. Dr. Kushner counsels that whenever things are discussed between residents and fellows in front of the patient that the attending physician turns to the patient and says “excuse us while we talk shop for a minute and then I will translate for you what we have said.”

Recommendation #4: The importance of offering hope with reference to the drinking glass. Always emphasize the positive. Be truthful to the patients. Don’t mislead them with false hope, but on the other hand, don’t dwell only on the negative findings.
**Recommendation #5**: Understanding the patients’ needs and wants with humor and a clinical pearl from Art Jampolsky, MD. When doing a refraction instead of saying, which is better 1 or 2? You ask, “Pick the worst choice.” The patient can always pick the worst choice because they love playing out the negative.

**Recommendation #6**: Expand your own horizons with words about Descartes’ Error. Descartes was famous for the statement, “I think therefore I am.” Descartes’ Error was reframed by Rousseau by declaring, “I feel, therefore I am.” To enhance the “feeling for the patient”, Dr. Kushner recommended reading fiction and poetry. Dr. Kushner felt that fiction was the best way to understand peoples’ plights, situations and make us more empathetic. He recommended the books *The Heart Is a Lonely Hunter* by Carson McCullers’, *Tunnel Visions* by Felix Pollak (book of poetry) and Lisel Mueller’s poem, *Monet Refuses the Operation*.

**Recommendation #7**: Take care of your heart and soul with intervention from a son of the Goddess Aphrodite. Dr. Kushner recommends being more heartfelt or compassionate and you will understandably make a more caring doctor.

**Recommendation #8**: Get to know your patients as people. Take the time to find out your patients’ job, family members, accomplishments, hobbies, etc.

**Recommendation #9**: The ultimate secret about caring for patients with teachings from renowned physician. “The secret of the care of the patient is to care for the patient.”

**Comment**: This is an extraordinarily fine article in summary from one of our greatest mentors, Dr. Burton Kushner. I personally have started reading poetry and fiction (2 areas that I have eschewed). I now use the words dilating drops will “relax your eyes” and that with dilated pupils you may be “slightly bothered by the light.”