

What's New and Important in Pediatric Ophthalmology and Strabismus for 2010

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**American Association for Pediatric Ophthalmology and
Strabismus – Professional Education Committee**

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I. AMBLYOPIA

Optical characterization of Bangerter foils.

Perez GM, Archer SM, Artal P. Invest Ophthalmol Vis Sci 2010; 51:609-13. (Jan 2010)

Purpose: Optical penalization is emerging as an alternative to patching for the treatment of amblyopia. Bangerter foils offer a form of optical penalization that is distinctly different from standard techniques making use of atropine or spectacle lens manipulation, or both, to produce defocus. The authors examined the optical properties of Bangerter foils and compared them with the effect of defocus.

Methods: Bangerter foils were evaluated on an optical bench to calculate point spread and modulation transfer functions. Retinal images through the foils were also simulated and qualitatively compared with those with defocus and Gaussian blur. Subjective visual acuity and contrast sensitivity were compared in two subjects wearing spectacles with foils and with simple defocus.

Results: The optical characteristics of the Bangerter foils do not correspond well with their labeled density designation. Bangerter foils and defocus affect the modulation transfer function similarly, with more attenuation of mid-range spatial frequencies than low spatial frequencies. However, Bangerter foils do not exhibit spurious resolution and phase shifts, as does defocus.

Conclusions: The blur resulting from Bangerter filters is qualitatively different from defocus. Whether this difference is of any consequence when these two methods of optical penalization are used for amblyopia treatment remains to be investigated.

Comment: This study is interesting because it shows that Bangerter foils produce blur that is qualitatively different from defocus. This may have implications for their use for amblyopia treatment, and may warrant further research.

Latent stereopsis for motion in depth in strabismic amblyopia.

Hess RF, et al. Invest Ophthalmol Vis Sci 2009; 50:5006-16. (Oct 2009)

Purpose: To investigate the residual stereo function of a group of 15 patients with strabismic amblyopia, by using motion-in-depth stimuli that allow discrimination of contributions from local disparity as opposed to those from local velocity mechanisms as a function of the rate of depth change.

Methods: The stereo performance (percentage correct) was measured as a function of the rate of depth change for dynamic random dot stimuli that were either temporally correlated or uncorrelated.

Results: Residual stereoscopic function was demonstrated for motion in depth based on local disparity information in 2 of the 15 observers with strabismic amblyopia. The use of a neutral-density (ND) filter in front of the fixing eye enhanced motion-in-depth performance in four subjects randomly selected from the group that originally displayed only chance performance. This finding was true across temporal rate and for correlated and uncorrelated stimuli, suggesting that it was disparity based. The opposite occurred in a group of normal subjects. In a separate experiment, the hypothesis was that the beneficial effect of the ND filter is due to its contrast and/or mean luminance-reducing effects rather than any interocular time delay that it may introduce and that it is specific to motion-in-depth performance, as similar improvements were not found for static stereopsis.

Conclusions: A small proportion of observers with strabismic amblyopia exhibit residual performance for motion in depth, which was disparity based. Furthermore, some observers with strabismic amblyopia who do not display any significant stereo performance for motion in depth under normal

binocular viewing may display above-chance stereo performance if the degree of interocular suppression is reduced. The authors term this phenomenon latent stereopsis.

Comment: This study shows that some persons with strabismic amblyopia can see motion in depth, and, contrary to a previous report, this ability is due to disparity rather than motion processing. This study also shows that some persons with strabismic amblyopia display a latent motion-in-depth performance when a neutral-density filter is placed over the fixing eye. The authors argue that this is the result of reducing the suppressive drive from the fixing eye.

Impaired temporal, not just spatial, resolution in amblyopia.

Spang K, Fahle M. Invest Ophthalmol Vis Sci 2009; 50:5207-12. (Nov 2009)

Purpose: In amblyopia, neuronal deficits deteriorate *spatial* vision including visual acuity, possibly because of a lack of use-dependent fine-tuning of afferents to the visual cortex during infancy; but *temporal* processing may deteriorate as well.

Methods: Temporal, rather than spatial, resolution was investigated in patients with amblyopia by means of a task based on time-defined figure-ground segregation. Patients had to indicate the quadrant of the visual field where a purely time-defined square appeared.

Results: The results showed a clear decrease in temporal resolution of patients' amblyopic eyes compared with the dominant eyes in this task. The extent of this decrease in figure-ground segregation based on time of motion onset only loosely correlated with the decrease in spatial resolution and spanned a smaller range than did the spatial loss. Control experiments with artificially induced blur in normal observers confirmed that the decrease in temporal resolution was not simply due to the acuity loss.

Conclusions: Amblyopia not only decreases spatial resolution, but also temporal factors such as time-based figure-ground segregation, even at high stimulus contrasts. This finding suggests that the realm of neuronal processes that may be disturbed in amblyopia is larger than originally thought.

Comment: This study shows that amblyopia strongly deteriorates temporal precision of visual perception for specific tasks, not just spatial vision.

Randomized Evaluation of Spectacles Plus Alternate-Day Occlusion to Treat Amblyopia

Agervi P., et al.

Ophthalmology 2010;117:381-387 (February)

Purpose: To compare spectacles plus patching ≥ 8 hours daily 6 days a week with spectacles plus patching ≥ 8 hours on alternate days to treat amblyopia in children 4 to 5 years of age. Prospective, randomized clinical trial in Stockholm, Sweden of forty children with untreated amblyopia.

Methods: Refractive correction was provided, and the children were randomized.

Main Outcome Methods: Median change in VCVA of the amblyopic eye after 1 year.

Results: The median change in BCVA of the amblyopic eye did not differ significantly between the 2 groups. Binocular function improved in both groups with no significant differences between the groups at 1 year. The median spherical equivalent refractive error did not change significantly during the study period in the amblyopic eyes in either group; however, a significant increase was found in the fellow eyes in both groups.

Conclusions: The improvement in visual acuity is a combined effect of spectacle wear and occlusion therapy.

Reviewer's Comments: Does duration or schedule of patching matter at all??

Amblyopia Therapy in Children Identified by Photoscreening

Teed RG, Bui CM, Morrison DG, Estes RL, Donahue SP.

Ophthalmology 2010;117:159-162 (January)

Design: A case series of 125 children diagnosed with amblyopia after referral from a community photoscreening program.

Methods: Treatment regimens included spectacles, patching, and/or atropine penalization. Successful treatment was defined as ≥ 3 Snellen line equivalent improvement in visual acuity and/or 20/30 visual acuity in the amblyopic eye in literate children. Successful treatment in initially preliterate children was defined as 20/30 or better visual acuity in the amblyopic eye.

Results: Of 901 children evaluated after being referred from photoscreening, 551 had amblyopiogenic risk factors without amblyopia, 185 were diagnosed with amblyopia, and 165 were false positives. Of 185 children with amblyopia, 125 met inclusion criteria for analysis and 78% (97 of 125) were successfully treated.

Conclusions: The success rate of amblyopia treatment in children identified through our photoscreening program is high. This study supports the role of photoscreening programs in prevention of amblyopia-related vision loss. Such early screening may translate to true visual acuity improvement.

Reviewer's Comments: An extension of Dr. Donahue's work in Tennessee

Prevalence of Amblyopia and Strabismus in White and African American Children Aged 6 through 71 months: The Baltimore Pediatric Eye Disease Study

Friedman DS, Repka MX, Katz J, Giordano L, Ibrinke J, Hawse P, Tielsch JM.

Ophthalmology 2009;116:2128-2134 (November)

Design: A cross-sectional, population-based study. Among 4132 children identified, 3990 eligible children (97%) were enrolled and 2546 children (62%) were examined.

Methods: Strabismus was defined as a heterotropia at near or distance fixation. Amblyopia was assessed in those children aged 30 through 71 months who were able to perform Optotype testing at 3 meters.

Results: Manifest strabismus was found in 3.3% of white and 2.1% of African American children. Esotropia and exotropia each accounted for close to half of all strabismus in both groups. Only 1 case of strabismus was found among 84 white children 6 through 11 months of age. Rates were higher in children 60 through 71 months of age (5.8% for whites and 2.9% for African Americans). Amblyopia was present in 12, (1.8%) white and 7 (0.8%) African American children. Only 1 child had bilateral amblyopia.

Conclusions: Manifest strabismus affected 1 in 30 Whites and 1 in 47 African Americans. National population projections suggest that there approximately 677,000 cases of manifest strabismus among children 6 through 71 months of age and 271,000 cases of amblyopia among children 30 through 71 months of age in the United States.

Reviewer's Comments: Prevalence of amblyopia <2%. Equally strabismic or anisometric

Different corrections of hypermetropic errors in the successful treatment of hypermetropic amblyopia in children 3 to 7 years of age.

Li CH, Chen PL, Chen JT, Fu JJ.

Am J Ophthalmol 2009 Feb; 147(2):357-63.

Purpose: To evaluate the improvement in visual acuity (VA) in children 3 to 7 years old with hypermetropic amblyopia after full or partial hypermetropic correction.

Methods: Medical records of 182 children with hypermetropic amblyopia treated with partial or full hypermetropic correction from January 1, 2001 to July 31, 2007 were evaluated. Improvement in the VA of the amblyopic eye, changes in the power of glasses, and the reduction in hypermetropia were assessed.

Results: Ninety-three children underwent full hypermetropic correction and the mean VA of their amblyopic eyes improved by 0.46 logarithm of minimal angle of resolution (logMAR). Eighty-one children underwent partial hypermetropic correction and the mean VA of their amblyopic eyes improved by 0.48 logMAR. The reduction in hypermetropia was 0.44 diopters (D)/year and 0.43 D/year, respectively. Changes in glasses at four to eight weeks of follow-up were noted in 11 children receiving full correction, all of whom were older than 5 years. Ten children, aged 3 to 5 years, with hypermetropia of more than 3 D and receiving partial correction, required a change of glasses and most (seven children) had underdiagnosed accommodative esotropia.

Conclusions: Both full correction and partial correction of hypermetropic errors improved the VA of 3 to 7-year-old children with hypermetropic amblyopia. The reduction in hypermetropia was similar after full and partial hypermetropic correction. However, for children older than 5 years, full correction should be undertaken with care because the accompanying blur at distance can hinder compliance. For younger children, especially with a high degree of hypermetropia, full correction might be required to avoid strabismus, which would cancel the effects of spectacle correction.

Amblyopia treatment: 1998 versus 2004.

Khazaeni L, Quinn GE, Davidson SL, and Forbes BJ.

J Pediatr Ophthalmol Strabismus 2009 Jan-Feb; 46(1):19-22.

A questionnaire survey was mailed to 1200 AAPOS members listed in the 2004 AAPOS directory. Seven scenarios were presented which included six treatment options. Respondents were asked to indicate their initial treatment preference in 1998 and in 2004. Three hundred eighty-nine surveys (33.1%) were returned. In four of seven scenarios, comments suggested that a change in practice was attributed to recent publications of Pediatric Eye Disease Investigator Group Trials. In all seven scenarios, atropine would have been offered in 2004 as an alternative to patching in 1998, and in five of the seven scenarios the combination of simultaneous atropine and patching would have been prescribed. In six of the seven scenarios some type of nonspecific near work would now be prescribed as an adjunct treatment.

Disrupted retinotopic maps in amblyopia.

Mansouri B, et al.

Invest Ophthalmol Vis Sci 2009 Jul; 50(7):3218-25.

Purpose: The amblyopic visual system exhibits both positional inaccuracy (uncertainty) and systematic biases (distortion). The fidelity of the retinotopic representation of the visual field driven by the amblyopic eye was studied for each of these aspects of position coding by using a dichoptic position-matching task.

Methods: Fifteen patients with amblyopia and five normal subjects were tested. The stimuli were luminance-defined Gaussian blobs that were presented within a circle of 15° diameter. Each Gaussian blob was seen only by the amblyopic eye. Moving a mouse marker seen only by the fellow fixing eye (perceptual matching measure), each subject had to localize the position of previously presented targets.

Results: The results confirm previous findings that there is significant distortion in the maps of the central visual field in amblyopic subjects. However, the uncertainty measure did not correlate with the measured distortion in amblyopic maps nor with the visual acuity. Also, regional analysis of the data showed that the distortion occurred heterogeneously in different parts of the visual field and had no relationship to the associated strabismus.

Conclusions: The underlying explanations for these three visual deficits—inaccuracy, distortion, and acuity loss—may be different.

Comment: Background about this paper is that humans with strabismic amblyopia (but not those with nonstrabismic anisometropic amblyopia) display increased uncertainty for positional tasks with their amblyopic eyes. This positional uncertainty is scale-invariant, meaning that it is elevated to a similar extent for large objects of low spatial frequency as it is for small objects of high spatial frequency. In addition, patients with strabismic amblyopia display fixed spatial biases (i.e., distortions) for positional judgments and perceive spatial distortions in general. The relationships among the deficits for uncertainty, distortion, and acuity are not well understood.

Treatment of anisometropic amblyopia with spectacles or in combination with translucent bangerter filters.

Agervi P., et al.

Ophthalmology 2009 Aug; 116(8):1475-1480.

Design: Prospective, randomized clinical trial (in Scandinavia) of 80 children (mean age, 4.4 years) with untreated anisometropic amblyopia and a median best-corrected visual acuity (BCVA) in the amblyopic eye of 0.4 logarithm of the minimum angle of resolution (logMAR).

Methods: Optimal refractive correction was provided, and the children were assigned to treatment with either spectacles or spectacles in combination with a Bangerter filter worn on the spectacle lens of the better eye.

Main Outcome Measures: The time course to resolution of amblyopia.

Results: The difference in the mean time to the resolution of amblyopia was 3.9 ± 3.2 months for the spectacles group versus 2.2 ± 1.9 months for the filter group, and the difference reached significance ($P < 0.05$). The BCVA in the amblyopic eye improved significantly ($P < 0.001$ for both comparisons) in both groups. After 1 year, there was no significant difference in the BCVA between the groups. The binocular function improved in both groups; at 1 year there was no significant difference between the groups. The median anisometropia decreased significantly from the first visit to the 1-year visit in both groups ($P < 0.001$ for both comparisons).

Conclusions: We found a more rapid visual acuity recovery with the Bangerter filters than with spectacles alone in eyes with anisometropic amblyopia. However, the 1-year visual acuity outcome was not statistically significantly different between the 2 treatments.

Bilateral uneven cataracts in children: Amblyopia management by sequential intraocular lens implantation.

Yu T, Dahan E.

Eye 2009 Jun; 23(6):1451-1455.

Children with bilateral uneven cataracts who needed bilateral cataract surgery were prospectively enrolled in Oxford Eye Center, Johannesburg, South Africa and Southwest Eye Hospital, Chong Qing, China. In the same patient, the amblyopic eye with the denser cataract underwent primary intraocular lens implantation, whereas the better eye was temporarily left aphakic as an alternative to patching. A secondary intraocular lens implantation was performed in the aphakic eye when best-corrected visual acuity in the amblyopic eye attained its best potential. Results: Thirteen children were included in this non-comparative study. Average age at surgery was 3.02 ± 1.87 years with an average follow-up period of 9.35 ± 5.23 years. In the amblyopic eyes, 10 out of 13 (77%) had less than 20/120 best-corrected visual acuity before amblyopia treatment. The optical penalization of the dominant eye (temporary aphakia) lasted on average 8.38 ± 4.05 weeks. The best-corrected visual acuity of the amblyopic eye improved to 20/50 or better in six eyes (46%), and ranged from 20/60 to 20/200 in five eyes (38%); in the remaining two eyes, the best-corrected visual acuity stayed below 20/200. Best-corrected visual acuity was restored to 20/30 or better following intraocular lens implantations in 12 of the dominant eyes (92%).

Treatment of severe amblyopia with weekend atropine: Results from 2 randomized clinical trials.

PEDIG.

J AAPOS 2009 Jun; 13(3):258-263.

A multicenter, prospective, randomized, clinical trial looking at effectiveness of atropine in severe amblyopia (20/125-20/400). Trial 1: 60 children 3-6 (mean 4.4 yrs) randomized to weekend atropine with a plano lens or weekend atropine with full correction. Trial 2: 40 children ages 7-12 (mean 9.3) randomized to weekend atropine or 2 hrs daily patching. Final acuity was determined at 18 wks in Trial 1 and 17 wks in Trial 2.

In Trial 1 visual acuity improved an average of 4.5 lines in atropine plus correction and 5.1 lines in atropine plus plano lens. In Trial 2, visual acuity improved 1.5 lines in the atropine group and 1.8 in the patching group.

Retinal nerve fiber layer thickness in amblyopic eyes.

Repka MX, Kraker RT, Tamkins SM, Suh DW, Sala NA, Beck RW; Pediatric Eye Disease Investigator Group.

Am J Ophthalmol 2009 Jul; 148(1):143-7.

Purpose: To compare the peripapillary retinal nerve fiber layer (RNFL) thickness of amblyopic and fellow eyes. We hypothesized that the RNFL of the amblyopic eye may be thinner.

Methods: Optical coherence tomography of the peripapillary RNFL thickness of amblyopic and fellow eyes was performed in 37 patients 7 to 12 years of age (mean age +/- standard deviation, 9.2 +/- 1.5 years) with unilateral strabismic, anisometropic, or combined-mechanism amblyopia enrolled in a randomized treatment trial.

Results: Mean global RNFL thickness of the amblyopic and fellow eyes was 111.4 and 109.6 microm, respectively (mean difference, 1.8 microm thicker in the amblyopic eyes; 95% confidence interval, -0.6 to 4.3 microm). The amblyopic eye was 8 microm or more thicker than the fellow eye in 9 patients (24%); the fellow eye was 8 microm or more thicker than the amblyopic eye in 2 patients (5%); and the difference was within test-retest variability (7 microm) in 26 patients (70%).

Conclusions: Our findings do not indicate that peripapillary RNFL thickness is thinner in eyes with moderate amblyopia compared with their fellow eyes.

Levodopa/Carbidopa in the Treatment of Amblyopia.

Dadeya S, Vats P, Malik KPS.

JPOS 2009 Mar-Apr; 46:87-90.

Thirty patients with strabismic amblyopia between the ages of 3 and 12 years were studied in double-blind, randomized fashion. Group A received levodopa/carbidopa three times daily after meals and Group B received placebo. Both groups received full-time occlusion until a visual acuity of 6/6 was achieved or for a maximum of 3 months. More than two lines improvement in visual acuity was noted in the levodopa group (15 of 15) than in the placebo group (9 of 15), and this effect was greater in patients younger than 8 years. There was also no significant reversal of the improved visual acuity in up to 6 months of f/u.

II. VISION SCREENING

Accuracy of the Welch Allyn SureSight for measurement of magnitude of astigmatism in 3- to 7-year-old children. Harvey EM, Dobson V, Miller JM, et al. J AAPOS 2009;13:466-471. Oct.

Welch Allyn SureSight has an upper limit for measuring astigmatism of 3.00 Diopters. The purpose of this study was to evaluate the accuracy of astigmatism magnitude measurements with the SureSight in noncycloplegic eyes, when compared to testing under cycloplegic conditions using the Retinomax K+ autorefractor. 825 children were enrolled from a community Head Start program. The study found that measurement success did not differ across the age range tested. The SureSight yielded an 89% high confidence reading, which was somewhat depressed by the high rate of astigmatism in the study population. The SureSight tended to overestimate the amount of astigmatism by approximately one-third. Therefore it was useful in categorizing the amount of astigmatism present (ie. > or < 2.00 Diopters), but not very useful in determining an exact amount.

Plusoptix Vision Screener: the accuracy and repeatability of refractive measurements using a new autorefractor.

Dahlmann-Noor AH, Comyn O, Kostakis V, Misra A, et al.

Br J Ophthalmol 2009 March; 93(3):346-349.

Background: The Plusoptix Vision Screener (PVS) is a new non-cycloplegic videoretinoscopy autorefractor. Refractive accuracy may affect its performance as a screening tool. Aims: Study 1: To determine the intra- and interobserver variability of PVS measurements. Study 2: To compare PVS measurements with gold-standard manual cycloplegic retinoscopy (MCR).

Methods: Study 1: PVS refraction of 103 children with mean (SD) age 5.5 (0.6) years by two observers. Study 2: PVS and MCR refraction of 126 children with mean (SD) age 5.5 (1.5) years, including 43 children with manifest strabismus >5 PD, comparing mean spherical equivalent (MSE) and Jackson cross cylinders J0 and J45.

Results: Study 1: Repeatability coefficients (observer 1): MSE: 0.63 D, J0: 0.24 D, J45: 0.18 D; those of observer 2 were nearly identical. The mean difference (95% limits of agreement) between the two observers for MSE, J0 and J45 were, respectively, 0.03 (20.62 to 0.68 D), 20.008 (20.25 to 0.23 D) and 0.013 (20.18 to 0.20) D. Study 2:

MSE tended to be lower on PVS than MCR, with differences of up to 8.00 D. Less than 20% of values were within ± 0.50 D of each other. Agreement was better for J0 and J45. Strabismus was associated with an odds ratio of 3.7 (95% CI 1.3 to 10.5) of the PVS failing to obtain a reading.

Conclusions: The PVS may underestimate children's refractive error.

Vision screening in children by Plusoptix Vision Screener compared with gold-standard orthoptic assessment.

Dahlmann-Noor AH, Vrotsou K, Kostakis V, Brown J, et al.

Br J Ophthalmol 2009 Mar; 93(3):342-345.

Background: To evaluate a new autorefractor, the Plusoptix Vision Screener (PVS), as a screening tool to detect risk factors for amblyopia by comparing it with gold-standard orthoptic vision screening in children.

Methods: Community-based screening study including 288 children age 4–7 years who were screened with the PVS and by orthoptic assessment (distance acuity, cover test, extraocular movements, 20 PD prism test, Lang stereotest). Follow-up comprehensive eye examination of screening-positive children included manual cycloplegic retinoscopy.

Results: Testability was high for both methods. Orthoptic screening identified 36 children with reduced vision and/or factors associated with amblyopia (referral rate 12.5%). The PVS identified 16 children with potential vision problems (referral rate 5.6%), indicating only moderate sensitivity (44%; 95% CI 27.9 to 61.9%), but high

specificity (100%; 95% CI 98.5 to 100%) to detect factors associated with amblyopia. The PVS underestimated visually significant refractive errors.

Conclusions: Use of the PVS as single screening test in young children may miss a significant number of children with amblyopia or amblyogenic risk factors.

Normative monocular visual acuity for early treatment diabetic retinopathy study charts in emmetropic children 5 to 12 years of age

Dobson V, Clifford-Donaldson CE, Green TK, Miller JM, Harvey EM.

Ophthalmology 2009 Jul; 116(7):1397-1401.

Objective: To provide normative data for children tested with Early Treatment Diabetic Retinopathy Study (ETDRS) charts.

Participants: A total of 252 Native American (Tohono O'odham) children aged 5 to 12 years. On the basis of cycloplegic refraction conducted on the day of testing, all were emmetropic.

Methods: Monocular visual acuity was tested at 4m, using 1 ETDRS chart for the right eye (RE) and another for the left eye (LE).

Main Outcome Measures: Visual acuity was scored as the total number of letters correctly identified and as the smallest letter size for which the child identified 3 of 5 letters correctly.

Results: Visual acuity results did not differ for the RE versus the LE, so data are reported for the RE only. Mean visual acuity for 5-year-olds was significantly worse than for 8-, 9-, 10-, 11-, and 12-year-olds. The lower 95% prediction limit for determining whether a child has visual acuity within the normal range was 0.38 (20/48) for 5-year-olds and 0.30 (20/40) for 6- to 12-year olds. Mean interocular acuity difference did not vary by age, averaging less than 1 logMAR line at each age, with a lower 95% prediction limit of 0.17 log unit (1.7 logMAR lines) across all ages.

Conclusions: For monocular visual acuity based on ETDRS charts to be in the normal range, it must be better than 20/50 for 5-year-olds and better than 20/40 for 6- to 12-year olds. Normal interocular acuity difference includes values of less than 2 logMAR lines. Normative ETDRS visual acuity values are not as good as norms reported for adults, suggesting that a child's visual acuity results should be compared with norms based on data from children, not with adult norms.

Testability of vision and refraction in preschoolers: the strabismus, amblyopia, and refractive error study in Singaporean children.

Trager MJ, Dirani M, Fan Q, Gazzard G, et al.

Am J Ophthalmol 2009 Aug; 148(2):235-241.e6.

Purpose: To determine the testability of several vision and refraction tests in preschool-aged children.

Methods: One thousand five hundred and forty-two Singaporean Chinese children aged 6 to 72 months were recruited through door-to-door screening of government-subsidized apartments in Singapore. Trained eye professionals administered all tests, including monocular logarithm of the minimum angle of resolution visual acuity with the Sheridan Gardiner chart, monocular Ishihara color testing (Richmond Products Inc, Albuquerque, New Mexico, USA), biometric measurements using IOLMaster (Carl Zeiss, Jena, Germany), and Randot stereoacuity (Stereo Optical Co, Chicago, Illinois, USA) for children 30 to younger than 72 months. Cycloplegic refraction and keratometry measurements also were determined using a table-mounted autorefractor (Canon Autorefractor RK-F1; Canon, Tokyo, Japan) in children 24 to younger than 72 months.

Results: Testabilities were 84.8% for visual acuity (40.7% for age 30 to < 36 months, 70.8% for age 36 to < 42 months, 86.7% for age 42 to < 48 months, 94.8 for age 48 to < 54 months, 98.6 for age 54 to < 66 months, and 98.7% for age 66 to < 72 months), 81.1% for the Ishihara color test, 82.2% for Randot stereoacuity, 62.2% for table mounted autorefraction, and 91.7% for IOLMaster. All testabilities significantly increased with age ($P < .0001$). Girls had higher testability rates than boys for the autorefraction and Randot stereoacuity tests ($P = .036$ and $.008$, respectively).

Conclusions: The vision and refraction tests were testable in a high proportion of preschool-aged Chinese Singaporeans. Preschool children in older age groups are likely to complete these tests successfully, with important implications for determining age limits for screening in the community and clinic.

Limits on improving the positive predictive value of the Welch Allyn SureSight for preschool vision screening.

Silverstein E, Lorenz S, Emmons K, Donahue S.
J APPOS 2009 Feb; 13(1):45-50.

The paper examines the usefulness of altering referral criteria to create high specificity for remote field screening where over-referral would be costly. Referral criteria were made increasingly more stringent to lower the rate of referral and the effect on positive predictive value (PPV) was determined. A total of 15,749 children were screened. This yielded a referral rate of 7.3% and a PPV of 48.2%. The PPV was >70% for children with unreliable screenings and with estimated refractive errors exceeding the instrument's range. Altering referral criteria decreased referral rate, but also decreased sensitivity. The SureSight usefulness for high specificity screening may be limited, but is sufficient for large screening programs.

III. Refractive Error

Height, stunting, and refractive error among rural Chinese schoolchildren: the See Well to Learn Well project.

[Sharma A](#), [Congdon N](#), [Gao Y](#), [Lu Y](#), [Ye Y](#), [Wu J](#), [Lam DS](#), [Li L](#), [Wu J](#), [Tse YK](#), [Zhang M](#), [Song Y](#), [Griffiths S](#).

[Am J Ophthalmol](#). 2010 Feb;149(2):347-353.e1. Epub 2009 Oct 29.

PURPOSE: To evaluate the hypothesis that changes in nutritional status could be partly responsible for observed increases in myopia prevalence among Chinese children.

METHODS: Rural Chinese secondary school children participating in a study of interventions to promote spectacle use were randomly sampled (20% of children with uncorrected vision >6/12 bilaterally, and 100% of remaining children) and underwent cycloplegic refraction with subjective refinement and measurement of height and weight. Stunting was defined according to the World Health Organization standard population.

RESULTS: Among 3226 children in the sample, 2905 (90.0%) took part. Among 1477 children undergoing refraction, 1371 (92.8%) had height and weight measurements. These children had a mean age of 14.5 +/- 1.4 years, 59.8% were girls, and mean spherical equivalent refraction was -1.93 +/- 1.82 diopters. Stunting was present in 87 children (6.4%). While height was inversely associated with refractive error (RE) (taller children were more myopic) among boys ($r = -0.147$, $P = .001$), this disappeared when adjusting for age, and no such association was observed among girls. Neither girls nor boys with stunting differed significantly in refraction from children without stunting, and neither stunting nor height was associated with RE when adjusting for age, height, and parental education. The power of this study to have detected a 0.75 diopters difference in RE between children with and without stunting was 0.96.

CONCLUSION: Results from this cross-sectional study are not consistent with the hypothesis that nutritional status is a determinant of RE in this setting.

The development of myopia among children with intermittent exotropia.

[Ekdawi NS](#), [Nusz KJ](#), [Diehl NN](#), [Mohney BG](#).

[Am J Ophthalmol.](#) 2010 Mar;149(3):503-7.

PURPOSE: To describe the long-term refractive error changes in children diagnosed with intermittent exotropia (IXT) in a defined population.

METHODS: Using the resources of the Rochester Epidemiology Project, the medical records of all children (<19 years) diagnosed with IXT as residents of Olmsted County, Minnesota, from January 1, 1975 through December 31, 1994 were retrospectively reviewed for any change in refractive error over time.

RESULTS: One hundred eighty-four children were diagnosed with IXT during the 20-year study period; 135 (73.4%) had 2 or more refractions separated by a mean of 10 years (range, 1-27 years). The Kaplan-Meier rate of developing myopia in this population was 7.4% by 5 years of age, 46.5% by 10 years, and 91.1% by 20 years. There were 106 patients with 2 or more refractions separated by at least 1 year through 21 years of age, of which 43 underwent surgery and 63 were observed. The annual overall progression was -0.26 diopters (SD +/- 0.24) without a statistically significant difference between the observed and surgical groups (P = .59).

CONCLUSION: In this population-based study of children with intermittent exotropia, myopia was calculated to occur in more than 90% of patients by 20 years of age. Observation versus surgical correction did not alter the refractive outcome.

Prevalence of Myopia and Hyperopia in 6 – to 72-month-Old African American and Hispanic Children: The Multi-Ethnic Pediatric Eye Disease Study

Multi-Ethnic Pediatric Eye Disease Study Group*

Ophthalmology 2010;117:140-147 (January)

Design: A population-based cross-sectional study. Of the prevalence of vision disorders in children aged 6 to 72 months in Los Angeles County, California. Seventy-seven percent of eligible children completed a comprehensive eye examination.

Results: Prevalence of myopia was higher in African American (6.6%) compared with Hispanic children (3.7%). Hispanics showed a higher prevalence hyperopia than African American children (26.9% vs. 20.8%). The prevalence of myopia showed a significant decreasing trend with age. Hyperopia prevalence reached a low point at approximately 24 months of age but increased and remained higher than that thereafter. No significant gender differences were found in the prevalence of refractive error for either ethnic group.

Conclusion: We observed ethnicity-related differences in both hyperopia and myopia prevalence in preschool children.

Anisometropia in Hispanic and African American Infants and Young Children The Multi-Ethnic Pediatric Eye Disease Study

Borchert M, Tarczy-Hornoch K, Cotter SA, Liu N, Azen ST, Varma R, for the MEPEDS Group
Ophthalmology 2010;117:148-153 (January)

Design: A population-based, cross-sectional study. 3030 Hispanic and 2994 African American children aged 6 to 72 months from Inglewood, California.

Methods: Retinomax autorefractometer was performed on all participants after cycloplegia. Strabismus was determined by prism-cover testing.

Results: The prevalence of SE anisometropia ≥ 1.0 diopter (D) was 4.3% for Hispanics and 4.2% for African Americans. Prevalence of cylindrical anisometropia ≥ 1.0 D was 5.6% and 4.5%, respectively. Prevalence of cylindrical or SE anisometropia ≥ 3.0 D was $\leq 0.4\%$ for both ethnic groups. The SE anisometropia decreased at age 1 year in Hispanics but not African Americans. Cylindrical anisometropia decreased in the first year of life in both ethnic groups. Anisometropia did not vary by gender. Strabismus was associated with all types of anisometropia. No association of anisometropia with gestational age, birth weight, cerebral palsy, family history, or prenatal exposure could be identified.

Conclusions: Spherical and cylindrical anisometropia (≥ 1.0 D) each affect 4% to 6% of Hispanic and African American preschoolers. Anisometropia ≥ 3.0 D is rare.

[Cheng D](#), [Schmid KL](#), [Woo GC](#), [Drobe B](#). Randomized trial of effect of bifocal and prismatic bifocal spectacles on myopic progression: two-year results. [Arch Ophthalmol](#). 2010 Jan;128(1):12-9.

The purpose of this paper was to determine if bifocal and prismatic bifocal spectacles could control progression of myopia in children with high rates of myopic progression. This study was a randomized controlled clinical trial which involved one hundred thirty-five (73 girls and 62 boys) myopic Chinese Canadian children. The children had myopia of $>$ or $= 1.00$ diopters [D] with myopic progression of at least 0.50 D in the preceding year. The patients were randomly assigned to 1 of 3 treatment arms: (1) single-vision lenses ($n = 41$), (2) +1.50-D executive bifocals ($n = 48$), or (3) +1.50-D executive bifocals with a 3-prism diopters base-in prism in the near segment of each lens ($n = 46$). The main outcome measures were to see assess myopic progression measured by an automated refractor under cycloplegia and increase in axial length (secondary) measured by ultrasonography at 6-month intervals for 24 months. Only the data of the right eye were used in each patient.

Mean age of the participants was 10.27 with SE of 0.15 years. Mean refractive error was -3.08 D [SE, 0.10 D]. 131 patients (97%) completed the trial after 24 months. Myopic progression averaged -1.55 D (SE, 0.12 D) for those who wore single-vision lenses, -0.96 D (SE, 0.09 D) for those who wore bifocals, and -0.70 D (SE, 0.10 D) for those who wore prismatic bifocals. Axial length increased an average of 0.62 mm (SE, 0.04 mm) for those who wore single vision lenses, 0.41 mm (SE, 0.04 mm) for those who wore bifocals, and 0.41 mm (SE, 0.05 mm) for those who wore prismatic bifocals. The treatment effect of bifocals (0.59 D) and prismatic bifocals (0.85 D) was significant ($P < .001$) and both bifocal groups had less axial elongation (0.21 mm) than the single-vision lens group ($P < .001$).

The authors conclude that bifocal lenses can moderately slow myopic progression in children with high rates of progression after 24 months and recommend that bifocal spectacles may be considered for slowing myopic progression in children with an annual progression rate of at least 0.50 D.

Given that myopic progression is a significant concern in many parents and a public health concern in some countries, this paper could provide a treatment option for some parents and also a forum for further study.

[Vitale S](#), [Sperduto RD](#), [Ferris FL 3rd](#). Increased prevalence of myopia in the United States between 1971-1972 and 1999-2004. [Arch Ophthalmol](#). 2009 Dec;127(12):1632-9.

The authors used the National Health and Nutrition Examination Survey (NHANES) to explore whether the prevalence of myopia was similar for persons aged 12-54 in 1971-1972 and persons of the same ages examined in 1999-2004. The 1971-1972 NHANES provided the earliest nationally representative estimates for US myopia prevalence; myopia was diagnosed by an algorithm using either lensometry, pinhole visual acuity, and presenting visual acuity (for presenting visual acuity \geq 20/40) or retinoscopy (for presenting visual acuity \leq 20/50). Using a similar method for diagnosing myopia, data from the 1999-2004 NHANES was used to determine whether myopia prevalence had changed during the 30 years between the 2 surveys. In this study, when using similar methods for each period, the prevalence of myopia in the United States appears to be substantially higher in 1999-2004 than 30 years earlier. Identifying modifiable risk factors for myopia could lead to the development of cost-effective interventional strategies.

Using the 1971-1972 method, the estimated prevalence of myopia in persons aged 12 to 54 years was 66.4% higher in 1999-2004 than in 1971-1972 (41.6% vs 25.0%, respectively; $P < .001$). Prevalence estimates were higher in 1999-2004 than in 1971-1972 for black individuals (33.5% vs 13.0%, respectively; $P < .001$) and white individuals (43.0% vs 26.3%, respectively; $P < .001$) and for all levels of myopia severity (> -2.0 diopters [D]: 17.5% vs 13.4%, respectively [$P < .001$]; ≤ -2.0 to > -7.9 D: 22.4% vs 11.4%, respectively [$P < .001$]; ≤ -7.9 D: 1.6% vs 0.2%, respectively [$P < .001$]).

Season of birth, daylight hours at birth, and high myopia.

McMahon G, Zayats T, Chen YP, Prashar A, Williams C, Guggenheim J.

Ophthalmology 2009 Mar; 116(3):468-473.

Purpose: Mandel et al recently reported that season of birth and daylight hours (photoperiod) at birth were associated with moderate and high levels of myopia Israeli conscripts. They sought to investigate whether these associations were evident in subjects from the United Kingdom (UK).

Design: Retrospective cross-sectional study of 74,459 subjects aged 18 to 100 years attending UK optometry practices for an eye examination.

Methods: The average monthly hours of daylight for London, UK, were classified into 1 of 4 "photoperiod categories," following Mandel et al. The odds ratio (OR) for each level of severity of myopia was calculated using multivariate logistic regression.

Results: Season of birth was significantly associated with the presence of high myopia: Subjects born in summer or autumn were more likely to be highly myopic compared with those born in winter. However, season of birth was not a significant risk factor for low or moderate myopia. Photoperiod category was weakly associated with low myopia, but with a direction of effect opposite to that observed by Mandel et al.

Conclusions: As in Israel, a disproportionate number of UK high myopes were born in the summer or autumn rather than in winter. However, unlike the situation in Israel, this association does not seem to be related to daylight hours during the postnatal period, implicating alternative physiologic influences that vary with season, such as birth weight.

Atropine for the treatment of childhood myopia; effect on myopia progression after cessation of Atropine.

Tong L, Huang XL, Koh AL, Zhang X, Tan DTH, Chua WH.

Ophthalmology 2009 Mar; 116(3):572-579

Purpose: The aim of this study was to assess the effect on myopia progression after cessation of topical atropine treatment.

Design: Parallel-group, placebo-controlled, randomized, double-masked study of 400 children aged 6 to 12 years with refractive error of spherical equivalent -1.00 to -6.00 diopters (D) and astigmatism of -1.50 D or less. Subjects were followed up for 12 months after stopping treatment, which consisted of either 1% atropine or vehicle eye drops once nightly for 2 years. Only 1 eye of each subject was chosen through randomization for treatment.

Main Outcome Measures: The main efficacy outcome measures were changes in spherical equivalent refraction as measured by cycloplegic autorefractometry and change in ocular axial length as measured by ultrasonography.

Results: After 3 years of participation in the trial (with 2 years on atropine treatment), eyes randomized to atropine have less severe myopia than other eyes. Over the 3 years, the increase in axial length of the atropine-treated eyes was 0.29 ± 0.37 mm compared with 0.52 ± 0.45 mm in the placebo-treated eyes

($P < 0.0001$). After cessation of atropine, the amplitude of accommodation and near visual acuity returned to pretreatment levels.

Conclusions: After stopping treatment, eyes treated with atropine demonstrated higher rates of myopia progression compared with eyes treated with placebo. However, the absolute myopia progression after 3 years was significantly lower in the atropine group compared with placebo.

Prevalence of refractive error among preschool children in an urban population: The Baltimore Pediatric Eye Disease Study.

Giordano L, Friedman DS, Repka MX, Katz J, Ibiwonke J, Hawes P, Tielsch JM.

Ophthalmology 2009 Mar; 116(3):739-746.

Design: The Baltimore Pediatric Eye Disease Study is a population-based evaluation of the prevalence of ocular disorders in children aged 6 to 71 months in Baltimore, Maryland. Among 4132 children identified, 3990 eligible children (97%) were enrolled and 2546 children (62%) were examined.

Methods: Cycloplegic autorefractometry was attempted in all children with the use of a Nikon Retinomax K-Plus 2. If a reliable autorefractometry could not be obtained after 3 attempts, cycloplegic streak retinoscopy was performed.

Main Outcome Measures: Mean spherical equivalent (SE) refractive error, astigmatism, and prevalence of higher refractive errors among African-American and white children.

Results: The mean SE of right eyes was $+1.49$ diopters (D) in white children and $+0.71$ D in African-American children. Mean SE refractive error did not decline with age in either group. The prevalence of myopia of 1.00 D or more in the eye with the lesser refractive error was 0.7% in white children and 5.5% in African-American children. The prevalence of hyperopia of $+3$ D or more in the eye with the lesser refractive error was 8.9% in white children and 4.4% in African-American children. The prevalence of emmetropia was 35.6% in white children and 58.0% in African-American children. On the basis of published prescribing guidelines, 5.1% of the children would have benefited from spectacle correction. However, only 1.3% had been prescribed correction.

Conclusions: Significant refractive errors are uncommon in this population of urban preschool children. There was no evidence for a myopic shift over this age range in the cross-sectional study.

Optical treatment reduces amblyopia in astigmatic children who receive spectacles before Kindergarten

Dobson V, Clifford-Donaldson CE, Green TK, Miller JM, Harvey EM
Ophthalmology 2009 Apr;116:1002-1008.

Design: Comparative case series of 73 astigmatic (right eye ≥ 1.50 diopters [D] cylinder) Native American children 5 to 7 years of age. All had with-the-rule astigmatism.

Intervention: Thirty-nine children (Treated Group) had spectacle correction of refractive error, prescribed for full-time wear, in preschool (0.8 – 2.4) years before testing). Thirty-four children (Untreated Group) had no prior correction.

Results: Mean ETDRS VA was significantly better in the Treated Group (20/37) than in the Untreated Group (20/48), difference between mean Lea Symbols VA in the Treated Group (20/33) and in the Untreated Group (20/38) was not significant.

Conclusions: Spectacle correction during the preschool years results in a significant improvement in best-corrected letter recognition acuity in astigmatic children by the time they reach kindergarten. However, grating acuity was not improved and magnitude of meridional amblyopia was not reduced in children who had received early spectacle correction.

Effect of topical atropine on astigmatism.

Chia A, Chua WH, Tan D.

Br J Ophthalmol 2009 May; 93(5):799-802.

Aim: The aim of this study was to determine if topical atropine, used to retard axial length elongation and myopia progression, had any effect on ocular astigmatism.

Methods: Data collected from subjects enrolled in the Atropine in the Treatment of Myopia (ATOM) study were analysed. In this study, 400 myopic children (aged 6–12 years) were randomly assigned to administer atropine 1% or a placebo daily to a randomly selected eye for 2 years. Cycloplegic autorefractometry and keratometry readings were measured using a Canon RK5 autorefractor. The refractive error was then split into its power vector components: J0 and J45.

Results: Astigmatism increased by 0.12–0.16 D per year in both treated and placebo groups. There was no difference between groups ($p=0.182$). The increase was mirrored by an increase in corneal astigmatism of 0.10–0.13 D per year, suggesting that most of the change was corneal in nature. There was an increase in J0 vector (with-the-rule astigmatism) with no change in the J45 (oblique) vector over time. The change in the J0 vector was significantly larger in the atropine-treated versus atropine-untreated eyes during the 2-year treatment period ($p=0.011$), but this difference disappeared after atropine was stopped.

Conclusions: The use of atropine on a daily basis over 2 years did not have any clinically significant effect on astigmatism.

Note: the findings of this study suggest that topical atropine does not have a clinically significant effect on the amount, axis or natural progression of astigmatism in myopic children (aged 6–12 years) with astigmatism (≤ 1.5 D).

IV. NEURO

Price SE. Multiple Sclerosis: Diagnostic issues and modern management.

Major Review. Br Ir Orthopt J 2009; (June) 6: 5-13.

This major literature-based review article provides insight into current issues in the diagnosis and management of MS. The results of the review show that the prevalence of MS may be increasing, especially in women. The United Kingdom has one of the highest prevalence levels in the world. An

increase, also more in women, has been noted in France, and that it is a more aggressive disease when seen in those of North African origin.

The incidence has also increased in the United States, especially in women. The female to male ratio has changed from 1.4:1 in 1955 to 2.3:1 in 2000. The possible infectious etiologies and potential environmental factors are reviewed. The role of imaging in the diagnosis and treatment is discussed. New and better disease-modifying therapies are emerging. [119 references.]

Hanif S, Rowe FJ, O'Connor, A. A comparative review of methods to record ocular rotations. Br Ir Orthopt J 2009; (June) 6: 47-52.

The authors reviewed articles from 1899-2007 that described methods of reporting ocular rotations. They looked at how methods have changed and progressed over the years. These can be divided into kinetic or static methods and many tests are described. The Hess and Lees screen tests are static methods in which the target remains still and the deviation is measured at a given point. Kinetic methods such as perimetry allow a moving target to be followed and the results plotted. Newer computerized versions of static and kinetic testing methods are described. Good historical perspective and extensive references.

Richardson GA, Firth AY. The effect of induced vertical divergence on horizontal fusional amplitudes. Br Ir Orthopt J 2009; (June) 6: 71-75.

The authors of this original article set out to determine whether horizontal fusion is compromised in the presence of slight vertical deviations induced by small vertical prisms.

Fifteen students with normal binocular single vision met the inclusion criteria. The dependent variable was the fusional amplitude and the independent variable was the amount of induced vertical divergence. The study design was well thought out.

Analysis of the raw data shows that with small vertical deviations induced by a prism, the greater the induced vertical divergence, the smaller the total horizontal fusional amplitude. The reduction in horizontal fusional amplitudes was statistically significant with 2 diopters of induced vertical divergence. [8 references.]

Piano M, Knox PC, O'Connor A: Grapheme-Colour Synaesthesia. Br Ir Orthopt J 2009; (June) 6: 34-40.

This is a fascinating article describing the condition of synaesthesia. This is a congenital condition with a strong familial component in which the individual perceives something not ordinarily seen by others and which is stimulated each time by a certain word or symbol. The stimulus induces the synaesthesia sensation and the individual experiences an extra perception known as the "concurrent." An example given was "tasting" chocolate whenever the word "oysters" was spoken or seeing the color red when viewing the letter A. This can cause great difficulty when reading or doing mathematics. The prevalence of grapheme-colour synaesthesia is 2 percent in UK adults and 1.3 percent in a group of 6-7 year-olds. Forty-three percent of children of parents with the condition are affected.

This article describes the condition and its neurophysiological basis. It is often associated with specific learning disorders such as dyslexia or other reading difficulties, problems that sometimes prompt a referral to an ophthalmologist or orthoptist. Therefore the authors thought it was reasonable to raise awareness of this condition among clinicians who may have to examine these children. [49 references]

Jones E, Rowe FJ: Ocular motility consequences following lesions of the thalamus: a literature review. Br Ir Orthopt J 2009; (June) 6: 40-46.

This excellent literature review concentrates on the anatomy and function of the thalamus and the types of thalamic lesions causing ocular motor deficits. The literature search revealed 32 papers published between 1939 and 2008 with a total of 599 patients studied.

The review found that the majority of thalamic lesions were vascular infarcts or hemorrhages. The differences in pathology between adults and pediatric cases were described. The eye movement deficits included, among others, vertical gaze palsies, skew deviation, convergence anomalies, III nerve palsy, nystagmus, and saccadic and pursuit deficits.

The authors wanted to determine whether the eye movement findings were caused by extension of the lesion into the midbrain. The thalamus makes up 4/5ths of the diencephalon, the remaining portion being the hypothalamus. The anatomy and vascular supply of each part is explained in detail.

The authors showed that bilateral thalamic lesions produce more severe ocular deficits than unilateral ones. Unilateral lesions produce upgaze weakness. Bilateral lesions cause paralysis of up or downgaze or both, skew deviation, dorsal midbrain signs, internuclear ophthalmoplegia and convergence paralysis. The authors questioned whether these unusual eye findings are caused by pure thalamic pathology or by involving the important ocular control centers in the midbrain. They conclude that a variant blood supply in some individuals may lead to midbrain involvement. [53 references]

Br J Ophthalmol 2010;**94**:146-149 doi:10.1136/bjo.2009.160713 **Optic neuropathy endemic in secondary school children in Dar es Salaam, Tanzania**

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7. C Gilbert²

Abstract

Aim To investigate the prevalence and causes of optic neuropathy, reported as epidemic in 1997, among secondary school students in Dar es Salaam, Tanzania.

Patients and methods First year students (n=10 892) from 63 secondary schools located within 30 km from the base hospital were interviewed and had a visual acuity (VA) screening test. Students failing the 6/12-line in either eye were defined as having "poor eyesight" and referred to the base hospital where an optometrist re-tested VA and refracted them. An ophthalmologist examined students with VA of 6/12 or worse in either eye and visual impairment was defined as VA of worse than 6/12 with best correction. Associations between optic neuropathy, socioeconomic status and educational results were investigated.

Results Students' ages ranged from 12 to 22 (mean 15.2) years; 50.6% were male. The prevalence of optic neuropathy was 0.3 (SD 0.051)%. The condition affected older students and was associated with the family having fewer economic possessions (car, computer, television). Optic neuropathy accounted for 19/33 (58%) of bilateral visual impairment cases. No effect of the disease on educational performance was identified.

Conclusion Optic neuropathy remains a significant problem in this population and can now be termed endemic rather than epidemic. Further research into its causes is required.

Comment: Large study, suggests that vitamin B deficiency as a cause for the optic neuropathy. Calls for Vitamin B supplementation programs to be created to reduce this endemic optic neuropathy.

Violation of the ISNT rule in nonglaucomatous pediatric optic disc cupping.

Pogrebniak AE, et al. *Invest Ophthalmol Vis Sci* 2010; 51:890-5. (Feb 2010)

Purpose: To determine whether nonglaucomatous optic disc cupping in children violates the ISNT rule (which states that for normal optic discs the neuroretinal rim width is greatest in the order inferior \geq superior \geq nasal \geq temporal).

Methods: Digital ocular fundus photographs from a random cohort of children with large optic disc cups of nonglaucomatous origin were analyzed in masked fashion by using computer graphic software. The diameter and perimeter of each optic disc and optic cup and the width of the neuroretinal rim were drawn and measured. Measurements were compared to a random cohort of normal pediatric optic discs.

Results: The ISNT rule was intact in 9 (16%) of 55 eyes of nonpremature children with nonglaucomatous cupping, in 6 (21%) of 28 eyes of children with a history of prematurity and nonglaucomatous cupping, and in 35 (73%) of 48 eyes with normal discs.

Conclusions: Violation of the ISNT rule occurs with greater frequency in the pediatric population with large optic disc cups of nonglaucomatous origin, compared with the pediatric population with normal optic discs. In discs with small cups, neuroretinal rim width conforms to the overall oval shape of the disc, which is usually greatest in vertical dimension, whereas discs with large cups possess greater variability of relative neuroretinal rim width around the disc, greater relative vertical cup/disc ratio versus horizontal cup/disc ratio, and lower predictability of the ISNT rule.

Comment: This study is interesting because the authors conclude that violation of the ISNT rule occurs in a majority of eyes in children with large optic disc cups of nonglaucomatous origin. The normal optic disc usually demonstrates a configuration in which the inferior neuroretinal rim is the widest portion of the rim, followed by the superior rim, and then the nasal rim, with the temporal rim being the narrowest portion. Violation of this "ISNT rule" may be used to identify adult glaucoma, which frequently damages superior and inferior optic nerve fibers before temporal and nasal fibers (i.e. leading to thinning of the superior and inferior rims and violation of the rule).

Grasping deficits and adaptations in adults with stereo vision losses.

Melmoth DR, et al.

Invest Ophthalmol Vis Sci 2009 Aug; 50(8):3711-20.

Purpose: To examine the effects of permanent versus brief reductions in binocular stereo vision on reaching and grasping (prehension) skills.

Methods: The first experiment compared prehension proficiency in 20 normal and 20 adults with long-term stereo-deficiency (10 with coarse and 10 with undetectable disparity sensitivities) when using binocular vision or just the dominant or nondominant eye. The second experiment examined effects of temporarily mimicking similar stereoacuity losses in normal adults, by placing defocusing low- or high-plus lenses over one eye, compared with their control (neutral lens) binocular performance. Kinematic and error measures of prehension planning and execution were quantified from movements of the subjects' preferred hand recorded while they reached, precision-grasped, and lifted cylindrical objects (two sizes, four locations) on 40 to 48 trials under each viewing condition.

Results: Performance was faster and more accurate with normal compared with reduced binocular vision and least accomplished under monocular conditions. Movement durations were extended (up to ~100 ms) whenever normal stereo vision was permanently (ANOVA $P < 0.05$) or briefly (ANOVA $P < 0.001$) reduced, with a doubling of error rates in executing the grasp (ANOVA $P < 0.001$). Binocular deficits in reaching occurred during its end phase (prolonged final approach, more velocity corrections, poorer coordination with object contact) and generally increased with the existing loss of disparity sensitivity. Binocular grasping was more uniformly impaired by stereoacuity loss and influenced by its duration. Adults with long-term stereo-deficiency showed increased variability in digit placement at initial object contact, and they adapted by prolonging (by ~25%) the time spent subsequently applying

their grasp (ANOVA $P < 0.001$). Brief stereoreductions caused systematic shifts in initial digit placement and two to three times more postcontact adjustments in grip position (ANOVA $P < 0.01$).

Conclusions: High-grade binocular stereo vision is essential for skilled precision grasping. Reduced disparity sensitivity results in inaccurate grasp-point selection and greater reliance on nonvisual (somesthetic) information from object contact to control grip stability.

Comment: Although the physiological basis of stereopsis has been studied extensively, the potential advantages of stereopsis for performing visually-guided tasks has received less attention. It has been suggested that “reaching and grasping” (prehension) movements are a main driving force for stereopsis. This study addresses the question of whether binocular stereopsis makes an irreplaceable contribution to prehension abilities, or whether permanently stereo-deficient subjects can compensate for its loss over time. For clinicians treating amblyopia, findings from this study suggest that prioritizing the recovery of high-grade binocular function (in addition to visual acuity) may provide long-term benefits for visuomotor control.

Birth weight and optic nerve head parameters.

Samarawickrama C, Huynh SC, Liew G, Burlutsky G, Mitchell P.

Ophthalmology 2009 Jun; 116(6):112-1118.

Purpose: To assess the relationship of birth weight, birth length, and head circumference as proxy markers of intrauterine growth, cup/disc ratio, and other optic disc parameters measured using optical coherence tomography (OCT).

Participants: The Sydney Childhood Eye Study examined 2353 primarily 12-year-old children.

Methods: Of 2353 children examined, 2134 (90.7%) had OCT scans and are included in this study. Birth weight, birth length and head circumference were ascertained from health records. Height and weight were measured using standardized protocols, body mass index (BMI), and sociodemographic information was collected in a questionnaire completed by parents. Low birth weight was defined as birth weight ≤ 2499 g, and prematurity was defined as gestation less than 37 weeks.

Main Outcomes Measures: Vertical optic disc and optic cup diameters, and cup/disc ratio.

Results: Children of low birth weight had decreased vertical disc diameter, increased cup diameter, and increased cup/disc ratio by 30 μm , 44 μm , and 0.03 respectively. After adjusting for age, gender, ethnicity, height, axial length, and BMI, birth weight remained positively associated with vertical optic disc diameter and inversely associated with both vertical optic cup diameter and vertical cup/disc ratio. These associations were not present in children with gestational age less than 33 weeks. Smaller birth length and head circumference were similarly associated with larger cup/disc ratio.

Conclusions: Low birth weight, short birth length, and small head circumference at birth were associated with larger cup/disc ratio in children aged 12 years. Our findings suggest that fetal growth restriction could adversely influence optic nerve head parameters. This may have implications for future risk of glaucomatous optic neuropathy.

Abnormal optic disc and retinal vessels in children with surgically treated hydrocephalus.

Andersson S, Hellstrom A.

Br J Ophthalmol 2009 Apr; 93(4):526-30.

Aims: To investigate the morphology of the optic disc and retinal vessels in children with surgically treated hydrocephalus.

Methods: A prospective, population-based study was performed in 69 children (median age 9.6 years) with early surgically treated hydrocephalus. All children were examined by ophthalmoscopy. Additionally, optic disc and retinal vessel morphology was evaluated in 55 children by digital image analysis of ocular fundus photographs.

Results: Optic atrophy was found in 10 of 69 children (14%). In comparison with a reference group, the median optic-disc area was significantly smaller ($p=0.013$) in the children with hydrocephalus. There was no corresponding difference in cup area, so the rim area was significantly smaller in the hydrocephalic children ($p=0.002$). Children with hydrocephalus had an abnormal retinal vascular

pattern, with significantly straighter retinal arteries and fewer central vessel branching points compared with controls ($p,0.001$ and $p,0.001$, respectively).

Conclusions: Hydrocephalus is associated with subnormal optic disc and rim areas and an abnormal vascular pattern, indicating a pre/perinatal disturbance of the development of these structures. A promising finding is that the frequency of optic atrophy in the present study was lower than previously reported, most likely reflecting improved perinatal care and better regulation of the intracranial pressure.

Note: nice descriptive study, hydrocephalus was associated more with small optic nerve size, retinal artery straightening. They also noted less optic atrophy in their patients likely related to improved care of children with hydrocephalus.

V. ROP

Importance of the ‘Third Criterion’ for Retinopathy of Prematurity screening in developing countries. Azad R et al. JPOS Nov-Dec 2009; 46:332-334.

With the use of current gestational age and birth weight guidelines, 86 of 1302 eyes (6.6%) were missed and 38 of these eyes (2.9%) had potentially treatable or more severe retinopathy of prematurity and were in need of treatment. Use of the “third criterion” (ie neonatologist referral of sick infants who were believed to be at high risk for ROP), enabled larger infants who were otherwise missed by the American guidelines to be included for screening. Even when the parameters were increased, a relatively small number of infants was still missed. Therefore, in view of the limited resources and manpower in developing countries, the American screening guidelines remain appropriate.

HMG-CoA Reductase inhibitors (statin) prevents retinal neovascularization in a model of oxygen-induced retinopathy

Bartoli M, et al. Invest Ophthalmol Vis Sci 2009; 50:4934-40. (Oct 2009)

Purpose: Retinal neovascularization (RNV) is a primary cause of blindness and involves the dysfunction of retinal capillaries. Recent studies have emphasized the beneficial effects of inhibitors of HMG-CoA reductase (statins) in preventing vascular dysfunction. In the present study, the authors characterized the therapeutic effects of statins on RNV.

Methods: Statin treatment (10 mg/kg/d fluvastatin) was tested in a mouse model of oxygen-induced retinopathy. Morphometric analysis was conducted to determine the extent of capillary growth. Pimonidazole hydrochloride was used to assess retinal ischemia. Western blot and immunohistochemical analyses were used to assess protein expression levels and immunolocalization. Lipid peroxidation and superoxide radical formation were determined to assess oxidative changes.

Results: Fluvastatin treatment significantly reduced the area of the capillary-free zone ($P < 0.01$), decreased the formation of neovascular tufts ($P < 0.01$), and ameliorated retinal ischemia. These morphologic and functional changes were associated with statin effects in preventing the upregulation of VEGF, HIF-1 α , phosphorylated STAT3, and vascular expression of the inflammatory mediator ICAM-1 ($P < 0.01$). Superoxide production and lipid peroxidation in the ischemic retina were also reduced by statin treatment ($P < 0.01$).

Conclusions: These data suggest the beneficial effects of statin treatment in preventing retinal neovascularization. These beneficial effects appear to result from the anti-oxidant and anti-inflammatory properties of statins.

Comment and Background: This study describes studies on the effects of statins on retinal neovascularization. This is interesting because recent studies have shown that the inhibition of VEGF expression and its activity in retina needs careful titration because of the physiological function of VEGF in promoting survival of the different retinal cell layers. Recently, attention has been focused on the use of the lipid-lowering drugs (statins) to prevent cardiovascular disease. This class of drugs consists of inhibitors of HMG-CoA reductase, a rate-limiting enzyme involved in the biosynthesis of mevalonate and cholesterol. The vasculoprotective effect of statins has been extensively documented, and numerous studies have suggested that the protective action of statins on the microvasculature is often independent of their cholesterol-lowering effects and involves their anti-oxidant and anti-inflammatory properties. The authors have previously documented that selective inhibition of NAD(P)H oxidase prevents VEGF overexpression and RNV in a mouse model of ROP. The authors and others have also shown that treatment with simvastatin (another statin) efficiently prevents hyperglycemia-induced retinal vascular permeability and leukostasis. That study demonstrated that statin effects in preventing diabetes-induced retinal vascular dysfunction are associated with the blockade of VEGF expression and NAD(P)H oxidase activation and with the inhibition of the transcription factor signal transducer and activator of transcription 3 (STAT3). Based on this evidence, the authors conducted studies in a model of oxygen-induced retinopathy to determine whether treatment with statins could be beneficial in preventing RNV, thus supporting their use in the treatment of advanced stages of ischemic retinopathies, among them proliferative diabetic retinopathy and retinopathy of prematurity.

Insights into Advanced Retinopathy of Prematurity Using Handheld Spectral Domain Optical Coherence Tomography Imaging

Sai H. Chavala, et. al

Ophthalmology 2009;116:2448-2456 (December)

Design: Prospective, observational case series of three low-birth-weight, severely premature infants.

Methods: Clinical examination was performed using using a portable slit lamp and indirect ophthalmoscope. Imaging was performed by using a handheld SD OCT device and Retcam (Clarity Medical Systems, Pleasanton, CA) or video-indirect recording.

Results: Linear and volumetric imaging was achieved with the handheld system in infant eyes despite tunica vasculosa lentis and vitreous bands. Imaging was not possible in eyes with notable vitreous hemorrhage. Analysis of SD OCT images revealed preretinal structures, retinoschisis, and retinal detachment in the posterior pole of patients with advanced ROP. Both the retinoschisis and the preretinal structures were not identified on conventional examination or imaging by expert pediatric ophthalmologists.

Conclusions: Handheld SD OCT imaging can be performed on the sedated or nonsedated neonate and provides valuable subclinical anatomic information. This imaging can reveal the location and extent of posterior ROP pathology not evident on standard examination.

Reviewer's Comments: May avoid exams under anesthesia

Wide-field digital retinal imaging versus binocular indirect ophthalmoscopy for retinopathy of prematurity screening: a two-observer prospective, randomized comparison.

Dhaliwal C, Wright E, Graham C, McIntosh N, Fleck, BW.

Br J Ophthalmol 2009 Mar; 93(3):355-359.

Aim: To compare the diagnostic accuracy of wide-field digital retinal imaging (WFDR) with the current “gold standard” of binocular indirect ophthalmoscopy (BIO) for retinopathy of prematurity (ROP) screening examinations.

Methods: A consecutive series of premature infants undergoing ROP screening at Edinburgh Royal Infirmary were eligible for recruitment into this prospective, randomized, comparative study. Infants were screened using both WFDR (Retcam II with neonatal lens) and BIO by two pediatric ophthalmologists who were randomized to the examination technique. Both examiners documented their clinical findings and management plans in a masked fashion. WFDR eye findings were compared with those of BIO.

Results: A total of 81 infants were recruited, and information from 245 eye examinations was analyzed. The sensitivity of WFDR in detecting any stage of ROP, stage 3 ROP and “plus” disease was 60%, 57% and 80%, respectively, and specificity 91%, 98% and 98%, respectively. The proportional agreement between WFDR and BIO was 0.96 for detecting stage 3 disease and 0.97 for detecting “plus” disease. There was very good agreement on management decisions (kappa 0.85).

Conclusions: When used in a routine ROP screening setting, a randomized comparison of WFDR and BIO, WFDR showed relatively poor sensitivity in detecting mild forms of ROP in the retinal periphery. This resulted in difficulty in making decisions to discharge infants from the screening program. Sensitivity was better for more severe forms of ROP, but at present WFDR should be regarded as an adjunct to, rather than a replacement for, BIO in routine ROP screening.

Astigmatism in the early treatment for retinopathy of prematurity (ETROP) study.

Findings to 3 Years of Age.

Davitt BV, Dobson V, Quinn GE, Hardy RJ, et al. On behalf of the Early Treatment for Retinopathy of Prematurity Cooperative Group.

Ophthalmology 2009 Feb; 116:332-339.

Purpose: To examine the prevalence of astigmatism (≥ 1.00 diopter [D]) and high astigmatism (≥ 2.00 D) at 6 and 9 months corrected age and 2 and 3 years postnatal age, in preterm children with birth weight of less than 1251g in whom high-risk prethreshold retinopathy of prematurity (ROP) developed in the ETROP Study. Randomized, controlled clinical trial of 401 infants in whom prethreshold ROP developed in one or both eyes and who were randomized after they were determined to have a high risk ($\geq 15\%$) of poor structural outcome without treatment using the Risk Management of Retinopathy of Prematurity program. Refractive error was measured by cycloplegic retinoscopy.

Intervention: Eyes were randomized to receive laser photocoagulation at high-risk prethreshold ROP (early treated [ET]) or to be conventionally managed (CM), receiving treatment only if threshold ROP developed.

Results: Astigmatism was classified as with-the-rule (WTR), against-the-rule (ATR), or oblique. The prevalence of astigmatism in ET and CM eyes was similar at each test age. For both groups, there was an increase in prevalence of astigmatism from approximately 32% at 6 months to approximately 42% by 3 years, mostly occurring between 6 and 9 months. Astigmatism was not influenced by zone of acute-phase ROP, presence of plus disease, or retinal residual of ROP. Eyes with astigmatism and high astigmatism most often had WTR astigmatism.

Conclusions: By age 3 years, nearly 43% of eyes treated at high-risk prethreshold ROP developed astigmatism of ≥ 1.00 D and nearly 20% had astigmatism of ≥ 2.00 D. Presence of astigmatism was not influenced by timing of treatment of acute-phase ROP or by characteristics of acute-phase or cicatricial ROP.

A Change in oxygen supplementation can decrease the incidence of retinopathy of prematurity.

Sears JE, Pietz J, Sonnie C, Dolcini D, Hoppe G.

Ophthalmology 2009 Mar; 116(3):513-518.

Design: Nonrandomized, retrospective study of all infants in a single Level III neonatal intensive care unit (Fairview Hospital, Cleveland Clinic) between the years of 2005 and 2007.

Methods: A prospective database recorded the gestational age, birth weight, stage and zone of ROP, threshold disease, treatment, final outcome and date of examination, maternal and infant demographics, and neonatal intensive care unit course. Year 1 (August 1, 2005 to July 31, 2006) includes a patient cohort who received the standard oxygen supplementation protocol, which has oxygen targets of 95% to 100% saturation. Year 2 (August 1, 2006 to July 31, 2007) includes a patient cohort who has strictly monitored oxygen targets of <34 weeks corrected gestational age oxygen limits of 80% to 95% and target 85% to 92% oxygen saturation and >34 weeks corrected gestational age limits of 85% to 100% and target 92% to 97% saturation.

Results: Ninety-eight infants were examined before and 92 infants were examined after the change in oxygen standards, comprising 190 consecutive patients examined between September 2005 and October 2007. ROP was present in 35% of infants in group 1 before the change in oxygen protocol compared with 13% after the change in oxygen standards ($P = 0.001$); stage 3 decreased from 11% to 2%; threshold disease decreased from 7% to 1%. Stage 0 (immature vessels, no ROP) incidence increased. There were statistically significant differences in mode of delivery, sepsis <3 days of life, and oxygen at discharge.

Conclusions: Lower oxygen targets at early gestational age and higher oxygen targets at older gestational age decrease the severity and incidence of ROP while inducing normal retinal development.

Vascular abnormalities in aggressive posterior retinopathy of prematurity detected by fluorescein-angiography.

Yokoi T, et al. National Center for Child Health and Development, Tokyo, Japan
Ophthalmology 2009 Jul; 116(7):1377-1382.

Purpose: A retrospective, nonrandomized case series of three patients (6 eyes) with AP-ROP. To evaluate fluorescein angiography (FA) in eyes with aggressive posterior retinopathy of prematurity (AP-ROP).

Methods: Fundus photographs and FA were obtained before and after laser and surgical treatment using a wide-field digital pediatric imaging system.

Results: At the initial stage of AP-ROP, FA showed vascular abnormalities, including capillary nonperfusion throughout the vascularized retina, shunting in the vascularized retina, a circumferential demarcation line, and limited vessel development, which was difficult to identify only by ophthalmoscopy. After treatment, FA showed poorly developed retinal vessels, including 4 small major vessels without an arcade pattern, small macular vessels, an inhomogeneous capillary bed, and absence of a capillary-free zone in the fovea.

Conclusions: Capillary bed loss throughout the vascularized posterior retina is characteristic of AP-ROP and may exacerbate retinopathy.

Wide-field digital retinal imaging versus binocular indirect ophthalmoscopy for retinopathy of prematurity screening: a two-observer prospective, randomised comparison.

Dhaliwal C, Wright E, Graham C, McIntosh N, Fleck BW.
Br J Ophthalmol 2009 Mar; 93(3):355-9.

Aim: To compare the diagnostic accuracy of wide-field digital retinal imaging (WFDR) with the current "gold standard" of binocular indirect ophthalmoscopy (BIO) for retinopathy of prematurity (ROP) screening examinations.

Methods: A consecutive series of premature infants undergoing ROP screening at Edinburgh Royal Infirmary were eligible for recruitment into this prospective, randomised, comparative study. Infants were screened using both WFDR (Retcam II with neonatal lens) and BIO by two paediatric ophthalmologists who were randomized to the examination technique. Both examiners documented

their clinical findings and management plans in a masked fashion. WFDR eye findings were compared with those of BIO.

Results: A total of 81 infants were recruited, and information from 245 eye examinations was analysed. The sensitivity of WFDR in detecting any stage of ROP, stage 3 ROP and “plus” disease was 60%, 57% and 80%, respectively, and specificity 91%, 98% and 98%, respectively. The proportional agreement between WFDR and BIO was 0.96 for detecting stage 3 disease and 0.97 for detecting “plus” disease. There was very good agreement on management decisions (kappa 0.85).

Conclusions: When used in a routine ROP screening setting, a randomised comparison of WFDR and BIO, WFDR showed relatively poor sensitivity in detecting mild forms of ROP in the retinal periphery. This resulted in difficulty in making decisions to discharge infants from the screening programme. Sensitivity was better for more severe forms of ROP, but at present WFDR should be regarded as an adjunct to, rather than a replacement for, BIO in routine ROP screening.

Note: WFDR should not replace BIO for screening at this time.

Evaluation of scleral buckling for stage 4A retinopathy of prematurity by fluorescein angiography.

Yokoi T, Yokoi T, Kobayashi Y, Hiraoka M, Nishina S, Azuma N.

Am J Ophthalmol 2009 Jul 8. [Epub ahead of print]

Purpose: To determine the early efficacy of scleral buckling for active neovascularization by fundus fluorescein angiography (FA) in eyes with stage 4A retinopathy of prematurity.

Methods: Patients who underwent scleral buckling for stage 4A ROP at the National Center for Child Health and Development, Tokyo, Japan, from October 2007 through November 2008 were included. Preoperative and postoperative FA and fundus photographs obtained with a wide-field digital pediatric imaging system were reviewed. Three patients (5 eyes; gestational ages at birth, 23 to 25 weeks; birth weights, 574 to 811 g) with zone II stage 4A ROP who underwent postoperative FA, 2 weeks or less after scleral buckling (range, 7 to 12 days; postmenstrual ages at postoperative FA, 41 to 45 weeks) were evaluated. Patients who underwent postoperative FA 2 weeks or more after scleral buckling were excluded.

Results: Despite fluorescein leakage from fibrovascular tissue in all eyes before surgery, markedly decreased leakage occurred only between 7 to 12 days after surgery. The retinas were reattached completely in all eyes after surgery.

Conclusions: Scleral buckling may prevent progression of retinal detachment in stage 4A ROP by reducing the tractional force and stabilizing the neovascular activity of the fibrovascular tissue.

Speed of telemedicine vs ophthalmoscopy for retinopathy of prematurity diagnosis.

Richter GM, Sun G, Lee TC, Chan RV, Flynn JT, Starren J, Chiang MF.

Am J Ophthalmol 2009 Jul; 148(1):136-42.e2.

Purpose: To compare the speed of retinopathy of prematurity (ROP) diagnosis using standard indirect ophthalmoscopy with that of telemedicine.

Methods: Three study examiners (2 pediatric retinal specialists [R.V.P.C., T.C.L.] and 1 pediatric ophthalmologist [M.F.C.]) conducted ROP diagnosis via standard indirect ophthalmoscopy and telemedicine. Each examiner performed: 1) standard ophthalmoscopy on 72 to 150 consecutive infants at his respective institution and 2) telemedical diagnosis on 125 consecutive de-identified retinal image sets from infants from an at-risk population. Time for ophthalmoscopic diagnosis was measured in 2 ways: 1) time spent by the examiner at the infant's bedside and 2) mean total time commitment per infant. Time for telemedicine diagnosis was recorded by computer time stamps in the web-based system. For each examiner, nonparametric statistical analysis (Mann-Whitney U test) was used to compare the distribution of times for examination by ophthalmoscopy vs telemedicine.

Results: Mean (+/- standard deviation [SD]) times for ophthalmoscopic diagnosis ranged from 4.17 (+/- 1.34) minutes to 6.63 (+/- 2.28) minutes per infant. Mean (+/- SD) times for telemedicine diagnosis

ranged from 1.02 (+/- 0.27) minutes to 1.75 (+/- 0.80) minutes per infant. Telemedicine was significantly faster than ophthalmoscopy ($P < .0001$). The total time commitment by ophthalmologists performing bedside ophthalmoscopy for ROP diagnosis, including travel and communication with families and hospital staff, was 10.08 (+/- 2.53) minutes to 14.42 (+/- 2.64) minutes per infant.

Conclusions: The ophthalmologist time requirement for telemedical ROP diagnosis is significantly less than that for ophthalmoscopic diagnosis. Additional time requirements associated with bedside ROP diagnosis increased this disparity. Telemedicine has potential to alleviate the time commitment for ophthalmologists who manage ROP.

Cost utility analysis of screening and laser treatment of retinopathy of prematurity.

Dunbar J, Hsu V, Christensen M, Black B, Williams P, Beauchamp G.

J AAPOS 2009 Apr; 13(2):86-190.

Long term study of 515 infants screened and treated for ROP from March 2004 and January 2005 from 3 NICUs in Louisiana and Texas. Cost model was determined by Current Procedural Terminology and cost of the study was funded by CMS. Ten year visual acuities post- laser were obtained compared to 10 yr visual acuities in untreated babies from the CRYO-ROP study. It required 3.4 exams per infant and 11.2% had laser for ROP. Mean visual acuity was 20/40 for laser treated eyes and 20/100 for untreated eyes. The cost-effectiveness of screening and laser treatment is \$650/quality-adjusted life years. The study clearly demonstrates that screening and treated for ROP is an extremely cost-effective intervention.

A neuroectodermal hypothesis of the cause and relationship of myopia in retinopathy of prematurity.

Beri S, Malhotra M, Dhawan A, Garg R et al.

JPOS 2009 May-Jun; 46:146-150.

A prospective study of 42 preterm infants screened for ROP was undertaken to determine the effect of presence of ROP on the development of myopia. Examination included fundus examination, cycloplegic refraction, and biometric measurements. Preterm infants with ROP who had myopia showed increased lens thickness with similar anterior segment lengths compared to preterm infants without ROP and preterm infants with ROP who did not have myopia. Increased lens thickness in the absence of anterior segment arrest seems to be the major contributing factor for myopia in ROP. This change may be associated with altered neuroectodermal development in ROP.

Spontaneous resolution of stage 4B retinopathy of prematurity.

Nayak H, Lim MK, Watts P.

JPOS 2009 May-Jun; 46:178-179.

An unfavorable outcome occurs in 31% of cases of treated severe threshold ROP and includes retinal detachment of the posterior pole. Early treatment with laser has significantly reduced this complication. Treatment of tractional partial retinal detachments involving the posterior pole (stage 4B ROP) is surgical. Successful reattachment of stage 4B ROP with lens-sparing vitrectomy is high. The authors describe an infant who had spontaneous reattachment after stage 4B ROP.

VI. PREMATURITY

Plus disease.

Davitt BV, Wallace DK. *Surv Ophthalmol* 2009; 54:663-70. (Nov-Dec 2009).

This article reviews the current conceptualization and research involving plus disease, which is an important sign of severe retinopathy of prematurity (ROP) has gradually been refined over the past 30 years. The authors review the history of plus disease, pathologic basis of plus disease, associations between plus disease and visual/structural outcomes, recognition of plus disease, and quantification of plus disease. As a result of the ETROP randomized trial, presence of plus disease is now the primary indication for laser treatment. Since the CRYO-ROP trial first introduced a standard photograph as the minimum abnormality necessary for diagnosing plus disease, an intermediate level of vascular dilatation and tortuosity (pre-plus disease) has been defined. However, the recognition of plus disease remains problematic, primarily because of its subjective nature. As our understanding of the pathologic basis for plus disease in ROP grows, objective methods of recognizing and measuring retinal vascular abnormalities are also being designed. Semiautomated methods are being developed to quantify the vascular morphologic changes seen in plus disease and show promise for augmenting clinical judgment in the recognition and timely treatment of ROP.

Telemedicine for retinopathy of prematurity diagnosis: evaluation and challenges.

Richter GM, et al. *Surv Ophthalmol* 2009; 54:671-85. (Nov-Dec 2009)

This article reviews retinopathy of prematurity (ROP) management, discusses potential applications of telemedicine in ROP care, summarizes findings from feasibility and evaluation studies in this field, and discusses current challenges and potential barriers such as cost-effectiveness of telemedicine. Although timely diagnosis and treatment of ROP can significantly reduce the risk of severe complications, this disease remains a leading cause of childhood blindness worldwide. Limitations of current disease management strategies include extensive travel and logistical coordination requirements for ophthalmologists and neonatologists, decreasing availability of adequately trained ophthalmologists at the point of care, variability in how retinal findings are diagnosed and documented, and a growing need for ROP care worldwide. Store-and-forward telemedicine is an emerging technology by which medical data are captured for subsequent interpretation by a remote expert. This has potential to improve accessibility, quality, and cost of ROP management.

Ophthalmic artery blood flow in very-low-birth-weight preterm infants.

Soares CRS, et al. *Invest Ophthalmol Vis Sci* 2010; 51:708-11. (Feb 2010)

Purpose: To evaluate normal blood flow velocity and Doppler indices of the ophthalmic arteries from birth to hospital discharge of inborn infants at birth weights between 500 and 1500 g and gestational age ≤ 32 weeks.

Methods: A longitudinal prospective study with Doppler ultrasound was conducted in both eyes at 24 hours, 7 and 28 days, and hospital discharge for systolic and diastolic velocities, pulsatility, and resistance indices. Retinopathy of prematurity stage 2 and higher, peri-intraventricular hemorrhage grades 3 and 4, and death were excluded.

Results: The authors studied 46 very-low-birth-weight infants (92 eyes; birth weight, 1215 ± 202 g; gestational age, 30.4 ± 1.3 weeks). Both eyes had similar Doppler findings at each study interval. Systolic velocity increased significantly from birth to hospital discharge ($P = 0.001$; right eye, 17.85 ± 5.3 cm/s and 23.18 ± 4.88 cm/s; left eye, 17.78 ± 5.19 cm/s and 23.51 ± 5.63 cm/s), as did diastolic velocity ($P = 0.02$; right eye, 6.17 ± 1.13 cm/s and 6.76 ± 1.12 cm/s; left eye, 6.34 ± 1.26 cm/s and 6.9 ± 1.53 cm/s). Pulsatility and resistance indices did not change during the entire period.

Conclusions: There is a typical pattern of ophthalmic artery systolic and diastolic blood flow velocities, and pulsatility and resistance indices during the neonatal period in very-low-birth-weight infants.

Comment: This study is clinically-relevant because peri-intraventricular hemorrhage and ROP are vascular-circulatory disorders related to altered blood flow. Studies have suggested that changes in retinal blood flow are involved in ROP pathogenesis by causing abnormal growth of vessels in the immature retina. In this paper, the authors present data about normal ranges for ophthalmic artery blood flow in preterm infants without significant ROP or peri-intraventricular hemorrhage.

Risk analysis and an alternative protocol for reduction of screening for retinopathy of prematurity. Yang MB, Donovan EF. J AAPOS 2009; 13:539-545. Dec.

Frequent ROP screening exams are often necessary in preterm infants but can cause complications. This study explored whether the number of screening examinations for infants with a birth weight of 401-1250 grams can be reduced without a loss of effectiveness by applying an alternative screening protocol. This less frequent screening protocol would be applied to infants felt to be at lower risk for developing prethreshold or threshold disease based on a predictive model with prognostic variables derived mostly from CRYO-ROP. The predictive variables included birth weight, gestational age, multiple birth, inborn status, race and gender. If the risk model showed the infant was at high risk, the conventional screening protocol was administered. However, if the risk model determined the infant was at low risk, the initial ROP screening exam was performed at 3 weeks postmenstrual age or 5-6 weeks chronological age (whichever was later). Followup exams were performed every 3 weeks thereafter. The study found that the significant predictors of risk were lower birth weight, younger gestational age at birth, and non-black race. Results were based on 712 eyes of 357 patients. No delays were noted in detecting threshold ROP. There was a delay in detecting 7% of prethreshold disease. Overall 13.4% fewer screening eye examinations were performed with this revised protocol. It is not clear if this modest reduction in eye examinations is worth the increased risk of missing significant ROP

Transscleral diode laser retinal photocoagulation for the treatment of threshold retinopathy of prematurity. Paravesh MM, Modarres M, Falavarjani KG, et al. J AAPOS 2009; 13:539-545. Dec

Traditional treatments for retinopathy of prematurity include cryo- or laser ablation. Cryoablation application can stress the premature infant, causing significant ocular and hemodynamic consequences. Laser ablation can produce lenticular opacities and/or iris atrophy. This report looked at the use of transscleral diode laser application under topical anesthesia for the treatment of threshold ROP. This was a retrospectively analyzed case report of 52 patients (103 eyes). Three patients (5 eyes) also received transpupillary diode laser photocoagulation because of posterior zone 2 or zone 1 ROP. A second treatment was required in 9.6% of patients. Complications were relatively mild. Five patients experienced mild bradycardia during treatment. Ten patients sustained small conjunctival lacerations. Two patients developed mild vitreous hemorrhages, which resolved within two weeks. All patients developed transient conjunctival injection and chemosis postoperatively. Complete regression of fibrovascular proliferation occurred in 96.1% of eyes. Of these, 3 eyes developed macular dragging, so 93.2% of eyes had a favorable result. This technique was found to be a good alternative, especially in cases with a poorly dilating pupil. This technique spares the risk of cataract development. Also, because the laser spots are twice the size of those obtained with transpupillary coagulation, fewer laser spots are needed. The results of this study are compromised by a lack of a control group.

Effect of granulocyte colony-stimulating factor on the incidence of threshold retinopathy of prematurity. Bhol R, Purkiss T, Hunter S, et al. J AAPOS 2009;13:450-453. Oct.

Granulocyte colony-stimulating factor (GCSF) is used clinically to mobilize hematopoietic stem cells from bone marrow in patients with hematologic disorders. GCSF has been shown to modulate and promote angiogenesis in ischemic tissue. It increases the release of VEGF. This retrospective study looked at the incidence of threshold ROP in infants who received exogenous GCSF. Fifty patients met study criteria and they were compared to a control group of 161 patients from the Vermont Oxford Network ROP database. The 2 groups had similar demographics. In the control group, 30/161 (18.6%) progressed to threshold ROP. In the study group, 5/50 (10%) progressed to threshold ROP. This difference was not statistically significant. This study is hampered by the fact that it was underpowered and retrospective. Also, the control group of patients was not from the same

institution. However the hypothesis that patients who receive exogenous GCSF have a lower incidence of threshold ROP is worth further investigation.

Retinopathy of prematurity in extremely low birth weight infants in Malaysia. Choo MM, Martin FJ, Theam LC, et al. J AAPOS 2009;13:446-449. Oct.

This paper analyzed the incidence of ROP and risk factors for the development of ROP requiring laser treatment among two birth weight categories. This prospective study divided subjects into 2 groups: <751 grams and 751-1000 grams. 70 infants were included. Of the 22 infants with birth weights <750 grams, half (11/22) required treatment for ROP. Of the 48 infants with birth weights from 751-1000 grams, 25% (12) required treatment for ROP. Zone 1 ROP was seen exclusively in the <751 gram group. The following were found to be risk factors for an increased risk of requiring ROP treatment: <751 grams (2x); gestational age ≤ 28 weeks (1.8x); intermittent positive pressure ventilation > 1week (1.5x) and IVH (2.4x). This study can help practitioners identify babies at especially high-risk for requiring treatment for their ROP.

Effect of Early Vitreous Surgery for Aggressive Posterior Retinopathy of Prematurity (APROP) Detected by Fundus Fluorescein Angiography

Nishina S, et al.

Ophthalmology 2009;116:2442-2447 (December)

Design: Retrospective, observational case series of Eleven eyes of 7 patients with APROP that underwent early vitreous surgery.

Methods: All eyes underwent vitrectomy with lensectomy that removed the vitreous gel around the fibrovascular proliferative tissue, but not the proliferative tissue when fibrovascular proliferation and retinal detachment occurred despite retinal photocoagulation. Dye leakage from the fibrovascular tissue, dilation and tortuosity of the retinal vasculature, and shunt vessels were evaluated by fundus fluorescein angiography.

Results: Nine eyes had severe dye leakage from the fibrovascular tissue and 2 eyes had moderate leakage seen by preoperative fluorescein angiography. Severe dilation and tortuosity of the retinal vessels were detected in 10 eyes and shunt vessels in 7 eyes. Six to 12 days after successful surgery, the retina reattached and dilation and tortuosity of the retinal vessels decreased substantially. Dye leakage diminished markedly in all eyes, resolved completely in 7 eyes, and was still apparent slightly in 4. At the final examination, fibrovascular proliferation and retinal detachment did not progress in any eyes; however, 2 eyes had a dragged or folded retina. Follow-up ranged from 6 to 19 months.

Conclusions: Early vitrectomy that removes vitreous gel from around the proliferative tissue promptly reduces vascular activity and may limit progression of retinal detachment in APROP.

[Austeng D](#), [Källén KB](#), [Ewald UW](#), [Jakobsson PG](#), [Holmström GE](#). Incidence of retinopathy of prematurity in infants born before 27 weeks' gestation in Sweden. *Arch Ophthalmol.* 2009 Oct;127(10):1315-9.

This paper looks at the incidence of retinopathy of prematurity (ROP) in extremely preterm infants born before 27 weeks' gestation in Sweden during a 3-year period. It was designed as a national, prospective, population-based study was performed in Sweden from April 1, 2004, to March 31, 2007. Screening for ROP was performed beginning postnatal week 5 using the criteria from the Early Treatment for Retinopathy of Prematurity Cooperative Group.

During the study, 506 of 707 live-born infants survived until the first eye examination. Of these, 368 (72.7%) had ROP: 37.9% had mild ROP and 34.8% had severe ROP. Ninety-nine infants (19.6%) were treated. Gestational age at birth was a stronger predictor of ROP than was birth weight. A log-linear relationship between severe ROP and gestational age at birth was found in the present cohort, and the risk of ROP was reduced by 50% for each week of increase in gestational age at birth

[Austeng D](#), [Källén KB](#), [Ewald UW](#), [Wallin A](#), [Holmström GE](#). Treatment for retinopathy of prematurity in infants born before 27 weeks of gestation in Sweden. [Br J Ophthalmol](#). 2009 Nov 30. [Epub ahead of print]

This study looks at the various aspects of treatment for retinopathy of prematurity (ROP) in a Swedish population of extremely preterm infants born before 27 weeks of gestation. It was a national, prospective and population-based study performed in Sweden from April 1, 2004 to March 31, 2007. The criteria for treatment of ROP was in accordance with the recommendations of the Early Treatment for Retinopathy of Prematurity Cooperative Group. The authors found that twenty percent of the infants (99/506) were treated for ROP. The likelihood of reaching treatment criteria nearly doubled for each week of reduction in gestational age (GA) at birth. The first treatment was performed at an earlier postmenstrual age in the most immature infants. One third of the infants had more than one session of laser treatment. Only a few infants progressed to ROP Stages 4 and 5. The study suggests that there is a need for improvement of the treatment routines in ROP, both with regards to the timing and number of laser spots at the first treatment.

VII. STRABISMUS

Comparison of quality-of-life instruments in adults with strabismus.

[Hatt SR](#), [Leske DA](#), [Bradley EA](#), [Cole SR](#), [Holmes JM](#).

[Am J Ophthalmol](#). 2009 Oct;148(4):558-62. Epub 2009 Jul 1.

PURPOSE: To compare two health-related quality-of-life (HRQOL) questionnaires in adults with strabismus: the new 20-item Adult Strabismus (AS-20) questionnaire (developed specifically for Adult Strabismus) and the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25).

METHODS: Eighty-four adult patients with strabismus (median age, 53 years; range, 18 to 81 years) completed the AS-20 and VFQ-25 HRQOL questionnaires. Patients were categorized as diplopic (n = 65) or nondiplopic (n = 19). Subnormal HRQOL was defined as less than the fifth percentile for adults with no visual impairment. The proportion of patients below normal was compared overall and by diplopia status.

RESULTS: Overall, more patients scored below normal with the AS-20 than with the VFQ-25 (90% vs 29%; P < .0001). Nondiplopic patients more often were below normal on the AS-20 psychosocial subscale than on the function subscale (95% vs 42%; P = .002), whereas diplopic patients were more

often below normal on the function subscale (85% vs 68%; $P = .01$). On the psychosocial subscale, more nondiplopic than diplopic patients scored below normal (95% vs 68%; $P = .01$); on the function subscale, more diplopic than nondiplopic patients scored below normal (85% vs 42%; $P = .0005$). The VFQ-25 seemed to be insensitive to nondiplopic strabismus: no patients scored below normal on composite score and no more than 11% scored below normal on VFQ-25 subscales. Of diplopic patients, 37% scored below normal on VFQ-25 composite score. No more than 38% scored below normal on VFQ-25 subscales.

CONCLUSIONS: The new AS-20 seems to be more sensitive than the VFQ-25 for detecting reduced HRQOL in Adult Strabismus, and therefore may be a more useful tool for clinical assessment and clinical trials.

A data-driven approach to the management of accommodative esotropia.

[Reddy AK](#), [Freeman CH](#), [Paysse EA](#), [Coats DK](#).

[Am J Ophthalmol](#). 2009 Sep;148(3):466-70. Epub 2009 May 23.

PURPOSE: To determine if key findings on initial examination are predictive of ability to achieve and maintain functional alignment (residual esotropia of less than 8 prism diopters) with single-vision spectacles, bifocals, or surgery in children with accommodative esotropia.

METHODS: Institutional review of 68 consecutive accommodative esotropia patients. Exclusion criteria included previous spectacles use, other ocular pathologic features or surgery, or follow-up of less than 2 years. The main outcome measure was the ability to achieve functional alignment.

RESULTS: Mean age at the time of single-vision spectacle prescription ($P = .02$), mean cycloplegic refractive error ($P = .016$), amblyopia ($P = .02$), uncorrected near deviation ($P < .001$), and uncorrected distance deviation ($P < .001$) differed significantly between children who achieved functional alignment with single-vision lenses and those who did not. The most parsimonious prediction model revealed that presence of amblyopia ($P = .113$; odds ratio [OR], 0.138; 95% confidence interval [CI], 0.012 to 1.59), uncorrected distance deviation ($P = .004$; OR, 1.156; 95% CI, 1.049 to 1.274), mean cycloplegic refractive error ($P = .008$; OR, 0.300; 95% CI, 0.123 to 0.732), and age at time of single-vision lens prescription ($P = .007$; OR, 0.259; 95% CI, 0.097 to 0.690) were the best predictors of ability to achieve orthotropia with single-vision spectacles with a sensitivity of 94% (95% CI, 71% to 99%) and specificity of 91% (95% CI, 75% to 98%).

CONCLUSIONS: Significant differences exist in the clinical presentations of children who achieve functional orthotropia with single-vision spectacles and those who require bifocals or surgery. An evidence-based algorithm may help practitioners predict which intervention is most likely to benefit an individual child.

Test-Retest Reliability of Health-Related Quality-of-Life Questionnaires in Adults with Strabismus.

[Leske DA](#), [Hatt SR](#), [Holmes JM](#).

[Am J Ophthalmol](#). 2010 Feb 5. [Epub ahead of print]

PURPOSE: To report the test-retest variability of two health-related quality-of-life instruments: the new Adult Strabismus 20 (AS-20) and the National Eye Institute 25-item Visual Function Questionnaire (NEI VFQ-25), in adults with strabismus.

METHODS: Fifty-five adult patients in a clinical practice with stable strabismus completed the AS-20 and the NEI VFQ-25 at 2 visits, without intervening treatment. Questionnaires were completed the second time either at a subsequent office visit, immediately before surgery, or by mail. Intraclass correlation coefficients were calculated. Ninety-five percent limits of agreement and 95% confidence intervals around the 95% limits of agreement also were calculated.

RESULTS: There was excellent agreement of overall questionnaire scores for the AS-20 (intraclass correlation coefficient, 0.92) and NEI VFQ-25 (intraclass correlation coefficient, 0.94). The 95% limits of agreement for overall scores were 14.3 points (95% confidence interval, 10.9 to 17.7) for the AS-20 and 11.1 points (95% confidence interval, 8.5 to 13.8) for the NEI VFQ-25. The lower test-retest variability of the VFQ-25 seemed to be partly the result of ceiling effects with many scores at the normal end of the range.

CONCLUSIONS: The new AS-20 and the NEI VFQ-25 show excellent test-retest reliability in adults with strabismus. Change exceeding 95% limits of agreement (14 points on the AS-20 and 11 points on the VFQ-25) is indicative of real change in an individual patient. The AS-20 may be more useful than the VFQ-25 because it is less prone to ceiling effects in adults with strabismus.

Br J Ophthalmol 2009;**93**:1620-1624 doi:10.1136/bjo.2008.152975

Presenting features and early management of childhood intermittent exotropia in the UK: inception cohort study

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Abstract

Aim: To investigate factors associated with early management of intermittent exotropia (X(T)) in hospital eye departments in the UK in a prospective cohort study.

Methods: An inception cohort of 460 children aged <12 years with previously untreated X(T) (mean age 3.6 years, 55.9% girls) was recruited from 26 UK hospital children's eye clinics and orthoptic departments. Participants received a standard ophthalmic examination at recruitment and orthoptic assessment at three-monthly intervals thereafter. The influence of severity of exotropia (control measured by Newcastle Control Score (NCS), and angle of strabismus, visual acuity and stereoacuity) and age on the type of management was investigated.

Results: Within the first 12 months following recruitment, 297 (64.6%) children received no treatment, either for impaired visual acuity or for strabismus. Ninety-six (21%) children had treatment for impaired visual acuity. Eighty-nine (19.4%) received treatment for strabismus (22 of whom also received treatment for defective visual acuity); in 54 (11.7%) treatment was non-surgical and in 35

(7.6%) eye muscle surgery was performed. Children with poor (score 7–9) control of strabismus at recruitment were more likely to have surgery than children with good (score 1–3) control ($p < 0.001$). Children who had no treatment were younger (mean age 3.38 years) than those who were treated (mean 4.07 years) ($p < 0.001$). Stereoacuity and size of the angle of strabismus did not influence the type of management received.

Conclusions: X(T) can be a presenting sign of reduced visual acuity. Most children with well controlled X(T) receive no treatment within 12 months following presentation.

Comment: prospective cohort study; 64% of the cohort did not receive treatment in the 1st year of the study, a reflection of the uncertainty that exists on how to manage the intermittent exotropia condition.

Exotropic Drift and Ocular Alignment after correction for Intermittent Exotropia. Leow Po-Lin et al. JPOS Jan-Feb 2010; 47:12-16.

Forty-eight patients aged from one to ten years who underwent bilateral lateral rectus muscle recession for intermittent exotropia were retro-spectively evaluated. The follow-up period ranged from 6 months to 3 years. Although most patients had exotropic drift, this drift was greater in patients with initial esotropia (86.7%) and orthophoria (70%) compared to patients with exotropia (26.1%). There was no statistical difference between ocular alignment at one week postoperatively and final motor success. The success rate appears to be unaffected by initial ocular alignment, suggesting that deliberate initial overcorrection may be unnecessary.

Relationship between static ocular counterroll and Bielschowsky head tilt phenomenon.

Hamasaki I, et al. Invest Ophthalmol Vis Sci 2010; 51:201-6. (Jan 2010)

Purpose: This study was conducted to assess how hyperdeviation of a paretic eye during ipsilesional head tilt—the Bielschowsky head tilt phenomenon (BHP)—can be explained by decreased compensatory ocular counterrolling (OCR) due to the depressed torque of the paretic superior oblique (SO) muscle.

Methods: Thirty-three patients with clinically diagnosed SO palsy and 11 control subjects were studied. With a head-mounted video camera, static ocular counterrolling (s-OCR) was determined by measuring the inclination of a line connecting the two centroids of the characteristic iris pattern and corneal reflex. The BHP was measured with the alternate prism and cover test.

Results: The mean (SD) amplitude of s-OCR in paretic eyes based on the fit of the regression sine curve against the ipsilesional head tilt angle was significantly decreased compared with that for contralesional head tilt, 6.3 (3.5)° for ipsilesional and 11.3 (3.9)° for contralesional ($P < 0.001$), and was significantly smaller than that in normal subjects: 10.9 (2.6)° ($P < 0.001$). No significant linear relation was noted between hyperdeviation on ipsilesional head tilt and the amplitude of s-OCR in paretic eyes ($r^2 = 0.04$; $P = 0.29$). However, the differences between the hyperdeviation with ipsilesional 30° head tilt and with head-upright position correlated significantly with the amplitudes of s-OCR in paretic eyes ($r^2 = 0.19$, $P = 0.01$).

Conclusions: The absolute value of the hypertropia on ipsilesional head tilt in clinically diagnosed SO palsy does not directly assess the function of the SO muscle. The difference in hypertropia between ipsilesional head tilt and the upright position, however, may be a better indicator of SO function.

Comment: The main findings of this study are that the amplitude of s-OCR was significantly decreased in paretic eyes during ipsilesional head tilt, but normal during contralesional head tilt. Furthermore, after IO weakening surgery, there was a significant decrease in s-OCR for contralesional head tilt.

The psychosocial aspects of strabismus: correlation between the AS-20 and DAS59 quality-of-life questionnaires. Durnian JM, Owen ME, Marsh IB. J AAPOS 2009;13:477-480. Oct

The AS-20 is a twenty item adult strabismus questionnaire. The Derriford Appearance Scale 59 (DAS59) is a well-established research tool looking at overall appearance. This study attempted to determine if there was any correlation between these scales and/or correlation between the subscales of both quality-of-life (QoL) scales. The study also tried to determine if there was a difference between control groups and strabismus groups on these questionnaires. This was a prospective, noninterventonal study of adult patients undergoing strabismus surgery (n=34) and a series of random controls (n=30). The study found that both questionnaires were easy to use. There was strong agreement between the scales and the AS-20 was specific for strabismus patients. Strabismus patients were found to have significantly more psychosocial distress than those without strabismus. The problem with this study is that the strabismus patients were self-selected in that they had all chosen to undergo surgery. This may overestimate the distress that patients with strabismus feel because this is biased towards those that elected to correct their strabismus. Also both the AS-20 and the DAS59 had over 10% of patients who either did not fill out the forms correctly or chose not to fill it out at all.

Dynamic Study of the Medial and Lateral Recti Capsulopalpebral Fasciae Using Cine Mode Magnetic Resonance Imaging

Kkakizaki H, Selva D, Leibovitch I.

Ophthalmology 2010;117:388-391 (February)

Design: Observational case series of ten patients (age range 8 – 75 years; mean age, 41.1 years) diagnosed with a unilateral orbital blowout fracture (medial wall, floor, or both) and having a normal contralateral orbit.

Results: In medial gaze, the medial part of the eyelid moves posteromedially, in synchronicity with medial rectus muscle contraction, mediated by the mrCPF. The lateral part of the eyelid moves anteromedially, synchronicity with lateral rectus muscle relaxation, mediated by the lrCPF. In lateral gaze, the lateral part of the eyelid moves posterolaterally, in synchronicity with the lateral rectus muscle contraction, mediated by the lrCPF. The medial part of the eyelid moves anterolaterally, in synchronicity with medial rectus muscle relaxation, mediated by the mrCPF. These findings were demonstrated in all 10 patients.

Reviewers' Comments: This is a baseline study which may allow a better understanding of the importance of these anatomic structures and may reduce functional and cosmetic complications during common oculoplastic and strabismus surgeries. The authors never distinguished the “why” or the difference in the eyes with a blowout fractures.

Congenital monocular elevation deficiency.

Kim JH, Hwang JM

Ophthalmology 2009 Mar; 116(3):580-584.

Objective: The pathophysiology of monocular elevation deficiency is poorly understood. The goal of this study was determine the appearance of the extraocular muscles and the oculomotor nerve.

Design: Observational case series of 6 patients with monocular elevation deficiency.

Main Outcome Measures: Ocular alignment and movement, Extraocular muscles, and the oculomotor nerve on MRI.

Results: One out of 6 patients with monocular elevation deficiency showed focal thickening of the inferior rectus muscle near the orbital apex. The 5 remaining patients showed normal extraocular muscles and the oculomotor nerves on MRI.

Conclusions: Focal thickening of the inferior rectus muscle may partially explain the cause of restricted gaze. In addition, the finding of normal oculomotor nerves might support an underlying deficit in the unilateral center for upgaze as the etiology of monocular elevation deficiency.

Reviewer Comments: Weak conclusions.

Splitting of the extraocular horizontal rectus muscle in congenital cranial dysinnervation disorders.

Okanobu H, Kono R, Miyake K, Ohtsuki H.

Am J Ophthalmol 2009 Mar; 147(3):550-556.e1.

Purpose: To analyze the horizontal rectus extraocular muscles (EOMs) by orbital magnetic resonance imaging (MRI) in patients with congenital cranial dysinnervation disorders that arises from abnormal development of cranial nerve nuclei or their axonal connections.

Methods: The morphology of the horizontal rectus EOMs was analyzed in orbital MRI on 4 patients with congenital oculomotor palsy, 26 with congenital superior oblique palsy, and five with Duane syndrome. Orbital imaging was performed by 1.5 tesla (T) and 3T MRI, and quasi-coronal and sagittal images perpendicular and parallel to the long axis of the orbit were obtained at slice thicknesses of 3 and 2 mm.

Results: The horizontal rectus EOMs were split in 4 of the 35 patients (11%). Splitting was observed in 2 of the five patients (40%) with Duane syndrome, one of the 26 patients (4%) with congenital superior oblique palsy, and 1 of the 4 patients (25%) with oculomotor palsy, but in none of the 6 normal subjects and 12 patients with acquired cranial nerve palsy.

Conclusions: Since splitting of the horizontal rectus EOMs was noted in patients with congenital dysinnervation disorders, including Duane syndrome, Sevel's theory that the horizontal rectus EOMs develop from the superior and inferior mesodermal complexes is considered to be reasonable.

Is the incidence of infantile esotropia declining?

A Population-Based Study from Olmsted County, Minnesota, 1965 to 1994.

Louwagie CR, Diehl NN, Greenberg AE, Mohny B G.

Arch Ophthalmol 2009 Feb; 127(2):200-203

Several reports from the United Kingdom have suggested that strabismus or strabismus surgery is occurring less frequently today than in previous years. This is a retrospective medical record review of all patients diagnosed with infantile esotropia within Olmsted County, Minnesota, from January 1, 1965, through December 31, 1994. The birth prevalence of infantile esotropia during the 30-year period was 1 in 403 live births. Although there were slightly more cases of infantile esotropia in the earlier years, the change in incidence over time was not statistically significant. The mean number of surgeries performed on each patient in this cohort was similar during the 30-year study: 1.8 for those diagnosed from 1965-1974, 1.9 for 1975-1984, and 1.6 for 1985-1994.

Effectiveness of placebo therapy for maintaining masking in a clinical trial of vergence/accommodative therapy.

Kulp M, et al, for the Convergence Insufficiency Treatment Trial (CITT) Study Group.

Invest Ophthalmol Vis Sci 2009 Jun; 50(6):2560-6.

Purpose: To evaluate the effectiveness of the Convergence Insufficiency Treatment Trial (CITT) placebo therapy program in maintaining masking of patients randomized to the office-based treatment arms, determine whether demographic variables affect masking, and determine whether perception of assigned treatment group was associated with treatment outcome or adherence to treatment.

Methods: Patients ($n = 221$, ages, 9–17 years) were randomized to one of four treatment groups, two of which were office-based and masked to treatment ($n = 114$). The placebo therapy program was designed to appear to be real vergence/accommodative therapy, without stimulating vergence, accommodation, or fine saccades (beyond levels of daily visual activities). After treatment, patients in

the office-based groups were asked whether they thought they had received real or placebo therapy and how confident they were in their answers.

Results: Ninety-three percent of patients assigned to real therapy and 85% assigned to placebo therapy thought they were in the real therapy group ($P = 0.17$). No significant differences were found between the two groups in adherence to the therapy ($P \geq 0.22$ for all comparisons). The percentage of patients who thought they were assigned to real therapy did not differ by age, sex, race, or ethnicity ($P > 0.30$ for all comparisons). No association was found between patients' perception of group assignment and symptoms or signs at outcome ($P \geq 0.38$ for all comparisons).

Conclusions: The CITT placebo therapy program was effective in maintaining patient masking in this study and therefore may have potential for use in future clinical trials using vergence/accommodative therapy. Masking was not affected by demographic variables. Perception of group assignment was not related to symptoms or signs at outcome.

Comment: Background about this paper is that the CITT study compared the effectiveness of home-based pencil push-ups, home-based computer vergence/accommodative therapy and pencil push-ups, office-based vergence/accommodative therapy with home reinforcement, and office-based placebo therapy as treatments for symptomatic CI. This study showed that 12 weeks of office-based vergence/accommodative therapy resulted in a significantly greater proportion of children being classified as having a successful or improved outcome in symptoms and clinical signs of convergence ability (near point of convergence and positive fusional vergence) when compared with home-based pencil push-ups, home-based computer vergence/accommodative therapy and pencil push-ups, and office-based placebo therapy (73% vs. 43%, 33%, and 35%, respectively). Although the placebo therapy arm was found to be effective in maintaining masking in the CITT pilot, its effectiveness in maintaining masking in the full-scale CITT has not been thoroughly investigated.

Intervention for intermittent distance exotropia with overcorrecting minus lenses.

Rowe FJ, Noonan CP, Freeman G, DeBell J.

Eye 2009 Feb; 23(2):320–325.

The aim of this prospective nonrandomised longitudinal cohort study is to evaluate the use of overcorrecting minus lenses as a primary treatment option for intermittent distance exotropia (IDEX) and determine ocular alignment status after 5 years from commencement of the study. Treatment was begun with the minimum minus lens required to achieve control of the manifest deviation. The strength of lenses was reduced over time while monitoring the results. Thirteen female and eight male patients were recruited with a mean age of 5 years at the start of treatment. There was a significant reduction in the angle of the deviation after treatment. Overcorrecting lenses did not appear to induce myopia. Twenty-four per cent of the patients had a successful outcome, 28% had a good outcome, and 33% required surgery at a later date. **Conclusions:** Fifty-two per cent of the patients achieved a successful or good outcome with overcorrecting minus lenses alone, and this was maintained for at least 1 year follow-up. The authors recommend overcorrecting minus lenses as a primary treatment option for IDEX with the knowledge that surgery, if subsequently required, is safely delayed to an older age without prior loss of binocular vision.

Aetiology and outcomes of adult superior oblique palsies: a modern series.

Mollan SP, Edwards JH, Price A, Abbott J, Burdon MA.

Eye 2009 Mar; 23(3):640–644.

A retrospective consecutive case series of 150 persons diagnosed with SOP between 1 January 1999 and 31 May 2005 at a neuro-ophthalmology centre in the West Midlands, the United Kingdom. The authors identified 133 unilateral isolated, 7 unilateral associated with other cranial nerve involvement, and 10 bilateral cases of SOP. Eighty-six were acquired, 51 congenital, and 13 undetermined. Of the unilateral isolated cases, 38.3% were considered to be congenital, 29.3% followed trauma, 23.3% were presumed to be vasculopathic in origin, and no cause could be established in 7.5%. All

presumed microvascular-associated palsies resolved within 6 months of presentation. Unilateral SOPs associated with other cranial nerve palsies were commonly caused by trauma (71.4%), followed by tumor and undetermined causes (both 14.3%). Trauma was the most frequent cause of bilateral SOP (50%), followed by tumors and undetermined causes (both 20%), with congenital causes being uncommon (10%).

Conclusions: Neuroimaging did not change the management for the vast majority of cases and should be prompted by atypical presentations.

Spontaneous resolution in patients with congenital Brown Syndrome.

Dawson E, Barry J, Lee John.

J AAPOS 2009 Apr; 13(2):116-118.

Retrospective review of pts from 1992-2002 with a diagnosis of constant congenital Brown syndrome presenting to Moorfields Eye hospital. A total of 32 pts were identified, females more than males, right eye more frequently than left and 3 patients had bilateral Brown. Ninety one percent had stereo vision and 19 had AHP. The authors found that 75% of patients had spontaneous resolution of symptoms ranging from 6 months to 9.5 yrs. Five patients required surgery.

The influence of head tilt on ocular torsion in patients with superior oblique palsy.

Kushner B.

J AAPOS 2009 Apr; 13(2):132-135.

Prospective study to determine the influence of head tilt on the hypertropia and the torsional component of superior oblique palsy. Twenty patients with unilateral superior oblique palsy had their hypertropia and torsion measured in both forced head-erect and preferred contralateral head tilt position. There was a 62% reduction of hypertropia in preferred head tilt compared to forced head-erect, but only 3% improvement in excyclotorsion. The purpose of the contralateral head tilt is reduce the vertical component of SO palsy, not the torsional component.

VIII. STRABISMUS SURGERY

Surgical procedure for correcting globe dislocation in highly myopic strabismus.

[Yamauchi M](#), [Yokoyama T](#), [Shiraki K](#).

[Am J Ophthalmol](#). 2010 Feb;149(2):341-346.e2. Epub 2009 Nov 24.

PURPOSE: To design a surgical procedure for correcting globe dislocation in strabismus in high myopia (highly myopic strabismus).

METHODS: We examined 36 eyes of 21 patients with highly myopic strabismus and 27 eyes of 27 healthy volunteers as controls at Osaka City General Hospital between 2000 and 2006. Anatomic relationships between the muscle cone and globe were analyzed using magnetic resonance imaging. Ranges of globe movement and angles of ocular deviation were measured quantitatively as angles of maximum abduction and sursumduction and angles of ocular deviation, respectively, using the Goldmann perimeter and alternate prism cover tests. A surgical procedure involving muscle union of the superior rectus and lateral rectus muscles was performed in 23 eyes of 14 patients to restore the dislocated globe back to the muscle cone.

RESULTS: After surgery, the angle of dislocation of the globe, defined as the angle formed by a line connecting the area centroid of the superior rectus muscle and the globe and a line connecting area centroid of the lateral rectus muscle and globe against the supertemporal wall of the orbit, was significantly decreased ($P < .001$), and angles of maximum abduction and sursumduction and the angle of ocular deviation improved significantly ($P < .001$).

CONCLUSIONS: This surgical procedure to restore the dislocated globe back into the muscle cone by uniting muscle bellies of the superior rectus and lateral rectus muscles is effective for highly myopic strabismus.

Effect of slow-releasing all-trans-retinoic acid in bioabsorbable polymer on delayed adjustable strabismus surgery in a rabbit model.

[Lee MJ](#), [Jin SE](#), [Kim CK](#), [Choung HK](#), [Kim HJ](#), [Hwang JM](#).

[Am J Ophthalmol](#). 2009 Oct;148(4):566-72. Epub 2009 Jul 9.

PURPOSE: To determine the usefulness of slow-releasing all-trans-retinoic acid (ATRA) in polytetrafluoroethylene (PTFE)/poly(lactide-co-glycolide) (PLGA) for delayed adjustable strabismus surgery.

METHODS: A prospective, masked-observer, controlled study was performed in 25 rabbits. Fifty rabbit eyes were divided randomly into three groups. After a recession of the superior rectus muscle, a PTFE/PLGA laminate containing ATRA, PTFE alone, or balanced salt solution was applied beneath and over the superior rectus muscle in the PTFE/PLGA/all-trans-retinoic acid group (ATRA group), the polytetrafluoroethylene group (PTFE group), and the control group, respectively. Delayed adjustment was performed once on each superior rectus muscle at 3 or 5 weeks after surgery by a masked observer.

RESULTS: In the control group, adjustment was possible in 2 of 5 eyes at 3 weeks after surgery and impossible in any eye at 5 weeks after surgery. In the PTFE and ATRA groups, adjustment was possible in all 10 eyes at 3 and 5 weeks after surgery. On comparing adjustability, a significant difference was observed between the PTFE group and the control group or between the ATRA group and the control group 5 weeks after surgery ($P = .0003$ and $P = .0003$, respectively). A significant difference was observed between the ATRA group and the control group in terms of adhesion between superior rectus muscles and sclerae at 5 weeks after surgery ($P = .006$).

CONCLUSIONS: Slow-releasing ATRA in PTFE/PLGA was found to reduce adhesion and to allow delayed adjustment in most eyes for up to 5 weeks after surgery.

Bilateral vs unilateral medial rectus resection for recurrent exotropia after bilateral lateral rectus recession.

[Yang HK](#), [Hwang JM](#).

[Am J Ophthalmol](#). 2009 Sep;148(3):459-65. Epub 2009 Jul 9.

PURPOSE: To compare outcomes after bilateral and unilateral medial rectus (BMR/UMR) resection for the treatment of recurrent exotropia after bilateral lateral rectus (BLR) muscle recession.

METHODS: Forty-four patients underwent BMR resection (BMR group) or UMR resection (UMR group) for recurrent constant exotropia of 25 prism diopters (PD) or less at distance after undergoing BLR muscle recession for intermittent exotropia in an institutional setting. The main outcome

measures were final success rates and improvement in stereopsis and were compared between the groups. The risk factors for recurrence after reoperation also were evaluated. Secondary outcome measures were evaluated based on the drift of ocular alignment toward exodeviation after surgery (exodrift) from postoperative day 1.

RESULTS: Thirteen (54%) of 24 patients in the BMR group had successful outcomes, 10 (42%) had overcorrection, and 1 (4%) had undercorrection at the last follow-up examination. Sixteen (80%) of 20 patients in the UMR group had successful outcomes, 2 (10%) had undercorrection, and 2 (10%) had overcorrection. The incidence of successful outcomes at the last follow-up examination and the incidence of recurrence were not significantly different between the 2 groups, whereas the incidence of overcorrection was significantly higher in the BMR group ($P = .017$).

CONCLUSIONS: Large UMR resection is a safe and effective procedure in the treatment of small to moderate angles of recurrent exotropia after BLR muscle recession. The overcorrection rate was significantly lower after UMR resection than it was after BMR resection.

Effect of 10-mm superior oblique posterior tenectomy combined with frenulum dissection in A-pattern with superior oblique overaction.

[Heo H](#), [Lee KH](#), [Ahn JK](#), [Kim DH](#), [Park YG](#), [Park SW](#)

[Am J Ophthalmol](#). 2009 Nov;148(5):794-9. Epub 2009 Aug 7.

PURPOSE: To evaluate the effect of 10-mm tenectomy of the posterior fibers of the superior oblique (SO) tendon combined with dissection of the frenulum for correction of A-pattern deviation and vertical deviation with SO overaction.

METHODS: Seventy-five patients with A-pattern strabismus associated with SO overaction who underwent surgery between March 1, 2004 and August 31, 2007. Retrospective analysis of A-pattern strabismus patients with SO overaction who underwent unilateral or bilateral 10-mm SO posterior tenectomy combined with frenulum dissection and who underwent at least 12 months of follow-up.

RESULTS: The mean preoperative amount of A-pattern for all patients was 21.20 +/- 7.25 prism diopters (PD), with a mean postoperative collapse of 17.63 +/- 5.33 PD (range, 10 to 30 PD), which was statistically significant ($P = .001$). After surgery, the mean A-pattern correction was 22.12 +/- 6.30 PD in the group that underwent bilateral posterior tenectomy and 13.33 +/- 5.20 PD in the group that underwent unilateral posterior tenectomy. The mean degree of preoperative vertical deviation in the group that underwent unilateral posterior tenectomy was 11.50 +/- 3.96 PD, and the mean correction was 9.21 +/- 4.22 PD ($P = .01$). There were no surgical complications, except in 5 patients, who manifested mild inferior oblique overaction.

CONCLUSIONS: We believe that 10-mm SO posterior tenectomy combined with frenulum dissection effectively collapses A-pattern deviation of less than 25 PD with mild to moderate SO overaction and reduces associated vertical deviation of 10 PD.

Br J Ophthalmol 2009;**93**:1616-1619 doi:10.1136/bjo.2008.156687

Residual torticollis in patients after strabismus surgery for congenital superior oblique palsy

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6. D S C Lam¹

Abstract

Aim: To study postoperative residual vertical deviation and abnormal head posture (AHP) after surgical treatment for congenital superior oblique palsy (SOP).

Method: Children with both SOP and AHP who underwent extraocular muscle surgery for correction of AHP were recruited. The patients received complete ophthalmic and orthopaedic examinations. Residual AHP was classified according to severity of face turn, head tilt and chin elevation.

Results: Thirty-two children with mean age at operation of 82.6 months were recruited, with mean follow-up of 37.9 months. Of these children, 65.6% had a postoperative vertical deviation of less than three prism dioptres. In addition, 34.4% patients had resolved (0°), 34.4% had mild (1° – 10°), and 31.3% had significant residual torticollis ($>10^\circ$). Of the patients with significant residual torticollis, 33.3% had ocular causes. The mean age at operation for the patients with residual torticollis (95.9 months) was older than those without torticollis (79.9 months) ($p = 0.018$). Residual torticollis was found to be related to sternocleidomastoid muscle tightness ($p = 0.013$).

Conclusion: The success rate for eliminating significant AHP after strabismus surgery for patients with congenital SOP was 68.8%. Early surgery was associated with a better outcome. Association was also found between sternocleidomastoid tightness and AHP. A multidisciplinary approach is recommended in the management of torticollis as ophthalmic and orthopaedic comorbidities can coexist.

Comment: Nice article reporting their results in a series of 32 patients with SOP. Anomalous head position was only relieved in 68% in this series. Residual anomalous head position was associated with tight sternocleidomastoid muscle, therefore these pts should have orthopedic consultation prior to further ophthalmic intervention.

Intraoperative adjustable suture surgery for excyclotorsion: a modification of the Harada-Ito procedure. Ameri A et al. JPOS Nov-Dec 2009; 46: 368-371.

Tucking of the anterior one-third of the superior oblique tendon was performed with nonabsorbable suture in two patients. The amount of tuck was adjusted until the fovea was at the level of the superior one-third of the disc through indirect ophthalmoscopy. In the patient with local anesthesia, a double Maddox rod test was used to evaluate subjective cyclotorsion intraoperatively. No regression was noted in 18 months of follow-up. This introduces a new therapeutic option for patients with BSO paresis and symptomatic excyclotorsion without vertical deviation in primary position.

Evaluation of Refraction in a Statistically Significant Sample: changes according to age and strabismus. Chiesi C et al. JPOS Sept-Oct 2009; 46:266-272.

A population-based sample of 12,534 subjects 6 months to 20 years of age were examined between 2004 and 2006. Patients were divided into those with orthophoria and those with strabismus and the latter group divided into esodeviation and exodeviation. Patients with esodeviation tend to share a higher initial degree of hyperopia than the general population. The myopic shift in these patients occurring in later years appears to be lower than the general population. Patients with exodeviation have similar refractive errors to those with orthophoria. Astigmatism often plays an important role in anisometropic amblyopia.

Detailed Magnetic Resonance Imaging findings of the Oculomotor nerves in Duane's Retraction Syndrome. Yonghong J et al. JPOS Sept-Oct 2009; 46: 278-285.

Eleven consecutive cases of DRS underwent MRI neuroimaging of the brain, brain stem, cavernous sinus, and orbits. This included five patients with type I, one patient with type II, four patients with type III, and one patient with inverse DRS. In ten patients, the abducens nerve was absent or showed hypoplasia in the brain stem, cavernous sinus, and orbit. The inferior division of the oculomotor nerve was traced to enter the lateral rectus muscle in nine patients. The aberrant branches likely correspond to the abnormal eye movement seen in patients with this disorder.

Duration of conjunctival redness following adult strabismus surgery. Escardo-Paton JA and Harrad RA. J AAPOS 2009;13:583-586.Dec

This study looked at the duration of post-strabismus surgery conjunctival injection, and whether or not prior surgery affects this duration. The method involved a postoperative questionnaire, given to adult strabismus patients. Limbal incisions were used. Only 53 of the 101 patients who received the questionnaire responded. Twenty-eight of the 53 patients had undergone prior strabismus surgery. The median duration of conjunctival injection was 9.5 weeks for 'virgin' muscles or recessed muscles and 10 weeks for nonadjustable muscles. Reoperations and adjustable suture procedures produced a reported 11 week postoperative period of injection. There were no statistically significant differences between these groups. These durations of conjunctival injection seem longer than what would be expected and the data culled from a questionnaire which had just over a 50% response rate must be questioned.

Precaruncular approach for medial orbital wall periosteal anchoring of the globe in oculomotor nerve palsy. Saxena R, Sinha A, Sharma P, et al. J AAPOS 2009;13:578-582.Dec

Globe fixation procedures are an option in patients with a third nerve palsy and minimal or absent medial rectus muscle action. Patients received a supramaximal recession of the lateral rectus muscle combined with periosteal anchoring of the globe to the medial orbital wall via a conjunctival incision nasal to the caruncle. Nonabsorbable sutures were passed through exposed periosteum and then anchored to the sclera on either end of the medial rectus muscle. Fourteen consecutive patients with isolated complete third nerve palsies (8 congenital and 6 post-trauma) were included. The mean preoperative deviation was 87.7 PD. The mean postoperative deviation was 10.7 PD (30 XT- 8 ET) over a mean followup period of 8.9 months. The advantages of this technique are avoidance of a skin incision or extensive dissection, and a reduced risk of globe injury or injury to the medial canthal tendon.

Effects of vertical offsets of the horizontal rectus muscles in V-pattern exotropia without oblique dysfunction. Oya Y, Yagasaki T, Maeda M, et al. J AAPOS 2009;13:575-577.Dec

The results of this study are compromised, by the small number of patients, and the multiple surgery types performed. A retrospective database analysis of strabismus surgery from 2002-2007 identified 11 patients who had a V-pattern exotropia and received full tendon offsets. Choice of surgery was not uniform. Three months postoperatively, the V-pattern decreased from 22 prism diopters preoperatively to 3.5 PD. The amount of correction effect was positively correlated with the size of the preoperative deviation

Predictive factors of surgical outcome in oculomotor nerve palsy. Cabrejas L, Hurtado-Cena FJ, Tejedor J. J AAPOS 2009;13:481-484.Oct

Surgical success in patients with 3rd nerve palsies is challenging. This review of patients who underwent eye muscle surgery for 3rd nerve palsies was undertaken to investigate potential predictive factors of surgical outcome. A retrospective chart review of patients from 1987-2007 was undertaken. Postoperative motor success was the main motor outcome. Twenty-two patients were identified (11 complete 3rd nerve palsies, 11 partial 3rd nerve palsies). Motor success in primary position was obtained in 14/22 and diplopia was reduced from 40% to 9% of patients. The main predictors of outcome success were: timing between onset of the 3rd nerve palsy and surgery; the size of the horizontal deviation. There was a trend towards partial 3rd nerve palsies faring better, but this did not reach statistical significance. The authors hypothesize that the longer duration of the condition lowering success rates might be due to secondary muscle overactions which could reduce the predictability of surgical results.

Results of extraocular muscle surgery for superior oblique myokymia. Agarwal S, Kushner BJ. J AAPOS 2009;13:472-476.Oct

Superior oblique myokymia can produce attacks of oscillopsia, often with associated vertical or torsional diplopia. The authors report their experience with surgery in patients who failed medical therapies. Surgery consisted of a nasal tenectomy of the ipsilateral superior oblique tendon and a myectomy of the ipsilateral inferior oblique muscle. Fourteen patients received this operation and were followed over a mean period of 4.1 years (0.5-10). All patients had complete elimination of their oscillopsia and were orthophoric in primary position postoperatively. Two of the 12 displayed a continuing hypertropia in 1' position with associated diplopia. Five of the 12 patients had diplopia in downgaze. This study showed that surgery can relieve the oscillopsia associated with SOM, but patients and their surgeons need to be aware of the postoperative risks of diplopia, especially in downgaze.

Nihalani BR, Whitman MC, Salgado CM, Loudon SE, Hunter DG. Short tag noose technique for optional and late suture adjustment in strabismus surgery. Arch Ophthalmol. 2009 Dec;127(12):1584-90.

This manuscript presents and evaluates a new technique that allows the second-stage suture adjustment in strabismus surgery to be skipped or delayed if the immediate postoperative alignment is satisfactory.

The technique described is the "short tag noose" technique and it replaces long sutures with short tags that can be left under the conjunctiva after adjustment. This was a retrospective study looking at the medical records of all patients treated by a single surgeon with this approach between January 1, 2005, and December 31, 2008. The patients were evaluated for a success rate of 10 prism diopters [PD] horizontal and 6 PD vertical, reoperation rate, and complications.

Of 120 procedures reviewed, 27 (22.5%) were performed in children; 97 procedures (80.8%) were performed in patients with complex strabismus. Mean follow-up of all patients was 6 months. The success rate was 81.0% for horizontal strabismus and 70.7% for vertical strabismus at 2 months. The reoperation rate was 10.0% for horizontal strabismus and 19.0% for vertical strabismus. The noose slipped in 1 patient (0.8%) and was corrected by readjustment on day 4. Two patients (1.7%) required in-office excision of cysts or granulomas.

The authors conclude that the short tag noose technique simplifies the logistics of suture adjustment and avoids the need for sedation in children who do not require adjustment. It also provides the ability to defer adjustment for days after surgery.

Role of the equator in the early overcorrection of intermittent exotropia.

Cho YA, Kim SH.

J Pediatr Ophthalmol Strabismus 2009 Jan-Feb; 46(1):30-34.

Ninety-two patients with intermittent exotropia were included, all of whom underwent recessions of both lateral rectus muscles (5-8 mm). Overcorrection was defined as esophoria in excess of five prism diopters, and all patients were followed for at least three months after surgery. Overcorrection was detected in 15 patients (16.3%). Overcorrection of intermittent exotropia did not appear to be related to the location of new insertions of the lateral rectus muscles of up to 8mm of recession. This may indicate the redistributing of relatively more innervational inputs to the medial rectus muscle after lateral rectus recession in consecutive esotropia.

Pain relief for strabismus surgery in children: a randomised controlled study of the use of preoperative sub-Tenon levobupivacaine.

Morris B, Watts P, Zatman T, Absolom M et al.

Br J Ophthalmol 2009 Mar; 93(3):329-32.

Aims: To compare the postoperative pain scores in children undergoing squint surgery administered with preoperative sub-Tenon levobupivacaine for postoperative pain relief versus controls.

Methods: A prospective randomised controlled clinical trial was performed. Children aged 1–16 years undergoing strabismus surgery were recruited. The test group received sub-Tenon levobupivacaine preoperatively and topical anaesthetic eye-drops at the end of the procedure. The control group received topical anaesthetic eye-drops only at the end of surgery. Pain scores were recorded at 30 min, 2, 4, 6 and 24 h postoperatively using the Wong–Baker Pain or FLACC (face, legs, arms, cry, consolability) assessment score. The principal outcome measured was the pain score at each time interval for both groups.

Results: 27 patients received sub-Tenon levobupivacaine, and there were 27 age- and sex-matched controls. The pain score in the test group was not lower than that of the control group ($p=0.22$ at 30 min, $p=0.37$ at 2 h).

Conclusions: Sub-Tenon levobupivacaine, which is widely used for postoperative pain relief in paediatric strabismus surgery, was not effective when administered preoperatively in this cohort.

Note: This article is interesting as it is the first to look at pre-operative levobupivacaine administration to control post-operative pain. Limitations are it is a small study and has a wide age range. Also placebo was not used in control group.

Drift of ocular alignment following strabismus surgery. Part 1: using fixed scleral sutures.

Pukrushpan P, Isenberg SJ.

Br J Ophthalmol 2009 Apr; 93(4):439-42.

Aims: To evaluate the postoperative alignment drift following traditional strabismus surgery utilizing direct attachment of muscle to sclera.

Methods: The ocular alignment drift (change from the first postoperative week) of 106 patients who underwent scleral fixation strabismus surgery at age 0.5 to 35 years with 5 years' maximal follow-up was analysed.

Results: There was a mean undercorrection drift of 4.6 (SD 8.9) prism dioptres (PD) at distance fixation ($p=0.025$) and 3.4 (7.6) PD at near ($p=0.053$) for all subjects, and 11.3 (8.6) PD distance ($p=0.008$) and 10.6 (6.0) PD near ($p=0.016$) for exotropic patients. Recession surgery produced an

undercorrection drift of 5.3 (8.8) PD ($p=0.021$) at distance fixation. Esotropic patients and those undergoing unilateral recession/resection surgery had no significant drift. Patients overcorrected at the 1-week postoperative visit later developed an undercorrection drift at distance (10.3) (7.9) PD, $p=0.002$) and near fixation (5.5 (9.2) PD at 36 months, $p=0.041$), while undercorrected patients showed no significant drift and largely stayed undercorrected.

Conclusions: Fixed scleral-suture strabismus surgery generally produces a postoperative undercorrection drift, especially following recession surgery, exotropia or overcorrection at the first postoperative week.

Note: Limitation of this study is that it was retrospective. It also lumped all strabismus together in the analysis. Would have been better to analyze each type individually. No new news.

Drift of ocular alignment following strabismus surgery. Part 2: using adjustable sutures.

Isenberg SJ, Abdarbashi P.

Br J Ophthalmol 2009 Apr; 93(4):443-7.

Aim: To measure the drift of ocular alignment following strabismus surgery utilising adjustable sutures.

Methods: 106 patients, aged 12 to 84 years, underwent adjustable suture strabismus surgery with a follow-up of 0.5–4 years (mean 24.3 months).

Results: For all subjects measured on distant fixation, there was a mean undercorrection drift of 8.3 (SD 2.3) prism dioptres (PD) from week 1 to 48 months postoperatively ($p=0.005$). Patients with exotropia demonstrated an undercorrection drift on distant fixation from week 1 to 2 years (mean 10.1 (3.5) PD, $p=0.023$). Patients who underwent recession surgery developed a mean 9.1 (3.3) PD undercorrection drift from week 1 to 3 years ($p=0.031$). Patients who had unilateral recession and resection surgery showed a mean 6.8 (2.9) PD undercorrection drift from week 1 to 18 months ($p=0.049$). Patients with constant or intermittent postoperative stereopsis had a statistically significant undercorrection drift ((5.1 PD) at certain postoperative periods ($p,0.042$), while those without stereopsis had no significant drift.

Conclusions: Most patients developed a general drift toward undercorrection, especially following recession or recession with resection surgery and those with exotropia. Surgeons should consider creating a mild overcorrection at the time of suture adjustment, while avoiding long-term diplopia.

Note: Limitation is that it is retrospective. No new news except adjustable suture technique may be a little better than scleral fixation.

Minimally invasive strabismus surgery (MISS) for rectus muscle transpositions.

Mojon DS.

Br J Ophthalmol 2009 May; 93(5):747-53.

Aims: To present two similar, minimally invasive strabismus surgery (MISS) techniques for rectus muscle transpositions.

Methods: The technique and results of 10 consecutive MISS muscle transpositions performed in eight patients by applying only small radial cuts between the insertion of the weak rectus muscle and the adjacent rectus muscles are presented.

Results: In nine eyes a minimal and in one eye a moderate lid and conjunctival swelling could be seen on the first postoperative day. The preoperative deviation at distance of 41.7 (SD 21.6) pdpt decreased to 2.3 (4.4) pdpt at 6 months ($p,0.01$). At 6 months, only one patient had an abnormal head posture at distance, and no patient experienced diplopia.

Conclusions: This study demonstrates that small incision, minimal dissection transposition techniques are feasible and effective in improving ocular alignment in patients with paralytic strabismus.

Note: Interesting new technique. Further study required.

Reversal of unilateral medial rectus recession and lateral rectus resection for the correction of consecutive exotropia.

Chatzistefanou KI, Droutsas KD, Chimonidou E.

Br J Ophthalmol 2009 May; 93(5):742-6.

Background/aims: To evaluate the effectiveness and dose–effect relationship of unilateral medial rectus advancement to the original insertion and lateral rectus recession in the surgical management of consecutive exotropia.

Patients/methods: The charts of 62 patients operated on for consecutive exotropia in a single-surgeon paediatric ophthalmology practice with a minimum follow-up time of 6 weeks were reviewed.

Results: Fifty-two patients were managed with unilateral surgery involving medial rectus advancement and lateral rectus recession. The medial rectus was advanced to the original insertion, and the lateral rectus was recessed by the amount of millimetres it had originally been resected for patients with precise records on previous surgery (within one millimetre of the above). The mean age at surgery for exotropia was 12.86 years. The mean postoperative follow-up time was 2.5 years. The mean preoperative distance exodeviation was 33.4 prism dioptres (PD), and the mean reduction in the angle of strabismus was 33.5 PD. A successful surgical outcome, defined as ocular alignment within 10 PD of orthophoria, was obtained in 41 patients (78.8%) at final follow-up. The mean dose–effect relationship between the reduction in the angle of deviation and the sum of millimetres of the reoperation was 2.9 PD/mm. It varied widely among patients and was strongly correlated with the amount of preoperative exodeviation, that is the patients tended to respond more per millimetre of surgical intervention the greater the preoperative exodeviation.

Conclusions: The standard reversal of unilateral medial rectus recession and lateral rectus resection is a simple and effective means for correcting secondary exotropia. The dose–effect relationship varied widely among patients and tended to correlate with the amount of preoperative exodeviation.

A randomised comparison of bilateral recession versus unilateral recession-resection as surgery for infantile esotropia.

Polling JR, Eijkemans MJ, Esser J, et al.

Br J Ophthalmol 2009 Jul; 93(7):954-7.

Aim: Infantile esotropia, a common form of strabismus, is treated either by bilateral recession (BR) or by unilateral recession–resection (RR). Differences in degree of alignment achieved by these two procedures have not previously been examined in a randomized controlled trial.

Methods: Controlled, randomised multicentre trial.

Setting: 12 university clinics.

Participants and intervention: 124 patients were randomly assigned to either BR or RR. Standardised protocol prescribed that the total relocation of the muscles, in millimetres, was calculated by dividing the preoperative latent angle of strabismus at distance, in degrees, by 1.6.

Main outcome measure: Alignment assessed as the variation of the postoperative angle of strabismus during alternating cover.

Results: The mean preoperative latent angle of strabismus at distance fixation was +17.2u (SD 4.4) for BR and +17.5u (4.0) for RR. The mean postoperative angle of strabismus at distance was +2.3u (5.1) for BR and +2.9u (3.5) for RR ($p=0.46$ for reduction in the angle and $p=0.22$ for the within-group variation). The mean reduction in the angle of strabismus was 1.41u (0.45) per millimetre of muscle relocation for RR and 1.47 (0.50) for BR ($p=0.50$ for reduction in the angle). Alignment was associated with postoperative binocular vision ($p=0.001$) in both groups.

Conclusions: No statistically significant difference was found between BR and RR as surgery for infantile esotropia.

The occurrence of monofixational exotropia after exotropia surgery.

Kushner BJ.

Am J Ophthalmol 2009 Jun; 147(6):1082-5, 1085.e1.

Purpose: To study patients with monofixation and presumed intermittent exotropia with monofixation with the specific intent of determining if they should be categorized as separate diagnostic entity than intermittent exotropes with bifoveal fusion.

Methods: A single-center institutional practice study of 215 patients from 2 separate consecutive randomized series undergoing surgery for presumed intermittent exotropia. Outcome measure was the presence of monofixation after surgery.

Results: Of 215 patients undergoing surgery for presumed intermittent exotropia, 194 were over 3 years of age at surgery, had bifoveal fusion, and did not have a preoperative manifest microtropia. None of them developed the monofixation syndrome after surgery. An additional 14 patients who had been previously excluded from those studies because they were too young for sensory testing were included in this study. Seven of them (50%) had the monofixation syndrome after surgery. A different 7 patients who had also been excluded from those prior studies because they had a constant microtropia prior to surgery which would build on alternate cover testing were also included in this study. All 7 had the monofixation syndrome after surgery.

Conclusions: The presence of the monofixation syndrome after surgery for presumed intermittent exotropia most likely reflects the fact that it was present preoperatively. Many of these patients manifest a constant microtropia preoperatively and hence should not be called intermittent exotropes. The term monofixational exotropia is more appropriately descriptive.

Effect of slow-releasing all-trans-retinoic acid in bioabsorbable polymer on delayed adjustable strabismus surgery in a rabbit model.

Lee MJ, Jin SE, Kim CK, Choung HK, Kim HJ, Hwang JM.

Am J Ophthalmol 2009 Jul 8. [Epub ahead of print]

Purpose: To determine the usefulness of slow-releasing all-trans-retinoic acid (ATRA) in polytetrafluoroethylene (PTFE)/poly(lactide-co-glycolide) (PLGA) for delayed adjustable strabismus surgery.

Methods: A prospective, masked-observer, controlled study was performed in 25 rabbits. Fifty rabbit eyes were divided randomly into three groups. After a recession of the superior rectus muscle, a PTFE/PLGA laminate containing ATRA, PTFE alone, or balanced salt solution was applied beneath and over the superior rectus muscle in the PTFE/PLGA/all-trans-retinoic acid group (ATRA group), the polytetrafluoroethylene group (PTFE group), and the control group, respectively. Delayed adjustment was performed once on each superior rectus muscle at 3 or 5 weeks after surgery by a masked observer.

Results: In the control group, adjustment was possible in 2 of 5 eyes at 3 weeks after surgery and impossible in any eye at 5 weeks after surgery. In the PTFE and ATRA groups, adjustment was possible in all 10 eyes at 3 and 5 weeks after surgery. On comparing adjustability, a significant difference was observed between the PTFE group and the control group or between the ATRA group and the control group 5 weeks after surgery ($P = .0003$ and $P = .0003$, respectively). A significant difference was observed between the ATRA group and the control group in terms of adhesion between superior rectus muscles and sclerae at 5 weeks after surgery ($P = .006$).

Conclusions: Slow-releasing ATRA in PTFE/PLGA was found to reduce adhesion and to allow delayed adjustment in most eyes for up to 5 weeks after surgery.

Effect of 10-mm superior oblique posterior tenectomy combined with frenulum dissection in A-pattern with superior oblique overaction.

Heo H, Lee KH, Ahn JK, Kim DH, Park YG, Park SW.

Am J Ophthalmol 2009 Aug 6. [Epub ahead of print]

Purpose: To evaluate the effect of 10-mm tenectomy of the posterior fibers of the superior oblique (SO) tendon combined with dissection of the frenulum for correction of A-pattern deviation and vertical deviation with SO overaction.

Methods: Seventy-five patients with A-pattern strabismus associated with SO overaction who underwent surgery between March 1, 2004 and August 31, 2007. Retrospective analysis of A-pattern strabismus patients with SO overaction who underwent unilateral or bilateral 10-mm SO posterior tenectomy combined with frenulum dissection and who underwent at least 12 months of follow-up.

Results: The mean preoperative amount of A-pattern for all patients was 21.20 +/- 7.25 prism diopters (PD), with a mean postoperative collapse of 17.63 +/- 5.33 PD (range, 10 to 30 PD), which was statistically significant (P = .001). After surgery, the mean A-pattern correction was 22.12 +/- 6.30 PD in the group that underwent bilateral posterior tenectomy and 13.33 +/- 5.20 PD in the group that underwent unilateral posterior tenectomy. The mean degree of preoperative vertical deviation in the group that underwent unilateral posterior tenectomy was 11.50 +/- 3.96 PD, and the mean correction was 9.21 +/- 4.22 PD (P = .01). There were no surgical complications, except in 5 patients, who manifested mild inferior oblique overaction.

Conclusions: We believe that 10-mm SO posterior tenectomy combined with frenulum dissection effectively collapses A-pattern deviation of less than 25 PD with mild to moderate SO overaction and reduces associated vertical deviation of 10 PD.

The incidence of asystole in patients undergoing strabismus surgery.

Min S-W, Hwang J-M.

Eye 2009 Apr; 23(4):864–866.

This is a retrospective, noncomparative interventional case series of patients aged six months to 80 years of age of 3628 consecutive patients who underwent strabismus surgery. Four patients (0.11%) under general anesthesia showed asystole during strabismus surgery. All four were adults of 28, 32, 50, and 53 years of age. Two patients had hypertension and three had preoperative electrocardiographic abnormalities. Three patients had previously undergone uneventful strabismus surgery.

Postoperative outcomes in children with intermittent exotropia from a population-based cohort.

Ekdawi N, Nusz K, Diehl N, Mohny B.

J APPOS 2009 Feb; 13(1):4-7.

The paper examines, retrospectively, the medical records of 184 patients less than 19 years old with intermittent exotropia between 1/1975 and 12/1994. 61 patients at a mean age of 7.6 had surgery. Twelve had to undergo a second surgery and no patient had 3 or more surgeries in a 10 yr follow up. After one surgery, 55% were within 9 pd of orthotropia and 45% had better than 60 seconds of stereopsis. The odds of developing > than 10 pd of misalignment after the first surgery was 54% by 5 yrs, 76% by 10 yrs and 86% by 15 yrs. Although only one in 5 had a second surgery, only 45% had excellent alignment and high grade stereopsis as of a follow up of 8 yrs post op.

Long-term follow-up of congenital esotropia in a population-based cohort.

Louwagie C, Diehl N, Greenberg A, Mohny B.

J AAPOS 2009 Feb; 13(1):8-12.

Retrospective review of medical records of patients with congenital esotropia from 1/1965 to 12/1994. A total of 130 congenital esotropic children with a median age of 7.4 months and a mean deviation of 30 pd underwent strabismus surgery. The authors found that the risk for a second surgery was greater in patients with a larger presenting angle and was 51% at 10 yrs and 66% at 20 years. They conclude that children with congenital esotropia, a second surgery is likely in 50% of patients after 10 years and were more likely in patients with a large angle at initial presentation.

Bupivacaine injection of the lateral rectus muscle to treat esotropia.

Scott A, Miller J, Shieh K.

JAPPOS 2009 Apr; 13(2):119-122.

Interesting report of a clinical pilot study examining the effect of Bupivacaine in an effort to enlarge and thus theoretically strengthen a muscle to treat strabismus.

Six patients with comitant esotropia had 1 lateral rectus muscle injected with Bupivacaine at various doses. MRI was obtained before and after to document the size of the lateral rectus and intervals to monitor effect. Two patients did require a second injection. In 4 patients, the deviation was, on average, 12 PD after one injection an average of 367 days post injection. Two patients had minimal to no change. Enlargement of all injected lateral muscles was noted on MRI, optimal dose has not yet be determined.

Toward an implantable functional electrical stimulation device to correct strabismus.

Velez F, Isobe J, Zealea D, Judy J et al.

JAAPOS 2009 Jun; 13(3):229-235.

Three feline lateral rectus muscles were injected with Botox and 4 feline control lateral rectus muscles were stimulated with a biphasic controlled current. In control muscles, a frequency of 170 Hz resulted in an abduction of 27 degrees while the chemically denervated muscles had increases in abduction of 17 degrees. The article is included for the novelty of the study.

Cyanoacrylate adhesive use in primary operation and reoperation in rabbit eye muscle surgery.

De Alba Campomanes A, Lim A, Fredrick D.

J AAPOS 2009 Aug; 13(4):357-63.

Very interesting study comparing the effectiveness of super glue with vicryl in strabismus surgery in rabbits.

Twenty rabbits underwent superior rectus muscle recessions in one eye using cyanoacrylate (superglue) and standard suture recession in the other eye. After 5 weeks, recessed muscles were advanced using cyanoacrylate in one eye and suture in the other. In both groups, the slippage was greater than 1 mm in 1.9% in both groups. After advancement, the slippage of > than 1mm was 36.8% in the suture group, but only 15.7% in the glue group. Surgery using cyanoacrylate was 3.85 mins faster than the suture group.

Augmented vertical rectus transposition surgery with single posterior fixation suture: Modification of Foster technique.

Struck M.

J AAPOS 2009 Aug; 13(4):343-349.

Article describes a technique to improve outcomes in Duane's and 6th nerve palsies. Full tendon transpositions of the vertical rectus muscle were performed on 5 pts with Duane's and 5 pts with CN VI palsies. Augmentation was created by use of a single lateral fixation suture incorporated in the bellies of both vertical muscles. The LR was disinserted and attached to the orbital wall in 4 patients with Duane's syndrome. Eight patients had improvement in alignment with deviations of less than 10 PD and the Duane's pts had marked improvement in torticollis.

Topical anesthesia in strabismus surgery: a review of 101 cases.

Seijas O, Gomez de Liano P, Merino P, Roberts CJ, Gomez de Liano R.

JPOS 2009 Jul-Aug; 46:218-222.

A total of 101 patients over a ten year period who underwent topical anesthesia for strabismus surgery were analyzed retrospectively. A good result (residual angle less than 10 pd, absence of diplopia) was obtained in 85% of patients at final follow-up (mean follow-up 3.1 years). The mean

operating time for each muscle was 29 minutes. Conversion to general anesthesia was not necessary in any case. Atropine was used in three patients due to activation of the vagal reflex. Topical anesthesia is a useful technique in the armamentarium of the strabismus surgeon. The oculocardiac reflex is infrequent. Appropriate anesthesia monitoring is necessary to ensure adequate control of pain and possible side effects.

IX. CATARACT

Cataract in children attending schools for the blind and resource centers in Eastern Africa.

Masukwa G, Njuguna M, Tumwesigye C, Shilio B, Courtright P, Lewallen S.

Ophthalmology 2009 May; 116(5):1009-1012.

Design: Cross-sectional study of children enrolled at schools for the blind in Kenya, Malawi, Tanzania, and Uganda.

Results: Of 1062 children examined, 196 (18%) had undergone cataract surgery or had cataract as the major cause of visual impairment; 140 (71%) had bilateral surgery, 24 (12%) had unilateral surgery, and 32 (16%) had not had surgery. Of operated eyes, 118 (41%) had visual acuity $\geq 20/200$. Intraocular lenses were implanted in 65% of the operated eyes. Eyes with intraocular lens were more likely to have better vision than those without. Amblyopia was the most common cause of poor visual acuity in children who had undergone cataract surgery.

Conclusions: The high rate of amblyopia highlights the critical need for programs to find children earlier and to ensure adequate follow-up after surgery. Without such programs, the value of training pediatric surgeons will not be fully realized.

X. CATARACT SURGERY

Infant Aphakia Treatment Study Group .The infant aphakia treatment study: design and clinical measures at enrollment. Arch Ophthalmol. 2010 Jan;128(1):21-7.

The Infant Aphakia Treatment Study (IATS) compares the use of contact lenses and intraocular lenses (IOLs) for the optical correction of unilateral aphakia during infancy, the purpose of which was to determine whether either treatment for an infant with a visually significant unilateral congenital cataract results in a better visual outcome. The IATS study is a randomized, multicenter (12 sites) clinical trial with 114 infants who had unilateral congenital cataracts. Each patient was assigned to undergo cataract surgery with or without IOL implantation. Children randomized to IOL treatment had their residual refractive error corrected with spectacles after surgery and children randomized to no IOL treatment had their aphakia treated with a contact lens. Patients were corrected to allow for near vision. The main outcome measure was grating acuity at 12 months of age and HOTV visual acuity at 4 1/2 years of age.

Enrollment began December 23, 2004, and was completed January 16, 2009. The median age at the time of cataract surgery was 1.8 months. Fifty patients were 4 to 6 weeks of age at the time of enrollment; 32 were 7 weeks to 3 months of age at time of surgery and the remaining 32 were more than 3 to less than 7 months of age at the time of surgery. Fifty-seven children were randomized to each treatment group. The eyes with cataracts had shorter axial lengths and steeper corneas on average than the fellow eyes.

Currently, the optimal optical treatment of aphakia in infants is unknown. However, the Infant Aphakia Treatment Study was designed to provide empirical evidence of whether optical treatment with an IOL or a contact lens after unilateral cataract surgery during infancy is associated with a better visual outcome. Future papers will be published regarding visual outcomes.

Role of ultrasound and biomicroscopy in evaluation of anterior segment anatomy in congenital and developmental cataract cases.

[El Shakankiri NM](#), [Bayoumi NH](#), [Abdallah AH](#), [El Sahn MM](#).

[J Cataract Refract Surg](#). 2009 Nov;35(11):1893-905.

PURPOSE: To investigate the role of ultrasound biomicroscopy (UBM) in the evaluation of anterior segment anatomy in cases of congenital and developmental cataract.

METHODS: In this cross-sectional nonrandomized unmasked study, ultrasound biomicroscopy (UBM) was used to evaluate the anterior segment anatomy of 32 eyes of 21 children with congenital and developmental cataract. The parents were questioned for details of the children's history. An initial office examination was done to detect visual function, pupil color, lens morphology, corneal clarity, and presence of gross anterior segment anomaly. If the fundus was visible, it was examined in cooperative children after mydriasis. Under general anesthesia, each child was examined by UBM.

RESULTS: The parameters detected by UBM included anterior chamber depth, lens thickness, zonular fiber length, ciliary process length, anterior chamber angle, and lens morphology. A-scan biometry was also performed to detect anterior chamber biometric characteristics.

CONCLUSION: Ultrasound biomicroscopy is a valuable tool for evaluating childhood cataracts and associated ocular anomalies as well as anterior segment biometric characteristics.

Br J Ophthalmol 2009;**93**:1495-1498 doi:10.1136/bjo.2009.160069 **Cataract surgery and primary intraocular lens implantation in children ≤ 2 years old in the UK and Ireland: finding of national surveys**

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Abstract

Background: Current patterns of practice relating to primary intraocular lens (IOL) implantation in children ≤ 2 years old in the UK and Ireland are investigated.

Methods: National postal questionnaire surveys of consultant ophthalmologists in the UK and Ireland.

Results: 76% of 928 surveyed ophthalmologists replied. 47 (7%) of the respondents operated on children aged ≤ 2 with cataract. 41 (87%) of respondents performed primary IOL implantation, but 25% would not implant an IOL in a child under 1 year old. 88% of surgeons used limbal wounds, 80% manual capsulotomies, 98% posterior capsulotomies and 100% hydrophobic acrylic lenses. The SRK/T formula was most commonly used (70%). Exclusion criteria for primary IOL implantation varied

considerably and included microphthalmos (64% of respondents), anterior and posterior segment anomalies (53%, 58%), and glaucoma (19%).

Discussion: Primary IOL implantation in children ≤ 2 has been widely adopted in the UK and Ireland. There is concordance of practice with regards to surgical technique and choice of IOL model. However, there is some variation in eligibility criteria for primary IOLs: this may reflect a lack of consensus on which children are most likely to benefit. Thus, there is a need for systematic studies of the outcomes of primary IOL implantation in younger children.

Comment: Large survey paper with a very high 76% response rate demonstrating that primary IOL in children less than 2 yrs old is becoming the standard of care in UK and Ireland.

Novel technique for Nd:YAG Posterior Capsulotomy in Pediatric Patients. Chen J, Frederick D. JPOS Jan-Feb 2010; 47: 41-42.

Overhead Nd:YAG lasers coupled with operating microscopes are ideal for patients requiring posterior capsulotomy while under general anesthesia. However, in many institutions the cost of such a device is prohibitive. The authors describe modifying the patient position (lateral decubitus) during general anesthesia in order to allow use of a standard upright Nd:YAG laser device. This approach was much preferred by the anesthesia team because it did not interfere with monitoring or airway management.

Refractive outcome with secondary intraocular lens implantation in children. Moore DB, Ben Zion I, Neely DE, et al. J AAPOS 2009;13:551-554.Dec

There are difficulties with the use of IOL calculation formulas when they are applied to pediatric cases. This study determined the accuracy of the actual postoperative refractive outcome with secondary IOL implantation in aphakic children. Fifty eyes from 35 consecutive patients seen over a ten-year period were evaluated. The average age of the secondary implantation was 6.5 years. The predictive error was found to be 1.64 +/- 1.58 diopters. The causes of error were felt to include 1.the effect of axial displacement of the lens is greater with stronger IOLs; 2.Biometry is complicated in aphakic patients by the absence of a lens spike; 3.shallower anterior chambers in pediatric patients; 4.proliferation of retained lens material from the initial cataract surgery; 5.posterior capsule contraction; 6.vitreous pressure; and 7.haptic angulation. The optimal approach to IOL selection in this patient population is still controversial.

Outcomes of cataract surgery following radiation treatment for retinoblastoma. Payne JF, Hutchinson AK, Hubbard III GB, Lambert SR. J AAPOS 2009;13:454-458. Oct.

This paper looked at the visual outcomes, complications and tumor recurrences in patients with a history of retinoblastoma who underwent cataract surgery for radiation-induced cataracts. Charts of 11 patients (12 eyes) who had received either external beam radiotherapy or I^{125} plaque brachytherapy to treat their retinoblastoma over a 5-year period were reviewed. Surgical technique consisted of a limbal-based approach with a scleral-tunnel wound. There were no intraoperative or postoperative complications. Eight patients required a Nd:YAG laser capsulotomy (including 3 patients who had already had a primary posterior capsulotomy and anterior vitrectomy). All ten patients who had preoperative acuity data experienced improved postoperative vision. Over a median follow-up period of six years, there were no metastasis or retinoblastoma recurrences. This

information is helpful for the cataract surgeon in regards to surgical technique and postoperative expectations in this challenging group of patients.

Central corneal thickness in children with congenital cataract and children with surgical aphakia: a case-control study.

Lupinacci AP, da Silva Jordao ML, Massa G, Arieta CE, Costa VP.

Br J Ophthalmol 2009 Mar; 93(3):337-341.

Aim: To measure the central corneal thickness (CCT) of children with congenital cataract and surgical aphakia.

Methods: Children with congenital cataract or surgical aphakia were prospectively recruited and divided into four groups: unilateral cataract (group 1, n=14), bilateral cataract (group 2, n=17), unilateral aphakia (group 3, n=32) and bilateral aphakia (group 4, n=44). An age-, sex-, and race-matched control group of normal individuals was selected. Ultrasonic pachymetry was performed by the same observer.

Results: The mean CCT of the control group was not significantly different from the normal ($p=0.747$) and cataractous eyes of group 1 ($p=0.252$). The mean CCTs of both eyes of group 2 were significantly higher than the control group ($p,0.01$). The mean CCT of the aphakic eyes in group 3 was significantly higher than the contralateral healthy eyes and control eyes ($p,0.001$). The mean CCTs of both eyes of group 4 were significantly higher than the control group ($p,0.001$). The mean CCT was significantly higher in aphakic eyes of groups 3 and 4 than in cataractous eyes of groups 1 and 2 ($p,0.001$).

Conclusions: Aphakic eyes due to congenital cataract show thicker corneas than normal phakic eyes. Aphakic eyes after congenital cataract extraction show thicker corneas than eyes with congenital cataracts, suggesting that the increase in CCT occurs postoperatively.

Cataract surgery in pediatric uveitis.

Zaborowski AG, Quinn AG, Dick AD.

J Pediatr Ophthalmol Strabismus 2008 Sep-Oct; 45(5):270-278.

The surgical management of uveitic cataracts in children is both challenging and controversial. Juvenile idiopathic arthritis occurs with an incidence of 1 in 1000 children in the United Kingdom. Between 12% and 25% of patients with JIA develop uveitis; it is by far the most common and the most severe cause of pediatric uveitis. The growing use of various immunotherapies and targeted biologic agents in childhood uveitis increases our potential to implant lenses and predict outcomes. The authors review preoperative management including supplemental steroid regimens, adjuvant immune suppression, surgical techniques, aphakia correction, complications, and postoperative management in this common condition.

Stereopsis in children with unilateral pseudophakia.

Kim SH, Plager DA.

Br J Ophthalmol 2009 Mar; 93(3):333-6.

Aim: To evaluate stereoacuity and the factors that can influence stereopsis in children with unilateral pseudophakia.

Methods: Charts of 38 patients who were diagnosed as having unilateral cataract and underwent cataract extraction with primary intraocular lens implantation were retrospectively reviewed. Data were collected on gender, age, race, age at presentation and the surgery, cataract types, the presence of strabismus before and after cataract extraction, refractive error and the presence of anisometropia, best corrected visual acuity (VA) of both eyes and stereoacuity.

Results: Thirty-eight patients were divided into two groups. Group I had 21 patients whose stereopsis was better than 400 s of arc. Seventeen patients in group II had stereopsis poorer than 400 s of arc. The mean ages at presentation and surgery were 4.9 and 6.3 years in group I and 2.7 and 3.0 in

group II, respectively ($p=0.046,0.007$). Posterior lenticonus was the most common cataract type in both groups ($p=0.20$). Strabismus was more frequently associated with group II. Those who had no strabismus before and after cataract surgery were 66.7% in group I and 47.1% in group II ($p=0.02$). Fifty-two per cent of patients in group I had a VA of 20/40 or better, but in group II, only one patient had a VA of 20/40 ($p,0.001$). With a VA of 20/40 or better as the reference level, the odds of having good stereopsis decreased significantly if VA in the eye with the cataract was less than 20/60 based on the multiple regression logistic analysis (OR 0.03, $p=0.0027$).

Conclusions: Stereopsis was better in children with later manifesting cataracts, in the absence of strabismus and in cases with a good postoperative VA. The postoperative VA was the most important factor affecting the outcome of stereopsis in children with unilateral pseudophakia.

Note: Limitations of this study are: the small sample size and they used the Titmus Fly test for measuring stereoacuity.

Management of congenital cataract in children younger than 1 year using a 25-gauge vitrectomy system.

Chee KY, Lam GC.

J Cataract Refract Surg. 2009 Apr; 35(4):720-4.

Purpose: To evaluate the safety and efficacy of a 25-gauge vitrectomy system for the management of congenital cataract in children younger than 1 year.

Methods: Children in a tertiary pediatric hospital and private practice had cataract extraction using a 25-gauge vitrectomy system between January 2005 and June 2008. Each eye had anterior vitrectorhexis, lens aspiration, posterior vitrectorhexis, and anterior vitrectomy through two 25-gauge limbal side ports. The ports were created with a 25-gauge trocar or a 0.6 mm paracentesis knife. The eyes were left aphakic.

Results: Nineteen (95%) of the 20 eyes (14 children) had a successful surgical outcome with the 25-gauge vitrectomy system. One eye was converted to the 20-gauge system because of an unusually tough and fibrous lens capsule. The limbal side ports in 16 of 17 eyes created with the 25-gauge trocar required suturing to seal the ports; none of the 3 eyes with side ports created with the paracentesis knife required suturing. There were no significant intraoperative or postoperative complications other than ocular hypertension in 1 eye.

Conclusions: The 25-gauge vitrectomy system appears safe and effective for the management of infantile cataract. Advantages include more precise manipulations with smaller instruments in infant eyes, a more stable anterior chamber, and less postoperative astigmatism.

Comparison of 2 techniques of intraocular lens implantation in pediatric cataract surgery.

Faramarzi A, Javadi MA.

J Cataract Refract Surg 2009 Jun; 35(6):1040-5.

Purpose: To compare the results of 2 intraocular lens (IOL) implantation techniques in pediatric cataract surgery.

Methods: This contralateral prospective randomized study comprised children with bilateral congenital or developmental cataract. In all cases, anterior capsulorhexis, lens aspiration, posterior continuous curvilinear capsulorhexis (PCCC), and anterior vitrectomy were performed. In 1 eye of each patient, a 3-piece AcrySof MA60BM IOL was implanted in the capsular bag. In the other eye, the same type of IOL was implanted in the ciliary sulcus and the optic was captured through the PCCC. Visual acuity, visual axis opacification, and complications were assessed.

Results: Twenty-eight eyes of 14 children were included in the study. The mean patient age at surgery was 5.1 years \pm 1.5 (SD) (range 2.5 to 8.0 years). The mean follow-up was 22.2 \pm 6.3 months (range 13 to 35 months). The visual axis remained clear in all eyes in both groups. There was no statistically significant difference between the 2 groups in best corrected visual acuity or complications (eg, postoperative uveitis, posterior synechia, significant IOL decentration).

Conclusions: In pediatric cataract surgery, placement of haptics in the ciliary sulcus and IOL optic capture through the PCCC was a safe alternative to IOL implantation in the capsular bag.

Surgical outcomes of primary foldable intraocular lens implantation in children: understanding posterior opacification and the absence of glaucoma.

Astle WF, Alewenah O, Ingram AD, Paszuk A.

J Cataract Refract Surg 2009 Jul; 35(7):1216-22.

Purpose: To evaluate visual and stereoscopic performance after pediatric cataract extraction with intraocular lens (IOL) implantation performed by the same surgeon over 24 years and to review the complications.

Methods: This retrospective review comprised children aged 1 month to 18 years who had small-incision cataract extraction with foldable posterior chamber IOL implantation from 1995 to 2008.

Results: The postoperative follow-up was 6 months to 12 years. Posterior capsule opacification (PCO) requiring secondary surgical membranectomy developed in 22.7% of the children. Younger children developed PCO more often than older children. The PCO rate was 70.8% in children younger than 1 year and decreased steadily to 6.1% in children older than 7 years. The mean onset of PCO was 6.1 months postoperatively. Other complications were vitreous tags (12.0%), IOL dislocation (4.7%), and loose corneal sclera sutures (2.7%). Of the eyes in which vision could be recorded, 89.5% had improved corrected visual acuity, with no eye losing acuity. Stereopsis was present in 35% of testable children preoperatively and 91% postoperatively.

Conclusions: Cataract surgery in children younger than 2 years should be considered a 2-stage procedure in view of the higher incidence of PCO. Secondary glaucoma decreased significantly when surgery was performed after 30 days of age and the eye was left pseudophakic after surgery. Further improvements in IOL design, surgical instrumentation, and implantation techniques will continue to improve the ability to visually rehabilitate children.

Changes in axial length growth after congenital cataract surgery and intraocular lens implantation in children younger than 5 years.

Hussin HM, Markham R.

J Cataract Refract Surg 2009 Jul; 35(7):1223-8.

Purpose: To study the axial length (AL) changes in children who had unilateral or bilateral congenital cataract surgery and intraocular lens (IOL) implantation when they were younger than 5 years.

Methods: Axial length measurements were obtained preoperatively and at the final follow-up. Axial length values were compared with those in a control group of children without cataract.

Results: Congenital cataract surgery and IOL implantation were performed in 18 patients (36 eyes) with bilateral cataract and 18 patients (18 eyes) with unilateral cataract. There was no statistically significant difference in AL growth between the operated eyes and the fellow eyes ($P = .12$, Wilcoxon signed rank test) or between the final AL in operated eyes and the AL in the age- and sex-matched control group ($P = .69$, Mann-Whitney U test). There was no statistically significant difference in AL growth between the right eyes of children with bilateral pseudophakia and the operated eyes of children with unilateral pseudophakia ($P = .26$, Mann-Whitney U test). There was no statistically significant difference between the final AL in the right eyes of children with bilateral pseudophakia and the AL in the age- and sex-matched control group.

Conclusions: No significant retardation or acceleration of axial growth occurred after congenital cataract surgery and IOL implantation. The AL in this group of patients followed a normal pattern, although the difference in AL between operated unilateral cataract eyes and control eyes and between operated unilateral cataract eyes and operated bilateral cataract eyes showed a trend toward significance.

Bilateral pediatric cataract surgery in the same session.

Totan Y, Bayramiar H, Imaz HY.
Eye 2009 May; 23(5):1199-1205.

The purpose of this study was to evaluate the results of bilateral pediatric cataract surgery in the same session with a focus on patient selection criteria, operative guidelines, and controversial issues. This retrospective noncomparative case series comprised 39 children (78 eyes), who underwent bilateral cataract surgery and/or primary or secondary IOL implantation in one sitting. Ten patients had bilateral lensectomy-primary posterior capsulotomy-anterior vitrectomy, and the remaining 29 patients had bilateral IOL implantation either primarily (20 cases) at the time of cataract extraction or secondarily for aphakic correction (9 cases). Both eyes were treated as two separate but consecutive surgeries in the same session. Maximum possible care was taken to ensure surgical asepsis. The age at surgery ranged from 2 months to 17 years. Average follow-up was 12 months. No serious intraoperative or postoperative complications occurred leading to permanent vision loss. During the last follow-up, 91% of eyes tested had a visual acuity of 20/40 or better. The authors conclude that bilateral pediatric cataract surgery in one session may be a safe and useful approach alternative to sequential surgery in selected patients, if operative guidelines and surgical asepsis are strictly followed.

The critical period for surgical treatment of dense congenital bilateral cataracts.

Birch E, Cheng C, Stager Jr D, Weakley D, Stager Sr D.
J AAPOS 2009 Feb; 13(1):67-71.

Purpose: To determine the critical period for deprivation amblyopia in a cohort of patients with dense bilateral congenital cataracts for optimal surgical timing.

Methods: Thirty seven infants with dense bilateral congenital cataracts that were extracted by 31 weeks of age were enrolled prospectively. VA was assessed at >5 years of age and assigned a statistical model. Additional adverse outcomes including strabismus, nystagmus, secondary membrane formation and glaucoma were evaluated.

Results: Statistically, a bilinear model with a critical age of 14 weeks provided the best data fit. During weeks 0-14 weeks, mean visual acuity decreased by 1 line with each 3 weeks delay in surgery. From 14 to 31 weeks, visual acuity was independent the subjects age at surgery, averaging 20/80. Surgery after 4 weeks was associated with a greater prevalence of strabismus and nystagmus than surgery before 4 weeks. However, surgery before 4 weeks was associated with a greater prevalence of secondary membrane formation and glaucoma.

Vitrectorhexis versus forceps capsulorhexis for anterior and posterior capsulotomy in congenital cataract surgery.

Hazirolan, DO, Altiparmak, UE, Aslan, BS, Duman, S.
JPOS 2009 Mar-Apr; 46:104-107.

Twenty-eight eyes with congenital cataract were included in the study. The anterior and posterior curvilinear capsulorhexes were created using microforceps in 17 eyes or with the vitrector in 11 eyes. Corneal edema, anterior chamber flare, and the time for optical axis clarity were similar between the groups. The current results suggest that the use of both techniques appears to be equally safe and effective for the treatment of anterior and posterior capsulorhexis.

XI. REFRACTIVE SURGERY

Photorefractive keratectomy in the management of refractive accommodative esotropia in young adult patients.

[Pacella E](#), [Abdolrahimzadeh S](#), [Mollo R](#), [Mazzeo L](#), [Pacella F](#), [Mazzeo F](#), [Gabrieli CB](#).
[J Cataract Refract Surg](#). 2009 Nov;35(11):1873-7.

PURPOSE: To evaluate the visual, motor, and sensory outcomes of photorefractive keratectomy (PRK) in the treatment of purely refractive accommodative esotropia in young adult patients.

METHODS: This prospective study comprised patients with hyperopia and purely accommodative hyperopic esotropia. A complete ophthalmologic examination was performed preoperatively and 1, 3, and 12 months postoperatively. The examination included uncorrected (UDVA) and corrected (CDVA) distance visual acuities and orthoptic and sensory tests. All patients also had keratometry, pachymetry, and corneal topography assessment before and after treatment. Treatment was performed using a Technolas 217 excimer laser.

RESULTS: Thirty eyes of 15 patients (mean age 30.8 years) were treated. Preoperatively, the CDVA was 20/30 or better in all eyes and the mean cycloplegic spherical equivalent (SE) was +3.50 diopters (D). One year postoperatively, the UDVA was 20/30 or better in all eyes and the mean SE was -0.01 D. The mean esotropic deviation for distance vision without correction preoperatively was 8.7 prism diopters. At 1 year of follow-up, 12 patients achieved orthophoria and 3 patients had a reduction in the angle of deviation. There were no intraoperative or postoperative complications. Stereopsis was unaffected by treatment in all patients.

CONCLUSIONS: Photorefractive keratectomy was effective in the treatment of purely accommodative esotropia in young adult patients at a follow-up of 1 year. There were no cases of visual acuity loss or complications from the laser treatment.

Laser-assisted subepithelial keratectomy for bilateral hyperopia and hyperopic anisometric amblyopia in children: one-year outcomes.

[Astle WF](#), [Huang PT](#), [Ereifej I](#), [Paszuk A](#).

[J Cataract Refract Surg](#). 2010 Feb;36(2):260-7.

PURPOSE: To assess the refractive, visual acuity, and binocular results of laser-assisted subepithelial keratectomy (LASEK) in children with bilateral hyperopia or hyperopic anisometric amblyopia.

METHODS: This retrospective review comprised children with bilateral hyperopia or hyperopic anisometric amblyopia who had LASEK. Refractive status, visual acuity, and binocular vision were assessed and recorded 2 months and 1 year postoperatively.

RESULTS: The mean spherical equivalent (SE) in all 72 hyperopic eyes (47 patients) was +3.42 diopters (D) (range 0.00 to +12.50 D) preoperatively and +0.59 D (range -1.25 to +2.00 D) 1 year postoperatively. After LASIK, 41.7% of eyes had improved corrected distance visual acuity (CDVA). No patient had reduced CDVA or loss of fusional ability; there was a 25.0% improvement in stereopsis at 1 year. The mean anisometric difference in the hyperopic anisometric amblyopia subgroup (18 eyes, 10 patients) was 4.39 D (range +1.75 to +7.75 D) preoperatively and +0.51 D (range 0 to +0.875 D) at 1 year. One year postoperatively, 83% of anisometric eyes were within +/-1.00 D of the fellow eye and 94.0% were within +/-3.00 D. Postoperatively, 64.7% of eyes had improved CDVA with no reduced CDVA or loss of fusional ability; there was a 22% improvement in stereopsis at 1 year.

CONCLUSION: Laser-assisted subepithelial keratectomy improved visual acuity in pediatric hyperopia with or without associated hyperopic anisometropic amblyopia.

XII. GENETICS

Preimplantation Genetic Diagnosis for Stargardt Disease.

[Sohrab MA](#), [Allikmets R](#), [Guarnaccia MM](#), [Smith RT](#).

[Am J Ophthalmol](#). 2010 Feb 9. [Epub ahead of print]

PURPOSE: To report the first use of in vitro fertilization (IVF) and preimplantation genetic diagnosis to achieve an unaffected pregnancy in an autosomal-recessive retinal dystrophy.

METHODS: An affected male with Stargardt disease and his carrier wife underwent IVF. Embryos obtained by intracytoplasmic sperm injection underwent single-cell DNA testing via polymerase chain reaction and restriction enzyme analysis to detect the presence of ABCA4 mutant alleles. Embryos were diagnosed as being either affected by or carriers for Stargardt disease. A single carrier embryo was implanted.

RESULTS: Chorionic villus sampling performed during the first trimester verified that the fetus possessed only 1 mutant paternal allele and 1 normal maternal allele, thus making her an unaffected carrier of the disease. A healthy, live-born female was delivered.

Br J Ophthalmol 2010;**94**:121-127 doi:10.1136/bjo.2008.154187

Ophthalmological findings in children and young adults with genetically verified mitochondrial disease

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Abstract

Aim: To describe ophthalmological phenotypes in patients with mitochondrial disease and known genotypes.

Methods: A retrospective study was performed on 59 patients (29 male, 30 female) with a mean age of 11.8 years who had mitochondrial disease with known DNA mutations. Fifty-seven of the 59 subjects underwent a detailed ophthalmological examination including visual acuity (VA), eye motility, refraction, slit-lamp examination, ophthalmoscopy and, in almost one-half of the cases, a full-field electroretinogram (ERG).

Results: Forty-six (81%) of the patients had one or more ophthalmological findings such as ptosis (n=16), reduced eye motility (n=22) including severe external ophthalmoplegia (n=9), strabismus (n=4), nystagmus (n=9), low VA (n=21), refractive errors (n=26), photophobia (n=4), and partial or total optic atrophy (n=25). Pigmentation in the macula and/or

periphery was noted in 16 patients. In 10/27 investigated individuals with full field ERG, retinal dystrophy was recorded in six different genotypes representing Kearns–Sayre syndrome (n=5), Leigh syndrome (n=1), Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) (n=1), Myoclonus epilepsy with red ragged fibres (MERRF) (n=1), Leber hereditary optic neuropathy (n=1) and mitochondrial myopathy (n=1).

Conclusion: The results show that a majority of patients with mitochondrial disorders have ophthalmological abnormalities. We recommend that an ophthalmological examination, including ERG, be performed on all children and adolescents who are suspected of having a mitochondrial disease.

Comment: weakness: it is a retrospective article, strength: largest cohort of these types of patients to date. Recommend ERG be performed on all pts that we suspect having mitochondrial disease.

Which Leber congenital amaurosis patients are eligible for gene therapy trials

Drack AV, Johnston R, Stone EM. J AAPOS 2009;13:463-465. Oct

Leber congenital amaurosis can be caused by mutations in at least 15 different genes. In 2001 a dog-model of RPE65LCA was treated with subretinal injection of a viral vector bearing a normal copy of the gene. In 2008 human gene therapy trials used a similar technique. Genetic testing must follow a multistep approach to ensure correct interpretation of variations found in patient genomes. Falsely identifying benign gene polymorphisms will cause incorrect patient enrollment and potentially lower outcome success rates. Conversely, incorrectly declaring a patient ineligible for a study prevents a good candidate patient from benefiting from a clinical trial. Only about 65% of LCA patients have a mutation that can be found with current technology. This paper presented case reports showing the value of a multistep approach in making correct genetic diagnosis. The case reports were very instructive and illustrative of potential pitfalls in genetic testing.

Axenfeld-Rieger syndrome and spectrum of *PITX2* and *FOXC1* mutations.

Tümer Z, Bach-Holm D.

Eur J Hum Genet 2009 Dec; 17(12):1527-39

This is an excellent review of the clinical features of the *PITX2* and *FOXC1* mutations and their relevant diagnostic approaches. Axenfeld-Rieger syndrome (ARS) is a dominantly inherited condition with genetic heterogeneity. Patients with ARS may have, in addition to their anterior segment abnormalities, systemic malformations with incomplete penetrance and variable expressivity. The major systemic features are mild tooth abnormalities (microdontia, hypodontia, oligodontia and adontia) and redundant periumbilical skin. Craniofacial dysmorphism such as maxillary hypoplasia, sensory hearing loss, hypertelorism and congenital heart defects may also be part of the clinical spectrum. Glaucoma is present in 50% of patients. Mutations in the transcription factors, *PITX2* and *FOXC1* lead to ARS. The mutations show great diversity from intragenic mutations to submicroscopic deletions or duplications (*FOXC1*) to chromosome rearrangements (*PITX2*). There is no clear genotype-phenotype relationship but ARS patients with systemic changes usually have *PITX2* mutations. The underlying genetic defect is unknown in 60% of the cases and there are at least two more loci associated with ARS, the genes involved are yet to be identified.

Novel *FOXG1* mutations associated with the congenital variant of Rett Syndrome.

Mencarelli MA, Spanhol-Rosseto A, Artuso R, Rondinella D et al.

J Med Genet 2010 Jan; 47(1):49-53

Rett syndrome (RTT) is a severe neurodevelopmental disorder representing one of the most common genetic causes of mental retardation in girls. The syndrome has a wide spectrum of clinical

phenotypes including the classic form, the early onset seizure variant, the Zappella variant, the congenital variant, the “forme frusta” variant and the late regression variant. Mutations in the *MECP2* gene, located on Xq28, are responsible for 95% of classic RTT and 50% of Z-RTT, while the early onset seizure variant results from mutation in the *CDKL5* gene on Xp22. These authors report on the phenotype associated with *FOXG1* mutations and confirm that the *FOXG1* gene is responsible for the congenital variant of RTT. The overall clinical phenotype is characterized by normal pregnancy and delivery, normal auzological parameters at birth followed by hypotonia, irresponsiveness and irritability in the neonatal period. Deceleration of head growth is one of the most important diagnostic signs; severe postnatal microcephaly evident before the age of 4 months. Additional features include severe psychomotor delay with inability to walk, poor eye contact, tongue stereotypes and jerky movements of limbs and corpus callosum hypoplasia.

Clinical and genetic aspects of neurofibromatosis 1.

Jett K, Friedman JM.

Genetics in Medicine 2010 Jan; 12(1):1-9.

This is an excellent review article. NF1 is an autosomal dominant condition caused by heterozygous mutations of the NF 1 gene. The diagnosis of NF1 is usually based on clinical findings: NIH Consensus criteria, two or more of following features:

1. 6 or more café-au-lait macules >5 mm in prepubertal children and >15 mm in postpubertal
2. Two or more neurofibromas of any type or one plexiform neurofibroma
3. Freckling in axillary or inguinal regions
4. Optic glioma
5. Two or more lisch nodules
6. Distinctive osseous lesion such as sphenoid dysplasia or tibial pseudarthrosis
7. First degree relative with NF1

Children who have inherited NF1 from an affected parent can usually be identified within the first year of life because they require only one feature. This feature is usually multiple café-au-lait spots, which develop in infancy in >95% of those with NF1. A definitive diagnosis of NF1 can be made in most of children by 4 years of age. The authors note that the value of a routine brain MRI at time of diagnosis remains controversial. Genetic testing is necessary to provide prenatal diagnosis and maybe used as an adjunct to clinical diagnosis in cases with an atypical presentation or if the child is too young to have developed most characteristic features. Almost one half of all affected individuals have de novo mutations. NF1 is characterized by extreme clinical variability, not only amongst unrelated individuals, but also among affected individuals with a single family. The frequency of more serious complications increases with age. The authors note several distinctive NF1 phenotypes including segmental NF1 who have typical features of NF1 restricted to one part of the body and whose parents are both unaffected. Also NF1-Noonan syndrome: features of Noonan syndrome such as ocular hypertelorism, down-slanting palpebral fissure, low-set ears, webbed neck and pulmonic stenosis occur in 12 % of individuals with NF1. They include a nice table of disorders resembling NF1 but which can be distinguished by clinical and/or histopathological features.

Neurofibromatosis 2 [Bilateral acoustic neurofibromatosis, central neurofibromatosis, NF2, neurofibromatosis type II].

Evans DGR.

Genetics in Medicine 2009 Sept; 11(9):599-567.

This is another good review article. NF2 is a dominantly inherited tumor predisposition syndrome caused by mutations in the NF2 gene on chromosome 22. Greater than 50% have NF2 as a result of a de novo mutation. Average age of onset is 18 to 24 years, with almost all affected individuals developing bilateral vestibular schwannomas by 30 years of age. In addition to vestibular

schwannoma, individuals with NF2 develop schwannomas of other cranial and peripheral nerves, meningiomas, ependymomas and very rarely astrocytomas. Diagnosis of NF2 is based upon clinical criteria. Diagnostic criteria for NF2 (NIH consensus criteria with additional modifications):

Bilateral vestibular schwannomas:

A first degree relative with NF2 AND

Unilateral vestibular schwannoma

Or

Any two of: schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacity

Unilateral vestibular schwannoma AND any two of: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacity

Multiple meningiomas AND

Unilateral vestibular schwannoma

Or

Any two of schwannoma, glioma, neurofibroma, cataract

Truncating mutations (nonsense and frameshifts) are the most frequent germline event and cause the most severe disease, single and multiple exon deletions are common. Variable expressivity of NF2 amongst individuals results in varying size, location, and number of tumors. Although the tumors are not malignant, their anatomic location and multiplicity lead to great morbidity and early mortality. One third of NF2 patients have decreased visual acuity in one or both eyes. PSC is the most common finding, though retinal hamartomas and epiretinal membranes are seen in 1/3 of individuals.

Eye anomalies and neurological manifestations in patients with PAX6 mutations.

Chien Y-H, Huang H-P, Hwu W-L, Chien Y-H et al.

Mol Vis 2009 Oct 22; 15:2139-45.

PAX6 is a transcriptional regulator in the early development of the ocular, central nervous and gastrointestinal system. This study identified five PAX6 mutations from 17 Taiwanese patients with congenital eye anomalies. This was a 30% detection rate (5/17) in all patients with congenital eye anomalies or 83% (5/6) in patients with aniridia. This study had an unexpectedly high incidence of developmental delay of 80% (4/5), though none of their patients had syndromic aniridia. Both novel and known PAX6 mutations were identified in the current study and PAX6 mutations were closely associated with aniridia. Absence of a positive family history did not exclude PAX6 mutation. The authors argue for a prompt diagnosis of the disease, give the frequent occurrence of development delay.

Clinical and molecular aspects of aniridia.

Kototas H, Petersen MD

Clin Genet 2010 Jan [Epub ahead of print]

Aniridia can appear in a highly penetrant form in association with a range of other ocular anomalies, resulting in poor vision or a less common form in which there is primarily iris involvement and retention of relatively good vision. One third of cases occur sporadically and of those about 1/3 also develop Wilms tumor. This article reviews the data regarding the mechanisms and the mutations that relate to aniridia. Paired box gene 6 (PAX6) has an essential roles as it encodes a phylogenetically conserved transcription factor almost universally employed for eye formation in animals with bilateral symmetry, despite widely different embryological origins. PAX6 is located in chromosome 11p13, and its mutations lead to a variety of hereditary ocular malformations of the anterior and posterior segment, among which aniridia and most probably foveal hypoplasia are the major signs. Aniridia occurs due to decreased dosage of the PAX6 gene. The spectrum of PAX6 mutations in aniridia patients is highly biased, with about 92% of reported mutations being nonsense, splicing, insertions and deletions,

leading to pre-mature truncation of the protein, causing haploin sufficiency and only 2% are missense mutations leading to a substitution of one amino acid by another. The human PAX6 gene harbors mutations that cause aniridia, but also non-aniridia phenotypes. To date the total number of unique DNA variants reported in the human PAX6 data base has increased to 313, the total number of individuals with variants reported is 646, and the total number of variants reported so far is 663.

Clinical and molecular features of Joubert syndrome and related disorders.

Parisi MA.

Am J Med Genet C Semin Med Genet 2009 Nov; 151C(4):326-40.

A good review article about Joubert syndrome (JBTS) an autosomal recessive disorder characterized by a specific congenital malformation of the hindbrain and a broad spectrum of other phenotypic findings now known to be caused by defects in the structure and/or function of the primary cilium. The features necessary for a diagnosis of classic JBTS include 1) the molar tooth sign on axial view of MRI with 3 findings: cerebellar vermis hypoplasia, deepened interpeduncular fossa, and thick elongated superior cerebellar peduncles; 2) intellectual impairment/developmental delay, 3) hypotonia in infancy 4) one or both of the following (not required, but supportive of dx): irregular breathing pattern in infancy and abnormal eye movements (nystagmus and/or oculomotor apraxia (OMA)). There is a broad spectrum of ocular findings in Joubert spectrum (JSRD). Abnormalities of ocular motility are very common, particularly nystagmus and OMA. Nystagmus and OMA are often present at birth and may improve with age. There are two basic forms of retinal disease, seen in about 1/3 of patients; form of Leber Congenital Amaurosis (LCA) and a later onset pigmentary retinopathy that often manifests with nyctalopia in childhood with a variable course. Additionally chorioretinal colobomas may be seen. Mutations in the 8 ciliary/basal body genes (INPP5E, NPHP1, CEP290, TMEM67/MKS3, RPGRIP, ARL13B, and CC2D2A) have been identified in patients with JSRD. The gene products associated with JSRD are known to localize to the primary cilium and/or basal body and centrosome apparatus. JSRD is considered a ciliopathy. The clinical features of JSRD are shared by many ciliary disorders, and typically involve the renal epithelium, retinal photoreceptor cells, central nervous system, body axis, and sensory organs.

Molecular modeling of retinoschisin with functional analysis of pathogenic mutations from human X-linked retinoschisis.

Sergeev YV, Caruso RC, Meltzer MR, Smaoui N et al.

Hum Mol Genet 2010 Jan. [Epub ahead of print]

Retinoschisin (RS1), a retinal secreted photoreceptor disulfide-linked oligomeric protein, is expressed exclusively in the retina and pineal gland and functions as an adhesion molecule, preserving the structural and functional integrity of the retina. To date, there is very little evidence of the mechanism by which protein changes are related to XLRS disease. The authors evaluated possible correlations of the molecular modeling with retinal function (as determined by ERG) in 60 XLRS patients who share 27 missense mutations. They sorted ERG b/a wave ratios by patient age and by the impact of mutation on protein atomic structure defined by homology modeling. Previous studies have looked for genotype-phenotype relationships in XLRS but none have been identified. Missense, splice site, frameshift, insertion and deletion mutations all result in a similar phenotype.

The authors sorted the ERG b/a wave ratios by patient age and by the mutation impact on protein atomic structure, modeled by homology. The majority of RS1 mutations caused minimal structural perturbation and targeted the protein surface. Patients' b/a ratios were quite similar across younger and older subjects. However, maximum structural perturbations, from either the removal or insertion of cysteine residues or changes in the hydrophobic core, were associated with a considerable age difference in the b/a ratio and caused a significantly smaller ratio at younger ages. The molecular modeling suggests an association between the predicted alteration and/or damage to the retinoschisin structure due to mutations and the severity of XLRS as measured by the ERG, analogous to ERG

changes with age observed in mice carrying a recombinant RS1 knockout gene. This indicates that mutational change in RS1 protein structure affects the phenotype of XLR5.

Human RPE65 gene therapy for Leber Congenital Amaurosis: Persistence of early visual improvements and safety at 1 year.

Cideciyan AV, Hauswirth WW, Aleman TS, Kaushal S et al.

Hum Gene Ther 2009 Sep; 20(9):999-1004.

This report extends the safety and efficacy data to 12 months for the 3 patients who previously underwent human gene therapy with rAAV2-vector for RPE 65 LCA. These 3 patients, now 22, 24 and 25, remain healthy and without vector related serious adverse events. Visual acuities, central retinal structure by OCT and standard kinetic visual fields at the 6, 9, and 12 month time points were not different from at the 3 month time point. Statistically significant increases in light sensitivity were noted 1-3 months post treatment and there were no further changes in the magnitude or retinal extent of visual sensitivity increase.

Age-dependent effects of RPE65 gene therapy for Leber's congenital Amaurosis: A phase 1 dose-escalation trial.

Maguire AM, Hugh KA, Auricchio A, Wright JF et al.

Lancet 2009 Nov; 374(9701):1597-605.

These are the results from the complete phase 1 dose-escalation study in 12 patients (ages 8-44years) with RPE65 associated Leber Congenital Amaurosis given one subretinal injection of adeno-associated virus (AAV) containing a gene encoding a protein needed for the isomerohydrolase activity of the retinal pigment epithelium (AAV2-hRPE65v2) in the worst eye with low (1.5×10^{10} vector genomes), medium ($4-8 \times 10^{10}$ genomes), or high (1.5×10^{11} vector genomes). The response duration was measured from 3 months to 2 years. AAV2-hRPE65v2 was well tolerated and all patients who sustained improvement in subjective and objective measurements of vision (i.e., dark adaptometry, pupillometry, ERG, nystagmus, and ambulatory behavior). All 12 individuals reported improved vision in dimly lit environments in the injected eyes starting 2 weeks post surgery. They noted an improvement in the visual fields of all 12 patients. The extent of improvement in visual fields in the injected eyes correlated with the amount of salvageable retina that was targeted, effects of immediate postoperative head-positioning on the borders of the detachment, and map of the VF at baseline. Pupillary responses improved in the injected eyes of all 11 patients tested. Overall the results of objective and subjective test supported their hypothesis that the greatest improvement in visual function with subretinal gene therapy will occur in younger individuals. Although young patients had better visual function at baseline than did older individuals, they also had the greatest overall improvement in vision. Subretinal gene therapy appeared safe at all administered doses. Treatment with the vector did not elicit local or systemic adverse events. The one foveal dehiscence during subretinal injection resolved immediately post op (and did not appear related to the investigational product) and they subsequently modified the procedure. They did note the presence of PCR detectable (but not quantifiable) vector in blood post injection in 2 patients suggesting that transient systemic exposure can occur after administration of a high dose or in individuals with widespread outer retinal atrophy. Thus in future studies they do not intend to use doses higher than 1.5×10^{11} vector genomes per injection.

Gene therapy for Leber's congenital Amaurosis is safe and effective through 1.5 years after vector administration.

Simonelli F, Maguire AM, Testa F, Pierce EA et al.

Molec Ther 2010 Mar; 18(3):643-650.

The groups' results showed improvement in both subjective and objective measurements of visual/retinal function observed as early as 1 month after subretinal administration of a low dose of

AAV@-hrPE65v2 in 3 patients persisting through the 1.5 year post injection period. They noted improvement in both velocity and amplitude of papillary light reflex testing (PLR) and felt it was particularly relevant, considering the objectivity of the test which is used to probe transmission of retinal signals to higher nervous centers. The test also revealed a sustained improvement in light sensitivity in each of the subjects. Additionally they noted a significant reduction in nystagmus in all subjects continuing thru 1.5 post injection. Even though the subjects received unocular treatment, the nystagmus showed binocular dampening. Two patients had at least 50% reduction in both monocular and binocular nystagmus amplitude in primary gaze. Visual acuity significantly improved in the injected eye in all 3 patients as early as 1 month post injection and continued to improve. An analysis of the mobility tests performed at various time points post injection showed a gradual and more confident behavior of the subjects when navigating the obstacle course. A better perception of the course and its obstacles was evident.

The authors drew several conclusions for the 1.5 year follow-up data in the LCA2 patients treated in this study; 1) transgene expression resulting from AAV delivery is stable over time, thus ruling out the possibility that the improvement in visual function observed is the result of a transient neurotrophic effect induced by the surgical procedure, 2) the kinetics of the improvement with early amelioration which stabilizes over time are consistent with AAV-hrPE65v2 mediated correction of a visual cycle enzymatic defect, 3) although longer term follow-up is required, efficacy of gene transfer seems not be affected by the progressive degenerative nature of LCA2 and 4) AAV2 mediated gene transfer to the human retina, similarly to what was observed in muscle and CNS does not elicit the cytotoxic T lymphocyte responses to AAV capsid observed in human liver. The safety and efficacy results reported suggest that the retina is an amenable target for stable AAV2-mediated gene transfer in humans.

Leber congenital Amaurosis: Clinical correlations with genotypes, gene therapy trials update, and future directions.

Chung DC, Traboulsi EI.

J AAPOS 2009 Dec; 13(6):587-92.

This article is a superb summary and review of the workshop previously presented at AAPOS. For the diagnosis of early onset childhood retinal dystrophies the authors state that both a thorough ophthalmic history as well as a skilled clinical evaluation is necessary. If the review of systems is normal and the retinal dystrophy appears isolated, they recommend additional testing: ERG, color vision testing, Goldman visual fields, and /or OCT. They note that characteristic OCT findings are present in Best disease, X-linked juvenile retinoschisis, Goldman Favre, and some forms of LCA. They included this succinct table delineating the genetic subtypes of LCA.

Symbol	Locus	Gene	Mutation frequency in %	Gene Function	Selected clinical/imaging findings
LCA 1	17p13.1	<i>GUCY2D</i>	11.7	Hydrolysis cGMP	Very poor vision, normal appearing fundus, photoaversion
LCA 2	1p31	<i>RPE65</i>	6	Vitamin A visual cycle	Night blindness, transient vision improvement, relatively good vision early in life
LCA 3	14q31.1	<i>SPATA7</i>	Unknown	Unknown	Poor vision, retinal atrophy, attenuated vessels
LCA 4	17p13.1	<i>AILP1</i>	5.3	Rod PDE chaperone	Atrophic maculopathy, poor vision, night blindness
LCA 5	6q11-q16	<i>Lebercillin</i>	1.8	Protein transport (cilia)	Coloboma-like macula, ciliary defect
LCA 6	14q11	<i>RPGRIP1</i>	4.2	Protein transport (cilia)	Severe vision loss, initially normal retinal appearance, progress to pigmentary retinopathy
LCA 7	19q13.3	<i>CRX</i>	1	Photoreceptor development	Severe vision loss, infantile nystagmus, some dominant cases

LCA 8	1q13.3	<i>CRB1</i>	9.9	Muller cell-photoreceptor interaction	PPRPE, Coats-like response, thickened and disorganized retina on OCT
LCA 9	1p36	<i>Unknown</i>	Unknown	Unknown	Single report of large Pakistani family
LCA 10	6q21.3	<i>CEP290</i>	15	Protein transport (cilia)	Most common, extremely poor vision in most patients
LCA 11	7q31.3-q32	<i>IMPDH1</i>	8.3	Guanine synthesis	Rare, diffuse RPE mottling, no pigmentary deposits
LCA 12	1q32.3	<i>RD3</i>	0.1	Unknown	Poor vision, atrophic macular lesion, rare
LCA 13	14q23.3	<i>RDH12</i>	2.7	Vitamin A visual cycle	Fundus pigmentary fishnet or reticular pattern, Coats-like response
Not numbered	4q31	<i>LRAT</i>	0.5	Vitamin A visual cycle	Clinically like juvenile retinitis pigmentosa
Not numbered	6p21.3	<i>TULP1</i>	0.8	Protein transport (cilia)	Pigmentary retinopathy, reading vision in early stages

Visual acuity in patients with Leber's congenital Amaurosis and early childhood-onset retinitis pigmentosa.

Walia S, Fishman GA, Jacobson SG, Aleman TS et al.

Ophthalmology 2010 Jan. [Epub ahead of print]

This is a multicentered retrospective observational study correlating the visual acuity of patients with LCA and early childhood onset RP with mutations in underlying LCA genes. They included 169 patients with the diagnosis of LCA and 27 patients with early childhood onset RP. There was a wide variation in BCVA, but overall median VA was better in patients with RDH12, RPE65, and CRB1 mutations in the LCA group. Those with AIPL1, GUCY2D, CRX, and RPGRIP1 Gene mutations were associated with severely decreased VA beginning in the first year of life. Patients with RPGRIP1 mutation had a median VA of CF, with 78% of patients with VA<20/200. A trend toward age-related loss of central vision was observed in patients with either an RPE65 or CRB1 mutation, whereas those with AIPL1 and CEP290 mutations were observed to have stable VA across different decades.

The Leber congenital Amaurosis protein, AIPL1, is needed for the viability and functioning of cone photoreceptors cells.

Kirschman LT, Kolandaivelu S, Frederick JM Dang L et al.

Hum Mol Genet 2010 Jan. [Epub ahead of print]

Amongst the causative genes for LCA, mutations in Aipl1 have been associated with the most severe form of LCA leading to the degeneration of photoreceptor cells. A mouse model of LCA lacking Aipl1 exhibited rapid degeneration of both rods and cones and did not produce any light-dependent electrical response, recapitulating the disease phenotype seen in humans. To decipher the need for AIPL1 in cone photoreceptor cells, this experimental design eliminated AIPL1 from cones in the presence of viable rod photoreceptors, thereby avoiding any bystander cone death as rod photoreceptor loss was prevented. Thus they created a transgenic mouse model that expressed AIPL1 exclusively in rods. Transgenic expression of hAIPL1 restored rod morphology and the rod-derived ERG response, but cone photoreceptors were non-functional in the absence of AIPL1. Additionally, the cone photoreceptors degenerated, but at a slower rate compared with the Aipl1 (-/-) mice. They linked the degeneration to the highly reduced levels of cone PDE6 observed in the hAIPL1 transgenic mice. Their studies demonstrated that AIPL1 is needed for the proper functioning and survival of cone photoreceptors. However, rod photoreceptors also provide support that partially preserves cone photoreceptors from rapid death in the absence of AIPL1.

From the laboratory to the clinic: Molecular genetic testing in pediatric ophthalmology

Drack AV, Lambert SR, Stone EM.

Am J Ophthalmol 2010 Jan; 149:10-17.

This is a good review article and addresses pertinent questions relevant to children. The authors note that an excellent first resource to query for testing for various diseases is www.genetests.org. There are links to laboratories at which fee-for service testing is performed as well as detailed information on sending samples. Labs offering fee-for service testing must be CLIA certified. Additionally information on labs offering research-based testing is also available. They also have a GeneReview section that discusses the current detection rates for different types of testing. At www.retinoblastomasolutions.org, nonprofit fee-for service testing is offered for RB. Fee for service labs generally send the results to the ordering MD. The ordering physician must have a plan in advance for who will discuss and interpret the results with the patient.

Not all genetic tests are alike: some tests are designed to examine rapidly multiple genes for mutations that previously were identified in other patients (allele-specific tests), whereas other tests are designed to examine the entire coding sequence of 1 or more genes in search of disease causing mutations that previously might never have been observed (DNA sequencing). Regardless of the specific method used to identify disease-causing mutations in a given proband, the authors suggest that it is usually a good idea to also obtain samples from additional family members to help with the proper interpretation of the findings. Prenatal diagnosis is in theory possible for all disease that can be diagnosed by direct analysis of DNA. However many labs that offer genetic testing for eye diseases are not set up to provide results with sufficient speed to make prenatal testing practical. Thus genetic tests with reasonably high sensitivity, high specificity, moderate cost, and a reasonably rapid turnaround time (weeks) are now available for dozens of inherited eye diseases.

Which Leber congenital Amaurosis patients are eligible for gene therapy trials?

Drack AV, Johnston R, Stone EM.

J AAPOS 2009 Oct; 13(5):463-5.

This article delineates the extreme care that must be taken to confirm the genetic diagnoses before proceeding with gene replacement therapy. Many disease-causing mutations are novel when they are observed and must be investigated in detail to determine their pathogenicity. There are many non-disease-causing variations in the genome that must be differentiated from disease causing mutations by a rational multistep approach, which usually includes genotyping family members to be sure that mutations are on different alleles. This study is a retrospective cases series of 5 probands and their families using the estimate of pathogenic probability (EPP) algorithm and genotyping of family members. Only about 65% of LCA patients have a mutation that can be found with current technology. This article nicely outlines how to screen for eligible patients and what to look for.

My child has Leber congenital Amaurosis: Why is he/she not eligible for gene therapy trials?

Heon E.

JAAPOS 2009 Dec; 13(6):533-6.

Elise Heon's editorial delineates the salient points from the Drack article: 1) the clinical diagnosis based on pattern recognition is no longer sufficient as pathologies with different genetic causes can lead to a similar phenotype, 2) LCA is genetically heterogeneous (>15 genes) and not all genes have been identified, 3) the identification of a genetic defect, even if it changes an amino acid, does not mean that it causes disease. We all carry several disease and non-disease producing DNA variants. What is an acceptable control population in terms of quantity and ethnic background? When mutations are rare, polymorphisms are likely also to be rare, which can pose some challenges. These genotype results, like any other test, must be interpreted in the clinical context and validated using standard criteria. 4) The right treatment must be given to the correct person. 5) the phenotype must be clearly defined and one needs surviving photoreceptors both to receive the restored

photopigment and for the outcome to be measured. She cautions that we as ophthalmologist should be cautious to first do no harm as well as avoid giving the wrong message to very hopeful families.

The natural history of patients treated for TWIST1-Confirmed Saethre-Chotzen Syndrome.

Foo R, Guo Y, McDonald-McGinn DM, Zackai EH et al.

Plast Reconstr Surg 2009 Dec; 124(6):2085-95.

This is a retrospective case series of 22 patients with molecular confirmation of Saethre Chotzen syndrome from CHOP. Saethre-Chotzen syndrome is an autosomal dominant genetic disorder characterized by craniosynostosis, dysmorphism, and mild limb deformities. Features include low frontal hairline, facial symmetry, ptosis, downward slanting lid fissures, depressed nasal bridge, prominent ear helical folds, and incomplete simple syndactyly of the index and middle fingers and the 3rd and 4th toes. It is a heterogenous craniosynostosis syndrome with variable expression. The TWIST1 gene located on 7p21 is associated with the syndrome. Currently >100 unique TWIST1 mutations have been described. The TWIST1 gene plays an important role in mesenchymal signaling during embryonic development. The TWIST1 protein product is a transcriptional factor. Neither the location nor type of TWIST1 mutation was found to have a direct relationship with the type or severity of craniosynostosis. All patients in this series had craniosynostosis, though not all patients with a genotypic diagnosis of Saethre-Chotzen syndrome have premature suture fusion. Additionally neither the location nor the type of TWIST1 mutation correlated with the severity of presenting cranial vault dysmorphism and subsequent need for secondary intracranial surgery. TWIST1 deletions and intragenic mutations manifested as either mild or severe craniofacial deformities.

Genotyping microarray for CSNB-Associated genes.

Zeitz C, Labs S, Lorenz B, Forster U et al.

Invest Ophthalmol Vis Sci 2009 Dec; 50(12):5919-26.

Congenital stationary night blindness (CSNB) is a clinically and genetically heterogeneous retinal disease. Although ERG measurements can discriminate clinical subgroups, the identification of the underlying genetic defects remains complicated because of the genetic heterogeneity, the uncertainty about the mode of inheritance, and time consuming and costly mutation scanning and direct sequencing approaches. The authors established a mutation detection tool for CSNB, which overcomes costly, low-sensitivity, and time consuming prescreening methods. The advantage of this CSNB microarray is that this method neither depends upon large family pedigrees with more than one affected patient nor on a precise clinical discrimination of the different subforms of CSNB (complete vs incomplete). This microarray was 100% effective in determining the expected sequence changes in all known samples asses. Additionally investigation of 34 patients with CSNB not previously genotyped revealed sequence variants in 18%, of which 15% were felt to be disease-causing mutations. The authors also believe that it can be used to test the hypothesis that CACNA1F plays an important role in more progressive retinal disorders like cone- or cone-rod dystrophies. And as new mutations are identified, updated versions of the microarray will be generated in regular time intervals.

Gene therapy for red-green colour blindness in adult primates.

Mancuso K, Hauswirth WW, Li Q, Connor TB et al.

Nature 2009 Oct; 46(17265):784-7.

Gene therapy was performed on adult squirrel monkeys that were missing the L-opsin gene and whom had been color blind since birth. This study showed that the addition of a third opsin in adult red-green color deficient primates was sufficient to produce trichromatic color vision behavior. Before treatment, monkeys were trained to perform a computer based color vision test. About 20 weeks post treatment, the trained monkeys' thresholds for blue-green and red-violet improved, supporting trichromatic vision. These experiments demonstrated that a new color-vision capacity, as defined by new discrimination abilities, can be added by taking advantage of pre-existing neural circuitry and

internal experience aside, full color vision evolved in the absence of any other change in the visual system except the addition of a third cone type.

Molecular and phenotypic aspects of CHD7 mutation in CHARGE syndrome.

Zentner GE, Layman WS, Martin DM Scacheri PC.

Am J Med Genet A 2010 Mar; 52A(3):674-86.

This is a compilation of 379 published cases of CHARGE syndrome patients, having undergone molecular testing. CHARGE syndrome (no longer just an association) includes Coloboma of eye, Heart malformations, Atresia of choanae, Retardation of growth, Genital hypoplasia, and Ear anomalies. Of the 379 individuals tested, 254 (67%) were CHD7 mutation-positive, with 125 (33%) mutation negative. Methods of mutation testing varied across sites, but all included full sequencing of coding exons. Of the CHD7 mutations reported thus far, about 72% were nonsense or frameshift, 13% splice site, and 10% were missense. Almost all cases of CHARGE syndrome patients were sporadic, a small number of cases of familial and parent-to-child transmission of CHD7 mutations have been reported. From the 254 CHD7 mutation-positive individuals reported since 2004, the most common clinical findings were temporal bone anomalies (98%) and hearing loss (89%). Ocular colobomas were more common in mutation-positive (75%) than in mutation-negative (65%) individuals. The ocular colobomas were typically bilateral and more frequently involved the optic nerve and/or chorioretina with less frequent involvement of iris and eyelids. The mutation positive individuals were more likely to have inner ear malformations, including semicircular canal aplasia/dysplasia, facial nerve palsy and ocular colobomas and less likely to have delayed growth and development. The authors highly recommend the use of temporal bone CT as a diagnostic tool for evaluation of CHARGE patients. The paper also highlights the recent genetic and genomic studies that have provided functional insights in CHD7 and the pathogenesis of CHARGE syndrome.

Albinism: Classification, clinical characteristics, and recent findings.

Summers CG.

Optom Vis Sci 2009 Jun; 86(6):659-62.

This is a superb review of albinism. The current classification of albinism is determined by the affected gene, making the previously used terminology “partial or complete” and “tyrosinase-positive or negative” obsolete. The prevalence of albinism in the US is estimated to be 1 in 18,000. The cutaneous phenotype often permits the clinical diagnosis to be made, although gene testing is sometimes required to specify the type. Ocular findings do not allow one to determine the type of albinism. Delayed visual maturation is reported. Nystagmus typically develops by 6-8 weeks of age. Nystagmus is initially slow and has large amplitude, but the amplitude typically decreases within the first year of life. A positive angle kappa may be present. Classic features are the iris transillumination and absent or poor foveal development. Recognition visual acuity varies from 20/20 to 20/400, but is commonly close to 20/80. She includes a table with guidelines for prescribing glasses in young children with albinism. Teller acuity testing in adults with albinism yielded significantly better vision when measured with vertical presentation than when measured with the standard horizontal presentation of the cards, likely due to the predominantly horizontal character of the nystagmus. She notes that there is an increased prevalence of attention deficit and hyperactivity disorder in albinism.

Evaluation of vision-specific quality-of-life in albinism.

Kutzbach BR, Merrill KS, Hogue KM, Downes SJ et al.

J AAPOS 2009 Apr; 13(29):191-195.

This study used the National Eye Institute Visual Function Questionnaire (NEI_VFQ) to determine the effect of albinism-associated ophthalmopathy on quality of life (QOL) on 19 male and 25 females (median age 30.5 years; range 18-79). Mean best corrected visual acuity was 20/83 (range 20/20-20/320). Forty eight percent reported that they currently were able to drive. Notable impairments in

vision-related QOL for the population studied included difficulties with activities requiring both near and distance vision. More surprising were the impairments in vision-specific mental health and vision-specific role activities, given the overall high level of education and vocational functioning demonstrated by the surveyed population.

Refining the residual vision in Leber Congenital Amaurosis caused by *RPE65* mutations.

Jacobson SG, Aleman TS, Cideciyan AV, Roman AJ et al.

Invest Ophthalmol Vis Sci 2009 May; 50(5):2368-75.

This study evaluates quantitatively the key features of the residual vision in 30 patients with *RPE65*-LCA (age range 4-55 years). ERGs were abnormal in all patients tested. There were no detectable waveforms in 41% of patients, and the other 59% had signals to only some stimuli. Full Field stimulus testing (FST) was performed on 22 patients. Thirteen of the 22 patients (59%) had rod mediation of the blue stimulus, indicating that there was severely reduced but detectable residual rod function. The remaining 9 patients detected both red and blue stimuli with cone mediated vision. They then concluded that residual rod function (and not only cone function) is detectable by psychophysics in patients with *RPE65* LCA. There was no clear relationship of patient age to presence of residual rod function. Kinetic visual fields were measurable in 29 patients. There was a wide variation in the first two decades of life. Only islands of vision of limited extent were measurable after the third decade of life. Colocalized measures of visual function and retinal structure by OCT showed that visual function was detectable when a photoreceptor layer was detectable. The finding of different regional patterns of visual loss in these patients suggests that the optimal retinal site(s) for subretinal gene delivery to achieve efficacy are likely to change with disease progression.

Human *RPE65* gene therapy for Leber Congenital Amaurosis: Persistence of early visual improvements and safety at 1 year.

Cideciyan AV, Hauswirth WW, Aleman TS, Kaushal S et al.

Hum Gene Ther 2009 July 7. [Epub ahead of print]

This report extends the safety and efficacy data to 12 months for the 3 patients who previously underwent human gene therapy with rAAV2-vector for *RPE 65* LCA. These 3 patients, now 22, 24 and 25, remain healthy and without vector related serious adverse events. Visual acuities, central retinal structure by OCT and standard kinetic visual fields at the 6, 9, and 12 month time points were not different from at the 3 month time point. Statistically significant increases in light sensitivity were noted 1-3 months post treatment and there were no further changes in the magnitude or retinal extent of visual sensitivity increase.

The predictive value of Café au Lait macules at initial consultation in the diagnosis of NF1.

Nunley KS, Gao F, Albers AC, Bayliss SJ, Gutmann DH.

Arch Dermatol 2009 Aug; 145(8):929-930.

This is a retrospective case study of 110 patients who presented with café au lait macules (CALMs) and no other diagnostic features of NF1. They defined "typical" CALMs as lesions with uniform pigmentation and distinct, regular borders, while "atypical" or "irregular" CALMs were lesions with irregular, smudgy borders or nonhomogeneous pigmentation. Median age at initial presentation was 33 months (range 1-206 months). The median number of CALMs at presentation was 6 (range 1->20). Thirty one percent of children ((34 patients) met criteria for diagnosis of NF1 during the study period. Thirty two of these children met criteria by age 72 months. (Thirteen patients with typical CALMs and 17 patients with atypical CALMs who were younger than 6 years at last follow up remained undiagnosed.) In children eventually diagnosed as having NF1 after an initial presentation with only CALMs, 76% met NF1 criteria by age 4 years, 94% met NF1 criteria by age 6 years, and all patients met criteria by age 8 years. (The 2 patients diagnosed after 72 months were both lost to follow up and possibly would have been diagnosed earlier if they had been seen.) They note that patients with

a higher number of CALMs at presentation were more likely to develop NF1: 77% with 6 or more CALMs at initial presentation were eventually diagnosed as having NF1. In children eventually diagnosed as having NF1, the most common second feature to establish the NF diagnosis was axillary or inguinal freckling, occurring in 77% of patients. Second confirmatory features included Lisch nodules in 6 children, plexiform neurofibroma in 2 and tibial pseudoarthrosis in one child. Thus, results from this, the largest series to date, confirm that patients who present with 6 or more CALMs will eventually meet criteria for NF1, even if they have no other signs at presentation. Their data indicates that children with <6 CALMs or atypical CALMs rarely become diagnosed with NF1. With few exceptions, the diagnosis of NF1 is established by 72 months of age. (Note: Solitary CALMs are common and may occur in as many as 3% of infants, and 25% of healthy children. The presence of >3 CALMS is seen in only 0.2% to 0.3% with children with no known underlying disorder).

Prospects for retinal gene replacement therapy.

Smith AJ, Bainbridge JW, Ali RR.

Trends Genet 2009 Apr; 25(4):156-65.

This is an excellent article reviewing the progress in development of gene replacement therapy for inherited retinal dystrophies. The technical advances in vector technology, particularly for AAV-based vectors and a better understanding of potential difficulties surrounding gene transfer to the retinal cells have led to impressive rescue of retinal degeneration. The authors discuss the potential for treating various forms of retinal degeneration focusing on those gene defects that are likely to be most amenable to treatment: the disease must be caused by loss-of-function mutations to enable gene replacement therapy. It is also very helpful for clinical trials if the disease pathology enables a rapid readout of success, either because therapy results in an improvement of vision or because it is able to slow a rapidly progressing vision loss. They summarize the results from the 3 LCA trials and discuss other potential genes.

AAV mediated gene therapy for retinal disorders in large animal models.

Stieger K, Lheriteau L, Moullier, P, Rolling F.

ILAR J 2009; 50(2):206-224.

This article presents a review and detailed discussion of the various large animal models available for the study of AAV-mediated gene-based therapies in the retina. They provide an overview of the different retinal degenerative and neovascular disorders in humans that may be suitable for potential gene-based therapies: RP, LCA, ARMD, and DR. They also review the basic mechanism of AAV mediated gene transfer, cellular tropism in the retina and biodistribution of AAV vectors after retinal gene transfer in large animals. They note that because of differences of retinal structures among species and unique structures (i.e. macula and fovea) in the primate retina, nonhuman primates are also useful as preclinical animal models.

Juvenile neuronal ceroid lipofuscinosis (JNCL) and the eye.

Bozorg S, Ramirez-Montealegre D, Chung M, Pearce DA.

Surv Ophthalmol 2009 Jul-Aug; 54(4):463-471.

This is an excellent review of the neuronal ceroid lipofuscinoses (NCL) with particular attention to Batten research. The NCL are a group of inherited lysosomal storage diseases that together constitute the most common neurodegenerative disorders of childhood. They are clinically and genetically heterogeneous and are characterized by intracellular accumulation of autofluorescent material, neurodegeneration, and blindness. JNCL is the most common type of NCL in the US and Europe and visual loss is almost invariably the presenting symptom. Mutations in CLN3, a gene localized to chromosome 16p12 that encodes a 438 amino acid protein of unknown function underlie JNCL. To date over 30 CLN3 mutations have been reported. Molecular testing is available. No unifying hypothesis presently exists to explain the molecular mechanisms leading to JNCL. It is not

known if storage of lipopigment is a cause or effect of disease. The development of visual failure in JNCL is poorly understood. The ophthalmologist must play a critical role in both early diagnosis and documentation of progression of the disease.

Funduscopy and angiographic appearance in the neuronal ceroid lipofuscinoses.

Hainsworth DP, Liu GT, Hamm CW, Katz ML.

Retina 2009 May; 29(5):657-668.

The authors characterize the retinal features of neuronal ceroid lipofuscinoses (NCLs) by evaluating 29 patients with NCL (3 with infantile form, 2 with late infantile and 24 with the juvenile form). Additionally 40 confirmed carriers (parents, grandparents or siblings) were examined. This series of patients indicated that the NCLs vary significantly in retinal appearance, even amongst children with the same form of the disorder. Optic disc pallor was observed in most of the affected children. They found that the bone spicule pigment changes of the peripheral retina (often described in this disease) was not uniformly observed. Juvenile retinal findings included macular RPE atrophy and pigment stippling (>50%), epiretinal membrane (33%), bull's eye maculopathy (25%) and peripheral bone spicules (46%). The most consistent finding in the juvenile form was the diffuse RPE atrophy of the macula that was most prominent on angiography (93%). Heterozygous NCL carriers had no identifying retinal abnormalities. Although no effective therapies for the NCLs have yet been developed, clinical trials of neural stem cell transplantation and gene therapy for some forms of NCL have been initiated. Thus early diagnosis is also important to possibly identify candidates for these trials.

Detailed ophthalmologic evaluation of 43 individuals with PAX6 mutations.

Hingorant M, Williamson KA, Moore AT, van Heyningen V.

Invest Ophthalmol Vis Sci 2009 Jun; 50(6):2581-2590.

This is a phenotype-genotype evaluation of 43 patients with aniridia or closely related ocular anomalies. *PAX6* mutations were identified for all cases and classified according to type. Every individual had iris anomalies, though extremely varied. Nystagmus and foveal hypoplasia were common, being present in 41 of the 43 patients. Thirty patients had cataracts, 16 had corneal abnormalities, 10 had optic nerve hypoplasia, 5 had glaucoma and 4 had bilateral ptosis. Eighteen individuals had mutations that are predicted to cause loss of function of one copy of *PAX6*. One had a whole gene deletion and the other 17 had mutations leading to nonsense-mediated decay of the mutant mRNA and failure of translation. Nine had missense mutations and this group contained the only 2 individuals in the entire cohort without nystagmus. The phenotypes observed in missense mutation carriers clearly overlap those associated with loss of function mutations, but they were significantly milder. Ten individuals had mutations predicted to result in a protein with a C-terminal extension (CTE). Exudative vascular retinopathy resembling that observed in Coats' disease was observed in 2 CTE cases. The severity of the anomalies in the CTE group was comparable to that seen with the loss-of-function mutations but the iris anomalies were generally milder. Their study is consistent with existing literature that both null mutations (gene deletions and PTCs) and CTE mutations tend to generate relatively severe phenotypes. Missense phenotypes are particularly difficult to predict because the outcome depends on the activity of the mutant protein and this will vary from mutation to mutation depending on the location and function of the substituted residue.

Axenfeld-Rieger syndrome and spectrum of PITX2 and FOXC1 mutations.

Tümer Z, Bach-Holm D.

Eur J Hum Genet 2009 Jun 10. [Epub ahead of print]

This is an excellent review of the clinical features of the *PITX2* and *FOXC1* mutations and their relevant diagnostic approaches. Axenfeld-Rieger syndrome (ARS) is a dominantly inherited condition with genetic heterogeneity. Patients with ARS may have, in addition to their anterior segment

abnormalities, systemic malformations with incomplete penetrance and variable expressivity. The major systemic features are mild tooth abnormalities (microdontia, hypodontia, oligodontia and adontia) and redundant periumbilical skin. Craniofacial dysmorphism such as maxillary hypoplasia, sensory hearing loss, hypertelorism and congenital heart defects may also be part of the clinical spectrum. Glaucoma is present in 50% of patients. Mutations in the transcription factors, *PITX2* and *FOXC1* lead to ARS. The mutations show great diversity from intragenic mutations to submicroscopic deletions or duplications (*FOXC1*) to chromosome rearrangements (*PITX2*). There is no clear genotype-phenotype relationship but ARS patients with systemic changes usually have *PITX2* mutations. The underlying genetic defect is unknown in 60% of the cases and there are at least two more loci associated with ARS, the genes involved are yet to be identified.

Novel FOXC1 mutations associated with the congenital variant of Rett Syndrome.

Mencarelli MA, Spanhol-Rosseto A, Artuso R, Rondinella D et al.

J Med Genet 2009 Jul 2. [Epub ahead of print]

Rett syndrome (RTT) is a severe neurodevelopmental disorder representing one of the most common genetic causes of mental retardation in girls. The syndrome has a wide spectrum of clinical phenotypes including the classic form, the early onset seizure variant, the Zappella variant, the congenital variant, the "forme frusta" variant and the late regression variant. Mutations in the *MECP2* gene, located on Xq28, are responsible for 95% of classic RTT and 50% of Z-RTT, while the early onset seizure variant results from mutation in the *CDKL5* gene on Xp22. These authors report on the phenotype associated with *FOXC1* mutations and confirm that the *FOXC1* gene is responsible for the congenital variant of RTT. The overall clinical phenotype is characterized by normal pregnancy and delivery, normal auzological parameters at birth followed by hypotonia, irresponsiveness and irritability in the neonatal period. Deceleration of head growth is one of the most important diagnostic signs; severe postnatal microcephaly evident before the age of 4 months. Additional features include severe psychomotor delay with inability to walk, poor eye contact, tongue stereotypes and jerky movements of limbs and corpus callosum hypoplasia.

Choroideremia: New findings from ocular pathology and review of recent literature.

MacDonald IM, Russell L, Can C-C.

Surv Ophthalmol 2009 May-Jun; 54(3):401-407.

This is an excellent review article coupled with the histopathology from a 30 year old man originally diagnosed with retinopathy at age 7 years. A living brother was available to confirm the clinical diagnosis of choroideremia (CHM) by immunoblot and molecular genetic analysis. Histopathology showed diffuse abnormalities of the retina, RPE, and choriocapillaris were noted that varied from different areas and appeared to occur independent of each other. Retinal degeneration was observed above RPE and choriocapillaris with either preserved architecture or severe atrophy. Areas of relatively well preserved retina were found abruptly adjacent to areas of severe degeneration. He found focally conspicuous presence of "ectopic" nuclei external to the external limiting membrane, apparently dropping into the subretinal space and occasionally appearing intermingled with RPE cells. There were mild inflammatory cellular infiltration in the choroid beneath the abrupt transitions between retinal degeneration (atrophy) and relatively preserved retina. Inflammatory cells were also identified surrounding choroidal vessels. Most of the inflammatory cells were T-lymphocytes. Because choroideremia presents with RPE and retinal degeneration, Dr. Macdonald believes the finding of inflammatory cells at the active lesion might imply a local immune response. Recently 21 CHM carriers, aged 6-61 were studied with scanning laser ophthalmoscopy and OCT. The earliest disease states involved thickening of the retina with normal lamination. This stage was followed by photoreceptor loss, independent of, or associated with RPE changes, and then thinning of the retina in later life.

Accommodation measured with optical coherence tomography in patients with Marfan's syndrome.

Konradsen TR, Kolvula A, Kugelberg M, Zetterstrom C.
Ophthalmology 2009 Jul; 116(7):1343-8.

This is a clinical case-control study of 31 Marfan syndrome (MFS) patients with 31 age and refraction matched controls. Exclusion criteria included previous intraocular surgery or corneal surgery. The Marfan patients were also subdivided into those with and those without subluxated lenses. Mean age was 35 years (range 12-63 years). Measurements were performed using the Visante OCT. There was no difference between the Marfan group and the controls in accommodative power, or between the eyes of the Marfan patients, with and without lens subluxation. (MFS spherical equivalent was $-3.5 \pm 4.0D$ at baseline and $-10.1 \pm 5.0D$ during full accommodation, with total accommodative power of $-6.6 \pm 2.2D$. In the control group, mean spherical equivalent changed from $-2.6 \pm 3.2D$ at baseline to $-9.4 \pm 4.0D$ during full accommodation, with an accommodative power of $-6.8 \pm 2.3D$.) There was no difference in the anterior chamber depth between the eyes of MFS patients and the control group. (MFS: 2.92 mm at baseline to 2.83 during accommodation, increasing to 3.05mm during dilation vs. controls of 3.05mm at baseline, 2.93mm during accommodation and 3.17 during dilation. In the MFS eyes the lens was thicker at all time points: 4.27mm baseline, 4.39mm during accommodation, and 4.19 mm during dilation vs. controls of 3.97mm at baseline, 4.19 at accommodation and 3.94mm at dilation. All differences between the groups were statistically significant. There was no difference in lens thickness within the MFS subgroups. The baseline pupil diameter was smaller in the MFS patients and increased more during dilation compared with the controls. No difference was found within the MFS lens subgroups.

This study suggests that MFS patients have the same ability to accommodate as the general population despite the fact that the lens and pupil may be affected. The current study does have some limitations: including the imprecise determination of the exact endpoint of accommodation with the OCT. The subjective minus-lens-to-blur method has been shown to induce accommodation even in pseudophakic eyes.

Update on Usher Syndrome.

Saihan Z, Webster AR, Luxon L, Bitner-Glindzicz M.
Curr Opin Neurol 2009 Feb; 22(1):19-27.

This is an excellent review article updating the pathogenesis and genetics of Usher syndrome. Usher syndrome (USH) is a group of recessively inherited disorders resulting in dual sensory impairment of the audiovestibular and visual systems. Historically they have been divided into 3 clinical subtypes, but since the advent of the first gene for USH in 1995, 11 loci including 9 genes have been identified. Mouse models of the USH genes have produced hearing deficits analogous to those observed in human USH, with impaired vestibular function and sensorineural hearing loss. It was not until 2007 that Liu reported the first murine model of any of the USH genes to demonstrate a clear retinal phenotype. The USH2A null mice showed an essentially normal retinal phenotype at birth, but went on to develop overt photoreceptor degeneration as demonstrated by light and EM and a decline in ERG responses. The large volume of USH mutation (>100 pathogenic mutations alone for the two most common molecular forms USH1B and USH2A) has led to the creation of a dedicated repository in the form of an online interactive database, housing a collection of phenotypic and molecular genetic data from many reports published. It is the first publically available comprehensive repository for sequence variants relating to USH and related nonsyndromic disorders.

FOXL2 mutations and genomic rearrangements in BPES.

Beysen D, De Paepe A, Baere E.
Hum Mutat 2009 Feb; 30(2):158-169.

The *FOXL2* gene is one of 10 forkhead genes, the mutations of which lead to human developmental disorders, often with ocular manifestations. The heterozygous mutations lead to blepharophimosis

(BPES) that can appear isolated (type II) or associated with ovarian dysfunction leading to premature ovarian failure (POF) (type I). This paper reviews the mutation spectrum, the genotype-phenotypes correlations and the effects of the mutations. Mutation studies of *FOXL2* in BPES *patients* revealed considerable allelic heterogeneity, which needs to be taken into account when performing genetic testing. To date all individuals carrying a *FOXL2* mutation display the BPES phenotype, leading to the conclusion that there is a nearly complete penetrance of the eyelid phenotype. The proportion of de novo mutations is estimated to be >50% (authors unpublished data). Germline mosaicism has been described in familial BPES in 3 families, which should be taken into account in genetic counseling, presumably at a rate comparable to other autosomal dominant disorders. For most classes of mutations both intra- and interfamilial variable expressivity of the POF phenotype have been observed. Predictive genetic testing for POF risk should always be complemented by clinical post pubertal endocrinological follow up. In general spontaneous pregnancies may occur in approximately 5-10% of patients after diagnosis of POF, fertility is usually lost. The authors emphasize that genetic testing should be performed in the context of genetic counseling, and should be systematically complemented by a multidisciplinary clinical follow-up.

Childhood macular dystrophies.

Moore AT.

Curr Opin Ophthalmol 2009 Aug; 20(5):363-368.

This is an excellent review article. He discusses the developmental macular disorders: foveal hypoplasia, nanophthalmos and North Carolina macular dystrophy and related phenotypes. Their molecular genetics and diagnostic tests are updated. Dr. Moore then reviews the childhood macular dystrophies: Best disease (noting 2 new phenotypes: biallelic mutations in the bestrophin gene. Affected patients had reduced vision, irregular RPE with scattered white flecks and also demonstrated retinal edema. The EOG was severely abnormal, BUT the Full field ERG was also abnormal. The 3rd phenotype is rarer, ADVIRC: autosomal dominant vitreochoroidopathy, with a characteristic 360 degree post-ora atrophy and angle closure glaucoma is seen in some families). He reviews X-linked retinoschisis and the new reports of treatment with dorsolamide with modest improvement in vision and a reduction in cystic changes as demonstrated on OCT. He also updates Stargardt disease and Bulls eye dystrophy. He concludes that although most forms of childhood macular dystrophy are currently not amenable to treatment, recent advances in molecular genetics, cell biology and the development of animal models of disease leads to optimism that the next decade will see the introduction of novel therapy into clinical practice.

XIII. RETINOBLASTOMA

The effect of race on the incidence of retinoblastoma. Krishna S et al. JPOS Sept-Oct 2009; 46: 288-293.

Age-adjusted incidence rates, rate ratios, and 95% confidence intervals were determined in 109 regions from 1993 to 1997 using compiled data from the International Agency for Research on Cancer. Because retinoblastoma is a genetic disease, its incidence is similar among varied populations.

Management and outcome of unilateral retinoblastoma. Mallipatna AC, Sutherland JE, Gallie BL, et al. J AAPOS 2009;13:546-550. Dec

Unilateral retinoblastoma is typically treated with enucleation. There are an increasing number of cases treated with chemotherapy. The authors reviewed management and

outcome of children with unilateral retinoblastoma at their facility over a 20 year period. One hundred and twenty-two cases of unilateral retinoblastoma were looked at. One hundred and six were treated with enucleation. In 16 cases an attempt was made to preserve the eye. Seven of these 16 eventually went on to receive an enucleation of the affected eye. One patient died from systemic metastasis because the family refused enucleation. The authors state that if the decision is made to try to avoid enucleation in unilateral retinoblastoma cases, careful classification and selection of eyes is mandatory. Also, the family must have a clear understanding of success and risks.

Recent advances in retinoblastoma genetic research.

Nichols KE, Walther S, Chao E, Shields C, Ganguly A.

Curr Opin Ophthalmol 2009 Sep; 20(5):351-355.

This article highlights the recent advances in RB research. In the review they note that the cumulative mortality of RB at 50 years was 25.5% for survivors with hereditary and 1.0% for those with nonhereditary disease. Additional data shows that retinomas represent true premalignant lesions and not regressed RB tumors, as previously thought. Translational advances in RB genetic research include development of an allele-specific assay that now enables the identification of mutational mosaicism thereby increasing the rate of RB1 mutation detection in bilaterally affected patients to as high as 95%.

Approximately 30% of RB is bilateral, with 80% of cases due to a sporadic mutation and 20% due to an inherited mutation. Unilateral RB accounts for 70% of cases of which 88% are sporadic and 12% familial. Genetic testing is often recommended for children with unilateral RB to guide the treatment of the primary tumor and direct clinical management in terms of anticipation for possible multifocal tumors and development of pineoblastoma or secondary malignancies. Genetic testing if offered to all affected children without fresh tumor available for analysis can yield equivocal results.

Trilateral retinoblastoma: Potentially curable with intensive chemotherapy.

Dunkel IJ, Jubran RF, Gururangan S, Chantada GL et al.

Pediatr Blood Cancer 2010 Mar; 54(3):384-7.

This is a retrospective multicenter review of 13 patients with trilateral Rb treated with intensive chemotherapy, defined as the intention to include high dose chemotherapy with autologous hematopoietic stem cell rescue. Twelve patients had bilateral intra-ocular Rb and one had unilateral disease. Median age at diagnosis of intra-ocular Rb was 8 months. Five patients had trilateral Rb at original diagnosis of intra-ocular Rb; 8 had later onset at median age of 35 months (range 3-60 months). Trilateral sites were pineal (11) and suprasellar (2). Seven patients had localized (M-O) disease while 6 presented with leptomeningeal dissemination (M-1+). One patient died due to toxicity (septicemia and multi-organ failure) while undergoing induction chemotherapy. Three patients developed tumor recurrence prior to receiving high dose chemotherapy with autologous hematopoietic stem cell rescue. Nine patients received high dose chemotherapy at a median of 5 months (range 4-9) post diagnosis of trilateral disease. Five patients survive event-free at a median of 77 months (range 36-104 months) and never received external beam radiation therapy. Four of seven patients with M-O disease survive event-free versus only 1 of 6 patients with M-1+ disease.

Whereas patients with intra-ocular Rb have an excellent prognosis for survival, trilateral disease is rare (6% of bilateral RB) and accounts for a significant proportion of the mortality. These results demonstrate that intensive chemotherapy is potentially curative for patients with trilateral Rb, including those who present symptomatically and with large tumors. There is now an ongoing prospective multi-center trial to better determine the role of intensive chemotherapy in the treatment of patients with trilateral Rb.

Does a nanomolecule of carboplatin injected periocularly help in attaining higher intravitreal concentrations?

Shome D, Poddar N, Sharma V, Sheorey U et al.

Invest Ophthalmol Vis Sci 2009 Dec; 50(12):5896-900

This is an experimental animal study which compared intravitreal concentrations (VC) of commercially available carboplatin (CAC) and a novel nanomolecule carboplatin (NMC) following periocular injection. Twenty four white rats were injected with CAC (1 ml) periocularly in the right eye and NMC (1ml) in the left eye periocularly. They found that the vitreous concentration of NMC was much higher compared to vitreous concentration of CAC in all the animals in the first week and statistically significant. Conversely on days 14 and 21, the vitreous concentration of CAC was found to be statistically significantly higher than the vitreous concentration of NMC. The authors propose that the NMC, being a smaller molecule, establishes a stronger osmotic gradient for transscleral migration initially in to the vitreous, compared to CAC. In the later stages this molecule probably also gets transported out of the vitreous cavity earlier than the conventional larger molecule. Clinically this might mean the use of sustained release devices for the release of this NMC for maintenance of vitreous concentrations similar to or great than the conventional molecule. The authors believe that nano-particulate bound carboplatin may help enhance the proven adjuvant efficacy of periocular carboplatin over and above systemic chemotherapy in treating human RB, especially those with vitreous seeds.

Canadian guidelines for retinoblastoma care.

Gallie B.

Can J Ophthalmol 2009 Dec; 44(6):639-42.

This editorial by Brenda Gallie outlines the newly established recommendations for RB care in Canada. She notes that achieving consensus in the first Canadian Guidelines is the initial step toward creating a National Retinoblastoma Strategy. These recommendations include; 1) Early detection and immediate referral of children with RB, 2) Canadian children with Rb must be managed by multidisciplinary teams with the necessary resources and sufficient experience, 3) Immediate referral upon suspicion of RB as timely diagnosis achieves good treatment outcomes, 4) genetic testing for RB1 gene mutation as it is the key to predicting disease, reducing risks, and supporting surveillance for mets of Rb, 5) current Rb treatment warranted for different stages and scenarios of disease, and suggest a standardized treatment plan for Canada, 6) long term follow-up as survivors of childhood cancer face potential chronic health issues, 7) psychosocial care and access to services guided by research and current best practice, and 8) increased public awareness and education about Rb.

Changing causes of enucleation over the past 60 years.

Setlur VJ, Parikh JG, Rao NA.

Graefes Arch Clin Exp Ophthalmol 2010 Apr; 248(4):593-7.

This is a retrospective clinicopathologic study of enucleated globes over the past 60 (1950-2006) years at Doheny Eye Institute. Over time, the total number of enucleated globes per decade decreased from a peak of 1,014 in the 60's to 275 in the 2000's. Glaucoma was the most common cause of enucleation early in the study, comprising 23% and 31% for the 50's and 1960's respectively. The next 3 decades showed a drop in enucleation due to glaucoma. Conversely, neovascular glaucoma increased from 21% to 57% of glaucoma in the same time period. The 1990 and 2000's each showed a higher proportion of neovascular glaucoma which was significantly different from the lower amounts seen in either 1950's or 60's. However, as the total number of enucleations for all causes steadily decreased, neoplasms represented an increasingly larger proportion. Within the category of neoplasms, a trend between melanoma and Rb was also seen. In the 1950's, 77% of enucleations secondary to neoplasm were due to melanoma. Rb was responsible for 17% of

enucleations in the 1950's. In each subsequent decade, Rb made up an increasingly larger share of neoplasms, while melanoma consistently decreased. Trauma did not show a consistent trend over time as glaucoma and tumor did. They did not see a decrease in trauma-related enucleations until after the 1980's. Trauma has then subsequently decreased in each of the last 3 decades, suggesting improved repair starting in the 1980's. Improved medical and surgical treatment of conditions that lead to end-stage eye disease have led to a decrease in total enucleated globes.

A visual approach to providing prognostic information to parents of children with retinoblastoma.

Panton RL, Downie R, Truong T, MacKeen L et al.

Psycho-oncology 2009 Mar; 18(3):300-4.

Providing information at diagnosis concerning long term treatment complexity helps parents of children with cancer. The authors developed a graphic tool, DePICT (Disease-specific Electron Patient Illustrated Clinical Timeline) to visually display entire RB treatment courses from real time clinical data. They retrospectively evaluated the effectiveness of DePICT by having 44 parents complete a 14 questionnaire to evaluate their understanding of RB treatment and outcomes. Their results showed that DePICT communicated complex health information in a manner that offset educational disadvantages often associated with understanding and using this knowledge. They showed that communication to parents is enhanced by graphic tools. Further, understanding risk is related to parent age, with older parents averaging higher scores, regardless of education attainment or first language. Their results implied that parental understanding of risk is related to their command of the language used by the clinician.

A Phase I study of periocular topotecan in children with intraocular retinoblastoma.

Chantada GL, et al.

Invest Ophthalmol Vis Sci 2009 Apr; 50(4):1492-6.

Purpose: To identify the maximum tolerated dose and dose-limiting toxicity of periocular topotecan in patients with relapsed or resistant intraocular retinoblastoma who are facing imminent enucleation.

Methods: For this phase I study, a starting dose of 0.5 mg of periocular topotecan administered through a 25-gauge needle was given with inpatient escalation at a rate of 0.5 mg/cycle according to toxicity, up to a maximum dose of 2 mg. Two courses separated by 2 weeks were scheduled. Plasma levels of topotecan were measured by high-performance liquid chromatography in patients with available intravenous catheters.

Results: Seven eyes of five patients were treated with a total of 14 courses of periocular topotecan. Only mild orbital edema occurred, and grade 1 vomiting developed in the first patient that was controlled with ondansetron for the following courses. Dose-limiting toxicity was not reached and the maximum tolerated dose was set at the target dose of 2 mg ($n = 5$ eyes). Lactone topotecan systemic exposure was lower than 55 ng/mL · h and it correlated linearly with dose in this small cohort. Even though the study was not designed to assess response, one eye was preserved after a partial response, but the remaining six were enucleated, either after a short period of disease stabilization followed by further therapy with other agents in five patients or by rapidly progressive disease in one.

Conclusions: The dose limiting toxicity was not reached. Up to 2 mg of periocular topotecan could be given safely, but further studies are necessary to determine its effect on retinoblastoma.

Comment: Periocular chemotherapy (subconjunctival, subtenon, retrobulbar) has potential to minimize systemic exposure to chemotherapy during retinoblastoma treatment. This may be associated with local or systemic toxicities. The use of intravenous and periocular topotecan has been studied for retinoblastoma, and this study provides new data about systemic absorption from periocular injection.

The success of primary chemotherapy for group D heritable retinoblastoma.

Cohen VM, Kingston J, Hungerford JL.

Br J Ophthalmol 2009 Jul; 93(7):887-90.

Aims: To report the ocular survival and event-free survival following primary multiagent chemotherapy for group D, heritable bilateral retinoblastoma (RB).

Methods: The RB database was used to identify children with heritable, bilateral RB treated with primary chemotherapy (six cycles of vincristine, etoposide and carboplatin). Only Group D eyes with more than 12 months' follow-up were analysed. The timing, number and type of salvage treatments were recorded. Kaplan–Meier estimates for the ocular survival and event-free survival (percentage of eyes that avoided external beam radiotherapy and/or enucleation) were performed as a function of time.

Results: Of 18 group D eyes, two (11%) were treated successfully with chemotherapy alone, nine (50%) underwent successful salvage treatment, and seven (39%) were enucleated. The median time from completing chemotherapy to enucleation was 9 months (range 4 to 25 months). Ocular survival was 67% at 2 years. External beam radiotherapy proved successful salvage treatment in five of nine eyes, so the event-free survival was 34% at 2 years.

Conclusion: Multiagent chemotherapy alone is rarely sufficient for the preservation of group D eyes. External beam radiotherapy and plaque radiotherapy remain important salvage treatments for advanced, heritable retinoblastoma.

Salvage external beam radiotherapy after failed primary chemotherapy for bilateral retinoblastoma: rate of eye and vision preservation.

Chan MP, Hungerford JL, Kingston JE, Plowman PN.

Br J Ophthalmol 2009 Jul; 93(7):891-4.

Background: Radiation is implicated in the induction of second malignancies in children with bilateral retinoblastoma. There is a need to determine whether this risk can be justified by good visual outcome when external beam radiotherapy (EBRT) is used as a salvage treatment.

Aim: To study the effectiveness of EBRT as a salvage treatment after failed primary chemotherapy and focal treatment in bilateral retinoblastoma.

Methods: This is a retrospective observational case series. The outcome measures after EBRT are: rate of eye preservation, rate of tumour control, visual potential, visual acuity and radiation-induced side-effects.

Results: Thirty-six eyes (22 patients) were included. The median follow-up after EBRT was 40 months (19–165 months). Thirty-two eyes received lens-sparing radiotherapy, and four received whole-eye radiation. The rate of eye preservation was 83.3% (30/36 eyes). Twenty-four eyes (66.7%) were controlled by EBRT and required no further treatment. Of the 30 preserved eyes, 20 eyes (66.7%) had extramacular tumours without retinal detachment and therefore potential for central vision. The final visual acuity was recorded for 19 eyes. Ten eyes (52.6%) read 6/9–6/5, three eyes (15.8%) read 6/18–6/36, and six eyes (31.6%) read 6/60 or worse. Significant radiation-induced side effects were limited to

cataracts and dry eyes with whole-eye radiation. There were no second cancers or deaths.

Conclusion: Salvage EBRT is highly effective in preserving eyes with useful vision in bilateral retinoblastoma after failed chemotherapy and focal treatments. These results will help the parents and ophthalmologists of such patients to reach an informed decision when weighing up the benefits of EBRT against its potential oncogenic effect.

Orbital recurrence of retinoblastoma following enucleation.

Kim JJ, Kathpalia V, Dunkel IJ, Wong RK, Riedel E, Abramson DH.

Br J Ophthalmol 2009 Apr; 93(4):463-467.

This is a retrospective case series of 1674 consecutive patients who underwent enucleation for RB between 1914 and 2006. This study identified 71 biopsy confirmed cases of orbital recurrence with an

overall incidence of 4.2%. The incidence before 1960 was 5%, whereas the incidence after 1960 was 4%. Among the 71 patients with orbital recurrences, there were 93 enucleated globes (22 bilateral enucleations). The diagnosis of orbital recurrence was made between 1 and 24 months after enucleation (mean 6 months) with 97% (69 of the 71) being diagnosed in the first 12 months. The most common presentation was a clinical complaint such as eyelid swelling or chemosis. Several histopathological features of enucleated eyes are recognized as risk factors for extraocular relapse: optic nerve invasion with tumor involvement of resection margin and extrascleral spread. In this series 75% of patients with orbital recurrence eventually died from systemic metastatic disease. These authors' current protocol for all patients with orbital tumor recurrence following enucleation is a full metastatic workup with a brain MRI, abdominal CT scan, lumbar puncture, bone scan and bone marrow aspirate and biopsy. The authors stress the importance of careful follow-up during the first 2 years after surgery. They emphasize that clinicians should be aware that patients may be asymptomatic or present with subtle, nonlocalising or even contralateral symptoms.

Microscopic scleral invasion in retinoblastoma. Clinicopathological features and outcome.

Cuenca A, Giron F, Castro D, Fandino A et al.

Arch Ophthalmol 2009 Aug; 127(8):1006-1010.

The authors report on 32 of 386 patients having undergone enucleation. Of those 32 cases, 21 were intrascleral and 11 cases were transcleral (invading the whole width of the sclera and invading periorbital tissue). Optic nerve invasion was present in 23 patients (72%). All patients had received chemotherapy (16 receiving moderate intensive therapy and 16 with a higher intensity regimen). Seven patients had an extraocular relapse at a median time of 9 months (range: 5-20 months). All patients who had a relapse died. Patients receiving the high intensity adjuvant chemotherapy had a better outcome compared with those receiving lower intensity regimens. The authors conclude, that microscopic sclera invasion is an uncommon feature in RB and is a marker for aggressive disease with the potential for systemic dissemination.

With CRD and lower dose P-EBR. Despite the attempt to avoid EBR in the CRD alone group, 30% eventually required T-EBR for globe salvage and the standard dose (3800-450cGy).

Chemoreduction for Group E retinoblastoma: Comparison of chemoreduction alone versus chemoreduction plus low-dose external radiotherapy in 76 eyes.

Shields CL, Ramasubramanian A, Thangappan A, Hartzell K et al.

Ophthalmology 2009 Mar; 116(3):544-551.

Group E RB typically has been managed with enucleation. Though there are circumstances in which globe retention is desirable, particularly when both eyes manifest group E disease or when the opposite eye is enucleated. In this paper, the authors retrospectively analyzed the results of chemoreduction (CRD) alone versus CRD and low dose-prophylactic external beam radiotherapy (P-EBR). Of 76 eyes treated between 1994 and 2007, 64 received CRD alone and 12 received CRD +P-EBR. Their data showed globe salvage in 25% of eyes managed with CRD alone, in 50% of eyes with CRD + T-EBR, and in 83% of eyes managed with CRD and lower dose P-EBR. Despite the attempt to avoid EBR in the CRD alone group, 30% eventually required T-EBR for globe salvage and the standard dose (3800-450cGy). At 5 years, there were no patients in either group with mets or pinealoblastoma or who had died.

Group E RB managed with CRD + P-EBR showed significantly less recurrence than CRD alone, thus allowing for more globe retention and avoidance of T-EBR. Their results indicated a greater chance for globe salvage with CRD +P-EBR, because enucleation at 2 years was necessary in 26 (48%) of 55 eyes in the CRD group and 1 (9%) of 11 eyes in the CRD + P-EBR group. This finding is important because the opposite eye generally was threatened with RB or had been enucleated previously.

Retinoblastoma regression patterns following chemoreduction and adjuvant therapy in 557 tumors.

Shields CL, Palamar M, Sharma P, Ramasubramanian A, et al.
Arch Ophthalmol 2009 Mar; 127(3):282-290.

This is a retrospective case series of 557 RBs from 157 patients with 239 affected eyes treated between 1994 and 2007. The authors evaluated tumor regression patterns following 6 cycles of chemoreduction (CRD) plus focal consolidation therapy. RB demonstrates a recognizable feature of intralesional calcification at presentation and the degree of calcification often increases following therapy. Calcification within RB is dystrophic and occurs within regions of necrosis. Regression patterns included type 0 (no remnant), type 1 (calcified remnant), type 2 (noncalcified remnant), type 3 (partially calcified remnant), and type 4 (flat scar). RB regressions were type 0 (n=10), type 1 (n=75), type 2 (n=28), type 3 (n=127) and type 4 (n=317). Small RBs of 3 mm or less (n=240) regressed most often to type 4 (92%), medium tumors of 3 to 8 mm (n=232) regressed most often to type 3 (34%) or type 4 (40%), and large tumors of >8mm (n=85) regressed most often to type 1 (40%) or type 3 (49%). By multivariate analysis, the main factors affecting the regression pattern were tumor size and location. Larger tumors and those nearer the foveola showed type 1 or type 3 regression patterns, whereas smaller tumors or those located more peripherally showed type 4 regression pattern. Older age was more predictive of type 3 pattern, possibly reflecting larger tumor size in older children, whereas familial hereditary pattern predicted type 4 pattern, and could reflect smaller tumor size in neonates. Following chemoreduction, most small RBs result in a flat scar, intermediate tumors in a flat or partially calcified remnant, and large tumors in a more completely calcified remnant.

Sudden dispersion of retinoblastoma shortly after initial chemotherapy treatment.

Parness Yossifon R, Bryer JP, Weinstein JL, Srikumaran D, Mets MB.
Am J Ophthalmol 2009 May; 147(5):903-906.

The authors present 3 cases of unilateral RB that demonstrated an atypical response with intraocular dissemination of RB shortly after initial chemotherapy treatment. One was an 8 week old with Group E tumor (per the International Classification), the second aged 3 years old with Group D1, and the third child was 2 years old with a tumor staged Group D1. There were no vitreous seeds or subretinal fluid at presentation. None had a positive family history of RB. Two cases received a 2 drug regimen of carboplatin and etoposide and one received a 3 drug regimen of carboplatin, etoposide, and vincristine. In each case the RB dispersed with tumor cells in the vitreous shortly after initial chemo, leading to subsequent enucleation of the eye. The cases were presented to raise awareness of the possibility of sudden dispersion after initiation of chemotherapy.

Quantitative analysis of tumor size in a murine model of retinoblastoma.

Dimaras H, Marchong MN, Gallie BL.
Ophthalmic Genetics 2009 Jun; 30(2):84-90.

The Tag-RB model is the most commonly used murine model of RB for pre-clinical studies. In this paper the authors describe a highly sensitive method to quantify tumor volume in a mouse model of RB, from the earliest stages of tumor initiation to large, advanced tumors. Their methodology combined immunohistochemistry, digital slide scanning and computer image analysis, and could be applied to quantitatively assess and characterize early tumor development in other models.

AAV-mediated local delivery of Interferon- β for the treatment of retinoblastoma in preclinical models.

Shih CS, Laurie N, Hotzmacher J, Spence Y et al.
Neuromol Med 2009 Mar; 11(1):43-52.

In this study, the authors tested the efficacy of AAV-mediated delivery of IFN- β using preclinical models of RB. They found that a potent anti-tumor effect can be achieved using with minimal

systemic exposure of IFN- β or spread of the AAV viral vector outside of the eye. This study differed from previously published data on gene therapy for RB in 3 ways. First, they delivered a cytokine that directly affected tumor survival and growth. The previous studies delivered the HSV-TK gene that sensitized the tumor cells to systemic delivery of ganciclovir. Second, in this study, infection of the tumor cells, the retina, or other ocular tissues is sufficient to deliver IFN- β to the vitreous and reduce tumor burden. Previously, only the infected tumor cells were sensitized to ganciclovir. Third, they used an AAV vector delivery method and the previous Study delivered HSV-TK using adenovirus. They also used the cell line Y79-Luc that was the least sensitive to IFN- β in the xenograph cell experiment.

Does a nanomolecule of carboplatin injected periocularly help in attaining higher intravitreal concentrations?

Shome D, Poddar N, Sharma V, Sheorey U et al.

Invest Ophthalmol Vis Sci 2009 Jul 23. [Epub ahead of print]

This is an experimental animal study which compared intravitreal concentrations (VC) of commercially available carboplatin (CAC) and a novel nanomolecule carboplatin (NMC) following periocular injection. Twenty four white rats were injected with CAC (1 ml) periocularly in the right eye and NMC (1ml) in the left eye periocularly. They found that the vitreous concentration of NMC was much higher compared to vitreous concentration of CAC in all the animals in the first week and statistically significant. Conversely on days 14 and 21, the vitreous concentration of CAC was found to be statistically significantly higher than the vitreous concentration of NMC. The authors propose that the NMC, being a smaller molecule, establishes a stronger osmotic gradient for transscleral migration initially in to the vitreous, compared to CAC. In the later stages this molecule probably also gets transported out of the vitreous cavity earlier than the conventional larger molecule. Clinically this might mean the use of sustained release devices for the release of this NMC for maintenance of vitreous concentrations similar to or great than the conventional molecule. The authors believe that nano-particulate bound carboplatin may help enhance the proven adjuvant efficacy of periocular carboplatin over and above systemic chemotherapy in treating human RB, especially those with vitreous seeds.

Recent advances in retinoblastoma genetic research.

Nichols KE, Walther S, Chao E, Shields C, Ganguly A.

Curr Opin Ophthalmol 2009 Sep; 20(5):351-355.

This article highlights the recent advances in RB research. In the review they note that the cumulative mortality of RB at 50 years was 25.5% for survivors with hereditary and 1.0% for those with nonhereditary disease. Additional data shows that retinomas represent true premalignant lesions and not regressed RB tumors, as previously thought. Translational advances in RB genetic research include development of an allele-specific assay that now enables the identification of mutational mosaicism thereby increasing the rate of RB1 mutation detection in bilaterally affected patients to as high as 95%.

Approximately 30% of RB is bilateral, with 80% of cases due to a sporadic mutation and 20% due to an inherited mutation. Unilateral RB accounts for 70% of cases of which 88% are sporadic and 12% familial. Genetic testing is often recommended for children with unilateral RB to guide the treatment of the primary tumor and direct clinical management in terms of anticipation for possible multifocal tumors and development of pineoblastoma or secondary malignancies. Genetic testing if offered to all affected children without fresh tumor available for analysis can yield equivocal results.

Frontiers in the management of retinoblastoma.

Lin P, O'Brien J.

Am J Ophthalmol 2009 Aug; 48(2):192-198.

This is a superb review article. Currently, the COG (Children's Oncology Group) is using the international classification system, which was formulated in 2003 and based upon the Murphree classification system, to predict outcomes in response to standardized protocols of chemotherapy used in conjunction with focal consolidative therapy. Most chemotherapy protocols for larger tumors use 2- or 3 drug chemotherapy with carboplatin, etoposide, and vincristine, but institutions vary on the exact protocol used. They include a table outlining the management strategy and prognosis of disease. They note that external beam radiation therapy has largely been replaced with aggressive chemoreduction and focal consolidative therapy for intraocular disease, but that it may still have usefulness in treating extraocular RB.

They briefly review the genetics of RB, noting that currently there are >900 mutations reported, many occurring within crucial areas of the protein involved in its binding to its normal targets, such as the E2F transcription factor. Additionally, genes other than RB1 undergo genetic alteration or amplification in the human RB cancer syndrome. N-myc is amplified in 10% of human RBs. In one series, 65% of human RBs have amplifications in the MDMX gene which produces a protein involved in the degradation of the RB and p53 protein products. Ten percent of RB tumor samples had extra copies of MDM2.

They review experimental treatment approaches including molecular targeting. One group recently found that a small molecule inhibitor of the MDM2/MDMX and p53 interaction, Nutlin 3A was able to induce cell death in human RB cell lines. Others demonstrated that when used in combination with another chemo drug, topotecan, Nutlin 3A killed human RB cell lines. This group also showed an 82 fold reduction in tumor burden in mice when Nutlin 3A was injected subconjunctivally with topotecan. They also note another approach using local delivery techniques to limit side effects. Abramson and associates have demonstrated good outcomes after direct intraophthalmic artery injections of melphalan. Unlike their Japanese colleagues, the Abramson group used selective catheterization of the ophthalmic artery, thereby theoretically avoiding toxicity to the brain.

XIV TRAUMA

Airsoft gun-related ocular injuries: novel findings, ballistics investigation, and histopathologic study.

[Kratz A](#), [Levy J](#), [Cheles D](#), [Ashkenazy Z](#), [Tsumi E](#), [Lifshitz T](#).

[Am J Ophthalmol](#). 2010 Jan;149(1):37-44. Epub 2009 Oct 29.

PURPOSE: To describe the ocular injuries related to airsoft gun bullets, investigate the ballistics of airsoft bullets, record real-time impact of the bullets on an eye, and investigate the histopathologic changes within the cornea after being hit by an airsoft gun bullet.

METHODS: All consecutive cases of patients with airsoft gun-related ocular injuries during 2006 to 2008 were included in this study. Porcine eyes were used for high-speed video photographs of bullet impacts. Rabbit eyes were used for the histopathologic investigation. All patients were treated in the Department of Ophthalmology at Soroka University Medical Center, Beer-Sheva, Israel. Laboratory investigations were performed at Ben-Gurion University of the Negev, Beer-Sheva, Israel. The main outcome measures were ocular injuries of the patients, ballistics of the airsoft bullets, nature of corneal deformation upon impact, and corneal histopathologic changes after the hit.

RESULTS: Fifty-nine patients with a mean age of 9.8 +/- 3.8 years (range, 2.8 to 26 years) were examined; 49 were male (83.1%). The ocular injuries included hyphema, corneal edema, corneal erosion, traumatic mydriasis, and posterior segment involvement. A novel, "donut" form of corneal erosion was seen and also demonstrated by the histopathologic investigation. Substantial anterior segment deformation was recorded in real-time using the high-speed video camera.

CONCLUSIONS: Airsoft gun injuries affect mainly young men and can be visually threatening. Typical ocular injuries along with a unique form of corneal erosion can be seen.

Use of digital camera imaging of eye fundus for telemedicine in children suspected of abusive head injury.

Saleh M, Schoenlaub S, Desprez P, et al.

Br J Ophthalmol 2009 Apr; 93(4):424-8.

Aim: Pilot study of the role of RetCam imaging for telemedicine in lieu of availability of ophthalmologist examination for cases of suspected abusive head injury.

Design: Cross-sectional observational study.

Participants: 21 children admitted in the paediatric units of the University Hospital of Strasbourg (France) with suspicion of abusive head trauma were included.

Methods: Children were examined by standard ophthalmoscopy. Photographs were taken using the RetCam-120 Digital Retinal Camera. Eye fundus images were stored and remotely read by an ophthalmologist. Patients also had radiographic skeletal series to look for bone fractures, and CT scan and/or MRI of the head to look for intracranial haemorrhages.

Main outcome measures: The absence or presence of retinal haemorrhages was assessed by both methods. Feasibility, sensitivity and specificity of the digital camera procedure were determined.

Results: 85.7% of the children presented cerebral bleeding, and 14 out of the 21 (66.7%) had retinal haemorrhages on ophthalmoscopy. The digital camera detected the retinal abnormalities in all cases. One false positive case was also reported. The sensitivity of the digital camera detection method was 100% with a specificity of 85.7%. 14 patients were eventually diagnosed as suffering from abusive trauma. RetCam helped establishing the diagnosis of abuse in 92.8% of these cases.

Conclusions: Digital photography compared with ophthalmoscopy has a good sensitivity and specificity in detecting retinal haemorrhages. Remote reading of RetCam-120 photographs could be a promising strategy in detecting children with abusive head trauma.

Note: Retcam can be used as a screening device for SBS. All positive screens should be confirmed by indirect ophthalmoscopy because Retcam produced some false positives.

Open globe injuries in children: factors predictive of a poor final visual acuity.

Gupta A, Rahman I, Leatherbarrow B.

Eye 2009 Mar; 23(3):621-625.

The authors describe the clinical characteristics and outcomes of open globe injuries presenting to a major UK centre and discuss factors affecting long-term prognosis. They identify demographic features, causes, types and location of injuries, initial clinical features and correlation with visual outcome, and predictors of poor visual outcome. They reviewed and analyzed records of 20 patients, aged 16 years and below, who had undergone repair of open globe injuries at the Manchester Royal Eye Hospital, UK. The study group comprised of 85% male subjects, 15% female subjects. The average age was 9.8 years (range: 1–15). Average follow-up was 16.3 months (range: 3–48 months). Sharp objects (mainly glass or knife) accounted for the majority (65%) of injuries. Initial clinical signs associated with poor visual outcomes included poor initial visual acuity, cataract, RAPD, and no initial red reflex. Younger patients and blunt injuries (especially BB gun injuries) had worse visual outcomes.

Ocular air gun injuries: a one-year surveillance study in the UK and Eire (BOSU). 2001–2002.

Shuttleworth GN, Galloway P, Sparrow JM, Lan C.

Eye 2009 Jun; 23(6):1370–1376.

Ocular air gun injuries were reported to the British Ophthalmic Surveillance Unit (BOSU; United Kingdom and Eire) for the period November 2001–December 2002 (13 months). Two questionnaires were used to collect demographic details, circumstances of injury, details of injuries, medical management and outcome. Results: A total of 105 initial and 99 follow-up questionnaires were returned. Eighty-six ocular air gun injuries occurred during the last 12 months of surveillance yielding a corrected, estimated incidence of 91–115 injuries/year. Injuries were most frequent in August/September, and 90% (95/105) of victims were men with mean age of 17.5 years (74% under 18 years). In all, 40% (32/81) of injuries occurred at home and 53% (43/81) in a public place. 23% (19/84) of injuries were deliberate, 66% (69/104) of injuries were severe and 20% (21/105) resulted in ruptured globes. In all, 54% (48/89) required hospital admission and 41 required surgery. A total of 11% (12/105) of eyes were either enucleated or eviscerated. Final visual acuity was ≤ counting fingers in 29% (26/91) but >6/12 (Snellen) in 65% (59/91). Moderate/significant cosmetic deformities were recorded in 10% (8/77) and restricted ocular movements in 5% (4/72). Conclusions: Ocular air gun injuries damage sight and leave lasting morbidity. The demographics and circumstances of injury are well documented with access to, and unsupervised use of, air guns, appearing the principal risks for injury.

Outcome and prognosis of pediatric patients with delayed diagnosis of open-globe injuries.

Acuna O, Yen K.

JPOS 2009 Jul-Aug; 46:202-207.

This study was a retrospective observational case series of patients who presented with open globe injuries diagnosed 24 hours or more after the injury between July 2002 and March 2007. Thirteen patients were included in the study with an average age of 5.8 years. Mean time of presentation after injury was 9.2 +/- 16 days. The most common complaints were chronic red eye (7 of 13 patients), eye pain (5 of 13 patients) and decreased vision (4 of 13 patients). All patients had self-sealing corneal wounds. One patient had sympathetic ophthalmia. No patient had endophthalmitis. Initial visual acuity was 20/200 or worse in ten patients, and final visual acuity was 20/40 or better in six patients. Pediatricians should be educated to maintain a high level of suspicion in the setting of chronic unilateral red eye, decreased visual acuity and abnormal red reflex even in the absence of a history of ocular trauma.

[Ho LY](#), [Goldenberg DT](#), [Capone A Jr](#). Retinal pigment epithelial tear in shaken baby syndrome. [Arch Ophthalmol](#). 2009 Nov;127(11):1547-8.

This is a case report that describes a retinal pigment epithelial tear in a patient with Shaken Baby Syndrome. Although RPE tears are a well known complication of neovascular macular degeneration, they have not been previously described in Shaken Baby Syndrome. The authors suggest that clot retraction from subretinal hemorrhages in SBS could lead to RPE tears.

XV UVEITIS

High-dose daclizumab for the treatment of juvenile idiopathic arthritis-associated active anterior uveitis.

[Sen HN](#), [Levy-Clarke G](#), [Faia LJ](#), [Li Z](#), [Yeh S](#), [Barron KS](#), [Ryan JG](#), [Hammel K](#), [Nussenblatt RB](#).

[Am J Ophthalmol](#). 2009 Nov;148(5):696-703.e1. Epub 2009 Aug 6.

PURPOSE: To provide preliminary data regarding the safety and efficacy of high-dose intravenous daclizumab (Zenapax; Roche Inc, Nutley, New Jersey, USA) therapy for the treatment of juvenile idiopathic arthritis (JIA)-associated active anterior uveitis.

METHODS: Six patients were recruited into the study and received daclizumab therapy at doses of 8 mg/kg at baseline, 4 mg/kg at week 2, and 2 mg/kg every 4 weeks thereafter, for a total of 52 weeks. The study was done at the National Eye Institute between June 29, 2005 and July 9, 2008. The primary outcome was a two-step decrease in inflammation grade assessed at week 12. Primary safety outcome was assessed at weeks 2 and 4. The ocular inflammation was assessed according to the Standardization of Uveitis Nomenclature criteria.

RESULTS: Four of the 6 participants achieved two-step reduction in anterior chamber cells according to Standardization of Uveitis Nomenclature Working Group grading scheme for anterior chamber cells 12 weeks into the study and met the primary efficacy endpoint. One additional patient responded to reinduction whereas 1 patient failed reinduction and was considered an ocular treatment failure. Visual acuity improved from a mean of 68 Early Treatment Diabetic Retinopathy Study letters in the worse eye to a mean of 79.6 letters (2 Snellen lines). Three participants were terminated before 52 weeks: First, because of a rash possibly induced by daclizumab; Second, because of ocular treatment failure; and Last, because of uncontrolled systemic manifestations of JIA.

CONCLUSION: High-dose intravenous daclizumab can help reduce active inflammation in active JIA-associated anterior uveitis; however, patients need to be monitored for potential side effects. Larger randomized trials are needed to better assess treatment effect and safety.

Epidemiology and course of disease in childhood uveitis.

Smith JA, et al. *Ophthalmology* 2009 Aug; 116(8):1544-1551.

Purpose: To describe the disease characteristics and visual outcome of pediatric uveitis. A retrospective, longitudinal observation (chart review) of 527 pediatric patients from the National Eye Institute, University of Illinois, Chicago, and Oregon Health Sciences University.

Main Outcome Measures: Demographics, uveitis disease characteristics, complications, treatments, and visual outcomes were determined at baseline and at 1-, 3-, 5-, and 10-year time points.

Results: The patient population was 54% female; 62.4% white, 12.5% black, and 14.61% Hispanic. Median age at diagnosis was 9.4 years. The leading diagnoses were idiopathic uveitis (28.8%), juvenile idiopathic arthritis-associated uveitis (20.9%), and pars planitis (17.1%). Insidious onset (58%) and persistent duration (75.3%) were most common. Anterior uveitis was predominant (44.6%). Complications were frequent, and cystoid macular edema and hypotony (OR, 4.54; P = 0.026) had the most significant visual impact. Ocular surgery was performed in 18.9% of patients. The prevalence of legal blindness was 9.23% at baseline, 15.15% at 5 years, and 7.69% at 10 years. Posterior uveitis and panuveitis had more severe vision loss. Hispanic ethnicity was associated with a higher prevalence of infectious uveitis and vision loss at baseline.

Conclusions: The rate and spectrum of vision threatening complications of pediatric uveitis are significant. Prospective studies using standard outcome measures and including diverse populations are needed to identify children most at risk.

Outcomes of cataract surgery in children with chronic uveitis.

Quiñones K, Cervantes-Castañeda RA, Hynes AY, Daoud YJ, Foster CS.
J Cataract Refract Surg 2009 Apr; 35(4):725-31.

Purpose: To evaluate the outcomes of cataract surgery in children with chronic uveitis.

Methods: This retrospective chart review was of patients younger than 17 years with a history of uveitis who had cataract surgery before June 2004.

Results: Thirty-four children (41 eyes) were identified. The mean age of the 10 boys and 24 girls was 9.8 years (range 4 to 17 years) and the mean total follow-up, 4.1 years (range 0.3 to 15.7 years). Twenty-one children had juvenile idiopathic arthritis-associated uveitis, 7 had pars planitis, and 6 had other conditions. Sixteen patients had concomitant posterior segment pathology, 25 received perioperative immunomodulatory therapy, and 13 had intraocular lens (IOL) implantation. The postoperative best corrected visual acuity improved in 35 of 41 eyes; 31 eyes had an improvement of 3.6 lines at 1 year. Most patients (92%) improved after IOL implantation. Most patients (88%) who received immunomodulatory therapy attained better vision, but this was not statistically significant compared with those who did not ($P = .47$). Similarly, there was no statistically significant difference between those with posterior pathology and those without. At the end of the analysis (1 year), the cumulative probability of improvement in visual acuity in 41 eyes reached 0.91.

Conclusions: In most cases, and with optimum control of intraocular inflammation, cataract surgery improved the visual outcome in children with chronic uveitis. Intraocular lens implantation was well tolerated in most cases, which may result in optimal vision.

XVI. ANTERIOR SEGMENT

Constant ocular infection with chlamydia trachomatis predicts risk of scarring in children in Tanzania.

Wolle MA, Muñoz BE, Mkocho H, West SK.

Ophthalmology 2009 Feb; 116(2):243-247.

Objective: To determine the 5-year incidence of scarring in children with a history of constant severe trachoma, constant infection, or both compared with children with a history of neither.

Design: Longitudinal observational study of children aged less than 10 years with data on trachoma and infection for 3 of the 5 visits in the first 18 months, and follow-up 5-year data on scarring.

Methods: Data were collected on clinical trachoma, and ocular swabs were taken to determine the presence of *C. trachomatis* in children in a hyperendemic village in Tanzania. Data were collected at baseline; 2, 6, 12, and 18 months; and 5 years from baseline. Severe trachoma was defined as the presence of 10 or more follicles, or trachoma intense. A child had constant infection (severe trachoma) if infection (severe trachoma) was present on at least 3 visits before the 5-year survey.

Results: Of the 189 children, 22 (11.6%) had constant severe trachoma, but not constant infection. Nine children (4.8%) had constant infection but not constant severe trachoma. Both constant severe trachoma and constant infection were present in 16 children (8.5%). The 5-year incidence of scarring was similar in all 3 groups and were most likely to develop scars compared with those with sporadic trachoma or infection (15.2%) or neither (6.8%)

Conclusions: Children with constant infection are also likely to have constant severe trachoma, and their 5-year risk of scarring is high compared with children with sporadic severe trachoma or infection. These data further support the presence of a subgroup of children who cannot clear infection with *C. trachomatis*, who may manifest a severe immunologic response to infection, and who are at increased risk of scarring sequelae.

XVII. CORNEA

Pediatric keratoplasty.

Vanathi M, et al.

Surv Ophthalmol 2009 Mar-Apr; 54(2):245-71.

Penetrating keratoplasty in children is a highly challenging and demanding procedure associated with a high risk of graft failure or failure of amblyopia therapy in clear grafts. Nonetheless, keratoplasty remains the surgery of choice for the management of pediatric corneal stromal opacities or edema. Allograft rejection, graft infection, corneal neovascularization, glaucoma, trauma to the anterior segment, vitreous pathology, and additional surgical interventions, especially those related to glaucoma management, are important risk factors. Successful penetrating keratoplasty in children requires careful preoperative evaluation and selection of patients follow-up by well-motivated parents, an expert corneal transplant surgeon, and a devoted pediatric ophthalmologist. This article reviews clinical features of the key indications for pediatric keratoplasty (e.g. congenital hereditary endothelial dystrophy, Peters anomaly, sclerocornea), operative technique, postoperative management, potential complications, and outcomes.

XVII. RETINA

25-Gauge vitrectomy for paediatric vitreoretinal conditions.

Gonzales CR, Singh S, Schwartz SD.

Br J Ophthalmol 2009 May; 93(5):787-90.

Summary: This is a retrospective study of 56 eyes of 49 children undergoing vitrectomy with 25-gauge instrumentation. There were no cases of endophthalmitis, wound leaks or hypotony requiring treatment. A modified approach in which the conjunctiva and sclera is sutured was used for young babies requiring a pars plicata approach.

Objective: To evaluate the feasibility and safety of 25-gauge vitrectomy for various vitreoretinal indications in the paediatric population.

Methods: Consecutive patients aged 18 years or less undergoing vitrectomy for various vitreoretinal indications over a 5-year period were studied retrospectively. Two different surgical techniques were used: a modified 25-gauge approach in which the sclerotomies and conjunctiva were sutured as described previously for most children under the age of 1 year, and a transconjunctival 25-gauge approach for older children

Results: 56 eyes in 49 children (16 girls and 33 boys) were included. Intraoperative unplanned events or complications included: conversion to 20-gauge vitrectomy (four), conversion of one port to a 20-gauge sclerotomy (two), suspected lens damage (one) and intraoperative bleeding from a vascular ridge (one). Postoperative complications included cataract (five), rhegmatogenous retinal detachment (four) and vitreous haemorrhage (three). The four retinal detachments were either recurrent or occurred in eyes with complex ocular pathology and were not felt to be related to the surgical technique. There were no cases of postoperative hypotony requiring intervention, choroidal detachment, endophthalmitis or sclerotomy-related retinal breaks.

Conclusions: 25-gauge vitreoretinal techniques can be used in various paediatric vitreoretinal conditions and facilitate easy access to small spaces in the paediatric

eye. To avoid postoperative hypotony, a modified technique is recommended for younger babies in which the conjunctiva and sclera is sutured.

Note: short follow up, retrospective, limited Va data. However this is the largest series employing this technique.

High Measured Intraocular Pressure in Children with recessive Congenital Hereditary Endothelial Dystrophy. Khan A et al. JPOS Jan-Feb 2010; 47: 29-33.

Five infants with significant congenital corneal haze had increased mea-

sured intraocular pressure that remained high despite drug treatment and surgery to decrease intraocular pressure. The clinical diagnosis of recessive congenital hereditary endothelial dystrophy without glaucoma was made based on the absence of buphthalmos, a distinct pattern of mosaic corneal haze with significant corneal thickness, and absence of cupping in healthy-appearing optic nerve heads. These findings contrast with previous reports that associate corneal edema with a falsely low measured IOP. The diagnosis of these two diseases in one patient should be made only with great caution.

Rare retinal hemorrhages in translational accidental head trauma in children.

Sturm V, Knecht PB, Landau K, Menke MN.

Eye 2009 Jul; 23(7):1535–1541.

The characteristic findings in accidental head injury consist of linear skull fracture, epidural hematoma, localized subdural hematoma, or cortical contusion because of a linear or translational impact force. Retinal hemorrhages have been found, although uncommon, in accidental head trauma. The authors performed a retrospective study of 24 consecutive cases of children with severe head injuries caused by falls. Inclusion criteria were skull fractures and/or intracranial hemorrhages documented by computerized tomography. All patients underwent a careful ophthalmic examination including dilated indirect funduscopy within the first 48 h following admission.

Results: No retinal hemorrhages could be found in patients whose accidents were plausible and physical and imaging findings were compatible with reported histories. Excessive bilateral retinal hemorrhages were found in only three children with the typical signs of shaken baby syndrome. In eight children, trauma had led to orbital roof fractures.

Conclusions: Retinal hemorrhages were not found in any of the patients with accidental trauma despite the severity of their head injuries. The authors feel that more evidence has been identified that there are strong differences between the ocular involvement in accidental translational trauma and those in victims of non-accidental trauma. Fall-related injuries carry a very low risk of retinal hemorrhages.

Odds of abuse associated with retinal hemorrhages in children suspected of child abuse.

Binbenbaum G, Mirza-George N, Christian C, Forbes B.

J AAPOS 2009 Jun; 13(3):268-272.

Retrospective study from CHOP of 110 children 15 months or younger suspected of abusive head trauma (AHT) who had an ophthalmological examination. The majority of the children (74%) were younger than 6 months old. Retinal hemorrhage was scored by type, size, location, and extent. The higher the score, the greater the severity.

Forty-five were known abuse and 37% were known accidental. Retinal hemorrhages were found in 32%. The presence of retinal hemorrhages was highly correlated with abuse and the severity was greater. Retinal hemorrhages were more commonly found the younger the child with AHT.

Paediatric retinal detachment: comparison of high myopia and extreme myopia.

Wang NK, Chen YP, Lai CC, et al.

Br J Ophthalmol 2009 May; 93(5):650-5.

Aims: To compare the clinical features and surgical outcomes of paediatric retinal detachment (RD) in high myopia and extreme myopia.

Methods: The clinical charts of 107 children who experienced RD and had a spherical equivalent (SE) of at least 6.00 dioptres (D) were reviewed. The patients were separated into a high myopia group (SE 6.0 to 10.0 D) and extreme myopia group (SE >10.0 D). RD characteristics and outcomes were compared between these two groups.

Results: There were significant differences between the two groups in total RD ($p,0.001$), the presence of posterior staphyloma ($p,0.001$) and some types of breaks. More eyes in the extreme myopia group required vitrectomy after the initial RD repair. In the high myopia group, retinal reattachment was achieved in 79 eyes (97.5%) at the end of the intervention, whereas in the extreme myopia group, retinal reattachment was achieved in 22 eyes (73.3%). Multiple logistic regression showed that a higher refractive error was the only negative predictor of surgical outcome ($p=0.026$).

Conclusions: Due to differences in aetiologies, clinical characteristics, required surgical procedure after initial repair, surgical and functional outcomes, paediatric RD with extreme myopia should be addressed differently from paediatric RD with high myopia.

Note: The strengths of this study include the large numbers of high and extreme myopic patients, and the long follow-up. The study's limitations include the fact that this is a nonrandomized retrospective review, and the patient population was based on referrals. They recommend a thorough retinal examination in extremely myopic children, especially in anisometropic and amblyopic children.

XIX. ORBIT

Evidence for visual compromise in preverbal children with orbital vascular birthmarks.

Good WV, Hou C, Frieden IJ, Norcia AM.

Am J Ophthalmol 2009 Apr; 147(4):679-682.e1.

Purpose: To learn whether electrophysiological changes indicating amblyopia occur even in the absence of clinically recognizable amblyopia.

Methods: Four consecutive infants between 7 and 19 months of age with unilateral periocular vascular lesions that intermittently obstructed vision in the affected eye and no clinical evidence of amblyopia were evaluated. No child had anisometropia greater than 0.50 diopter in the greatest meridian or strabismus. Sweep visual evoked potential vernier acuity was measured under monocular viewing conditions with the fellow eye tested as the control.

Results: Response amplitudes and acuity thresholds were significantly diminished in the affected eyes. A phase analysis showed slowing of the response in the affected eyes compared with the control eyes.

Conclusions: An amblyopia-like effect on vernier acuity occurred in infants with unilateral periocular vascular birthmarks when the lesion caused intermittent occlusion of the eye. Whether long-term effects will occur is unknown, but children with no clinically apparent amblyopia in the setting of a vascular mark or other cause of intermittent occlusion of the visual axis should be followed, since these electrophysiology findings suggest amblyopia may be present.

Well-circumscribed orbital venous-lymphatic malformations with atypical features in children.

Gunduz K, Kurt RA, Erden E.

Br J Ophthalmol 2009 May; 93(5):656-9.

Aim: To report well-circumscribed orbital lymphaticvenous malformations (VLMs) with atypical clinical, imaging and pathological features in four paediatric patients.

Methods: Retrospective non-comparative case series of four patients aged 5–18 years old having a well circumscribed orbital mass diagnosed histopathologically as orbital VLM. All patients underwent orbitotomy and total excision of the VLM. Pre- and postoperative visual acuity, proptosis and globe displacement produced by the orbital VLM, MRI findings, histopathological features, treatment, follow-up and prognosis were evaluated.

Results: No proptosis, visual acuity change or globe displacement was induced by the orbital VLM. One lesion was located superiorly, one medially and two inferonasally. On MRI, the orbital VLMs were isointense on T1-weighted images and hyperintense on T2-weighted images, demonstrated moderate contrast enhancement and had a heterogenous internal structure. Signal void areas and fluid–fluid levels were not observed on MRI. At a mean follow-up of 50 months, all patients remained

free of recurrence clinically and retained preoperative visual acuities. Several histopathological features of the excised lesions supported an initial diagnosis of cavernous haemangioma, but the lesions were subsequently rediagnosed as orbital VLM when aggregates of lymphocytes and randomly arranged smooth muscle were noted.

Conclusions: Well-circumscribed orbital VLMs in children can display atypical clinical, imaging and pathological features. MRI features of this entity are not characteristic of typical orbital VLMs. It may be possible to totally excise well-circumscribed orbital VLMs as in this series of four patients. Careful histopathological evaluation indicates the correct diagnosis.

Note: nice case report of four cases.

XX. PLASTICS

Relationship of infantile periocular hemangioma depth to growth and regression pattern.

Tambe K, Munshi V, Dewsbery C, et al. J AAPOS 2009;13:567-570.Dec

This retrospective case review evaluated all patients with periocular hemangiomas who fulfilled inclusion criteria and were seen at a tertiary eye care center over seven years. Forty-two patients met inclusion criteria. Thirty-four of the 42 patients were female. Fourteen patients presented with superficial hemangiomas. They presented earlier and reached peak growth by 3 months of age. This was followed by an involutational phase and 5/14 (38%) completely resolved by 24 months of age. Thirteen patients presented with deep (subcutaneous) hemangiomas. These were noticed later and only 2/13 (15%) completely resolved by 24 months of age. The behavior of the 8 hemangiomas that were mixed (deep and superficial components) was based on the dominant component. Seven patients had hemangiomas with orbital extension. Only one of these 7 (14%) completely resolved by 24 months of age. This data is clinically useful for physicians counseling families on the natural course of periocular hemangiomas.

[Fay A, Nguyen J, Jakobiec FA, Meyer-Junghaenel L, Waner M. Propranolol for isolated orbital infantile hemangioma. Arch Ophthalmol. 2010 Feb;128\(2\):256-8.](#)

The authors describe the use of systemic propranolol in an infant who had an isolated and extensive, deep orbital infantile hemangioma. The child presented at 4 months of age with painless protrusion of the eye. Propranolol treatment was initiated at 2mg/kg/day IV for 5 days and then continued at home orally. By 6 weeks after initiating treatment, the proptosis had resolved and the patient was treated with the propranolol until 1 year of age without adverse effects or regrowth. This report suggest that propranolol is a promising alternative agent for treatment of deep orbital or other inaccessible infantile hemangiomas.

Frontalis sling operation using silicone rod compared with preserved fascia lata for congenital ptosis. A Three-Year Follow-up Study.

Lee MJ, Oh JY, Choung HK, Kim NJ, et al.
Ophthalmology 2009 Jan; 116:123-129.

Design: Retrospective, nonrandomized, comparative, interventional case series. One hundred twenty-three patients with congenital ptosis over 3years.

Methods: Patients were divided into 2 groups according to the sling material used; a preserved fascia lata group (n = 63) and a silicone rod group (n = 60). Cosmetic results and recurrence rates were compared between these 2 groups. The cosmetic results of the frontalis sling operation were assessed as good, fair, or poor based on the habitual upper lid heights and symmetry, and bilateral

cases and unilateral cases were compared separately. Recurrence was defined as the conversion of the cosmetic result from good or fair to poor category.

Results: At the 3- and 6-month follow-ups, the cosmetic results were not significantly different between the 2 groups. However, the silicone rod group showed significantly better cosmetic results than the preserved fascia lata group at 1, 2, and 3 years after surgery in both bilateral and unilateral cases. At 3 years after surgery, the recurrence rates were 29.2% (7/24 bilateral cases) and 11.1% (3/27 unilateral cases) for the silicone rod group, and 63.2% (12/19 bilateral cases) and 41.4% (12/29 unilateral cases) for the preserved fascia lata group.

Conclusions: However, only prospective randomized studies can give a more accurate conclusion in that regard.

Long-term functional and cosmetic outcomes after frontalis suspension using autogenous fascia lata for pediatric congenital ptosis.

Yoon JS, Lee, SY.

Ophthalmology 2009 Jul; 116(7):1405-1414.

Design: Retrospective, observational case series of 239 Asian children who underwent frontalis suspension using fascia lata autografts from 1998 through 2006 with a minimum of 6 months of follow-up.

Methods: Functional success was assessed by review of photographs and medical charts.

Results: The follow-up time ranged from 6 to 144 months. The functional success rates were 100% at 1 month after surgery and 94% at the last follow-up. In the early postoperative period, 96.7%, 91.6%, and 97.5% of patients showed excellent cosmetic success rates regarding lid contour, symmetry, and lid crease, respectively. However, these rates decreased to 85.4%, 65.7%, and 66.9% at 6 months after surgery, respectively. Similarly, the mean grades for lid contour, symmetry, and crease were lower at 6 months compared with early after surgery ($P < 0.001$).

Conclusions: The use of fascia lata autografts for pediatric congenital ptosis resulted in high functional success rates in both the short-term and long-term. In contrast, whereas cosmetic success rates were high in the short-term, they decreased by 6 months after surgery. This deterioration in cosmetic outcome was the result of gradual elevation of lid height, medial inversion of eyelashes, and poor lid creases, possibly resulting from contracture of the grafted fascia lata and the anatomic characteristics of Asian eyelids.

Pediatric blepharoptosis: a 10-year review.

Berry-Brincat A, Willshaw H.

Eye 2009 Jul; 23(7):1554–1559.

One hundred and fifty five children (186 eyes) underwent blepharoptosis surgery. One hundred and ten patients (71%) were treated with a levator resection procedure, 28 (18%) underwent a brow suspension using Mersilene mesh, 15 (10%) with Fasanella Servat procedure and 2 (1%) with La Mange procedure. The mean post-operative follow-up was 30.82 months with 84 children completing a minimum of 12 months follow-up. Overall, 70.97% lids were successfully corrected with a single operation. In 9.14% of lids, the results were fair but no further surgery was carried out. Reoperation was required in 19.89% of lids with the mean time to second surgery being 32.69 months. Amblyopia was found in 26.45% (41 children); in 3 patients, their amblyopia became manifest after the ptosis surgery. Strabismus was present in 14.19%, and 18.70% had a significant refractive error requiring spectacles prescription, with anisometropia present in more than 72% of these patients. The authors conclude that early referral to an ophthalmologist is necessary even though surgical correction may be delayed. Children with congenital ptosis need to be monitored for amblyopia both pre- and post-operatively, as the incidence of strabismus and refractive errors is much higher than the general population and these may develop even after ptosis surgery.

Balloon catheter dilation for complex congenital nasolacrimal duct obstruction in older children.

Maheshwari R.

JPOS 2009 Jul-Aug; 46:215-217.

The case records of 65 eyes in 59 children aged 2-6 years who underwent probing for congenital nasolacrimal duct obstruction were retrospectively reviewed. Complex obstruction was noted in 21 of the 65 eyes in children older than two years who underwent probing. Secondary balloon dacryoplasty was performed under general anesthesia in eight of these 21 lacrimal systems. Success was defined as the resolution of all clinical signs and symptoms of lacrimal obstruction. Secondary balloon dacryoplasty was successful in seven of the eight lacrimal systems. Balloon catheter dilation can be considered an alternative to silicone intubation and dacryocystorhinostomy in older children after unsuccessful probing.

XXI. GLAUCOMA

[Fay A](#), [Nguyen J](#), [Jakobiec FA](#), [Meyer-Junghaenel L](#), [Waner M](#). Topical treatment for capillary hemangioma of the eyelid using Beta Blocker solution [Arch Ophthalmol](#). 2010 Feb;128(2):255.

This is a case report describing the use of topical Timolol in the treatment of a large capillary hemangioma on a child's left upper eyelid. The patient was 4 months old at presentation and had a large hemangioma of the left upper eyelid with associated ptosis and evidence of poor fixation in the involved eye as well as astigmatic anisometropia. The Timolol 0.5% was used twice daily on the surface of the hemangioma and within 5 weeks of treatment, the hemangioma was significantly reduced in size, thickness, and color with decrease of astigmatism in that eye. The patient did not suffer any adverse effects.

This report suggests that topical Beta blockers should be considered in the treatment of capillary hemangiomas.

Deep sclerectomy combined with trabeculectomy in pediatric glaucoma.

Feusier M, Roy S, Mermoud A.

Ophthalmology 2009 Jan; 116:30-38.

Design: Retrospective, nonconsecutive, noncomparative, interventional case series (over 10 years).

Methods: A primary combined deep sclerectomy and trabeculectomy was performed in 35 eyes of 28 patients. Complete examinations were performed before surgery, postoperatively at 1 and 7 days at 1, 2, 3, 4, 6, 9, and 12 months, and then every 6 months after surgery.

Main Outcome Measures: Surgical outcome was assessed in terms of intraocular pressure (IOP) change, additional glaucoma medication, complication rate, need for surgical revision, as well as refractive errors, best-corrected visual acuity (BCVA), and corneal clarity and diameters.

Results: The mean age before surgery was 3.6 years, and the mean follow-up was 3.5 years. The mean preoperative IOP was 31.9. At the end of follow-up, the mean IOP decreased by 58.3%, and from 14 patients with available BCVA 8 patients (57.1%) achieved 0.5 (20/40) or better. Six patients (43%) were affected by myopia. The complete and qualified success rates, based on a cumulative survival curve, after 9 years were 52.3% and 70.6% respectively ($P < 0.05$). Sight-threatening complications were more common (8.6%) in refractory glaucomas.

Conclusions: Combined deep sclerectomy and trabeculectomy is an operative technique developed to control IOP in congenital, secondary, and juvenile glaucomas. The intermediate results are satisfactory and promising. Previous classic glaucoma surgeries performed before this new technique had less favorable results. The number of sight-threatening complications is related to the severity of glaucoma and number of previous surgeries.

Complications and 2-year valve survival following Ahmed valve implantation during the first 2 years of life.

Al-Mobarak F, Khan AO.

Br J Ophthalmol 2009 May; 93(5):795-8.

Aim: To report complications and 2-year valve survival following Ahmed valve implantation during the first 2 years of life.

Methods: Retrospective institutional case series.

Results: Forty-two eyes of 36 patients with Ahmed valve implantation (without prior drainage device surgery) during the first 2 years of life and 2 years' postsurgical follow-up were identified. Most eyes had primary congenital glaucoma (28/42, 66.7%), aphakic glaucoma (5/42, 11.9%) or Peters anomaly (5/42, 11.9%). All but three eyes had prior ocular surgery. Surgery was at a mean age of 11.83 months (m) (SD 5.63). The most common significant postoperative complications were tube malpositioning requiring intervention (11/42, 26.2%), endophthalmitis (3/42, 7.1%; one with tube exposure) and retinal detachment (3/42, 7.1%). Thirty-six eyes (85.8%) required resumption of antiglaucoma medications to maintain intraocular pressure (IOP) (22 mm Hg a mean of 7.2 m (SD 6.8) postoperatively. Cumulative probabilities of valve survival (IOP(22 mm Hg with or without medication) by Kaplan–Meier analysis were 73.8% and 63.3% at 12 months and 24 months, respectively.

Conclusions: Postoperative tube malpositioning that required surgical revision was common in this age group. Infectious endophthalmitis and retinal detachment are known potential complications following any incisional surgery for advanced buphthalmos; however, tube exposure is a unique potential problem following aqueous shunt implantation that can lead to intraocular infection. Cumulative valve survival 2 years following implantation was 63.3%.

Comparison of polypropylene and silicone Ahmed valve survival 2 years following implantation in the first 2 years of life.

Khan AO, Al-Mobarak F.

Br J Ophthalmol 2009 May; 93(5):791-4.

Aim: To compare the 2-year survival rates of polypropylene and silicone Ahmed glaucoma valves (AGVs) implanted during the first 2 years of life.

Methods: Retrospective analysis of polypropylene and silicone AGV implantation during the first 2 years of life in children with 2 years' postoperative follow-up. Patients with prior aqueous drainage device implantation were excluded.

Results: Forty-two eyes of 36 children were reviewed. Thirty-one eyes received a polypropylene AGV (six S1, 25 S2), and 11 eyes received a silicone AGV (11 FP7). The average survival time (maintenance of intraocular pressure (22 mm Hg with (or without) medications and without significant complications) was significantly longer ($p=0.001$ by the logrank test) for the silicone group (23.36 months, standard error (SE) 1.64, 95% confidence interval (CI) 20.16 to 24.00 months) than for the polypropylene group (19.10 months, SE 1.53, 95% CI 16.1 to 22.12 months). Cumulative probabilities of survival at 2 years by Kaplan to Meier analysis were 90.9% (SE 8.7, 95% CI 70 to 100%) and 54.8% (SE 8.9, 95% CI 23 to 87%), respectively ($p=0.001$ by the logrank test). All eyes implanted with silicone AGVs had the diagnosis of congenital glaucoma, which was independently associated with 2-year survival.

Conclusions: Two years after surgery, silicone AGVs survived longer than polypropylene AGVs. However, all eyes that received silicone AGVs in our cohort had congenital glaucoma, which had a

better survival than other paediatric glaucoma diagnoses. A study of silicone AGV implantation in other paediatric glaucoma diagnoses is needed to determine whether or not silicone AGVs independently have a better survival after implantation in the first 2 years of life.

The spontaneous resolution of primary congenital glaucoma.

Nagao K, Noel LP, Noel EM, Walton DS.

JPOS 2009 May-Jun; 46:139-143.

The records of 356 patients with primary congenital glaucoma were reviewed. Nine patients were identified with spontaneous resolution of PCG after four months of age. Fourteen of 18 eyes demonstrated evidence of early glaucoma, were found to have normal intraocular pressure, and were determined to have had spontaneous resolution of PCG. All 14 eyes had corneal enlargement and 10 of 14 had Haab's striae. Angle abnormalities were noted to be less severe than in three fellow eyes which did eventually require glaucoma treatment. The mechanism of spontaneous resolution could be related to continued post-natal development of the angle structures in eyes possessing milder angle abnormalities.

Corneal anomalies in newborn primary congenital glaucoma.

Thiagalingarn S, Jakobiec F, Chen T, Michaud M et al.

JPOS 2009 Jul-Aug; 46:241-244.

The corneal specimen of a four-month-old infant with primary congenital glaucoma and cloudy corneas who had undergone penetrating keratoplasty was examined by light and electron microscopy. Findings included a thinned epithelium, thickening of Bowman's layer and a thickened and disorganized corneal stroma. Decemet's membrane was intact, and the endothelium was mildly attenuated. The corneal changes seen in this patient may be specific to primary congenital glaucoma and may contribute to the corneal clouding seen so frequently in these patients.

Br J Ophthalmol 2010;**94**:33-35 doi:10.1136/bjo.2008.148122

Intraocular pressures after ketamine and sevoflurane in children with glaucoma undergoing examination under anaesthesia

1. L Jones¹,
2. V Sung¹,
3. G Lascaratos¹,
4. H Nagi²,
5. R Holder³

Abstract

Aim: For accurate intraocular pressure (IOP) measurement in very young children examination under anaesthesia (EUA) may be necessary. Most anaesthetic agents used for EUA have some effect on IOP. We compared IOPs in children after ketamine and sevoflurane anaesthesia.

Methods: Consecutive patients with definite or suspected glaucoma, uncooperative for reliable IOP measurement in clinic and requiring EUA, were included in this study. IOPs were measured after intramuscular injection (5 mg/kg) or intravenous injection (2 mg/kg) of ketamine using a Perkins applanation tonometer. Three measurements were taken from each eye. The IOPs were rechecked after sevoflurane, given for maintenance anaesthesia. Mean IOPs were used for analysis. Paired t test was used to assess the differences in IOPs for the whole group and one-way ANOVA for the three subgroups (ketamine IOP <20, 20–30, >30 mmHg).

Results: The records of eight patients (16 eyes) were available for review. The mean age was 55.42 (SD 25, range 26–89) months. Seventy data-points from both eyes (35 EUAs) were used for the analysis. The mean IOP after sevoflurane (17 (SD 10) mmHg) was statistically lower than after ketamine (24.4 (SD 12.7) mmHg, $p < 0.001$). The percentage difference was 28.5 (SD 20.8; 95% CI 23.5 to 33.4). The difference between the subgroups was not statistically significant ($p = 0.192$).

Conclusion: Sevoflurane lowers the IOP significantly compared with the IOP measured after ketamine. This difference is independent of the IOP level. It may be important to use ketamine as the induction anaesthetic agent when accurate IOP measurement is necessary during EUA for children.

Comment: many weaknesses to this paper: retrospective study, small number of pts ($n=8$). Sevoflurane IOP was measured after ketamine was given, so there could be an additive effect confounding the results. Ketamine can raise IOP; another confounding factor. Same person did the IOP measurements so there is a possible reproducibility bias confounding factor.

Br J Ophthalmol 2009;**93**:1325-1330 doi:10.1136/bjo.2008.142562

Correlation between optical coherence tomography and glaucomatous optic nerve head damage in children

1. M A El-Dairi,
2. S Holgado,
3. S G Asrani,
4. L B Enyedi,
5. S F Freedman

Aim: To compare analysis of macular and nerve fibre layer thickness by optical coherence tomography (OCT) with optic nerve head (ONH) morphology based on stereophotography.

Design: Prospective observational case–control series.

Methods: Normal and glaucomatous eyes of children (age 4–17 years) were scanned using Stratus OCT (Carl Zeiss Meditec, Dublin, California, USA). Fast macular and retinal nerve fibre layer (RNFL) thickness map were performed on 372 eyes of 222 children. ONH stereophotographs were taken and evaluated by two masked observers using a grading system of 0 to 5 based on both cupping ratio and morphology. OCT3 analyses were compared across ONH grades for different areas around the macula and the peripapillary RNFL.

Results: Analysis included OCT values and ONH grading for 139 eyes of 139 children. There was a negative correlation between ONH grade and both macular thickness and RNFL thickness in all areas measured. There was a difference in the correlation identified for black versus white children.

Conclusion: OCT measurements of RNFL and macular thickness declined with increasing grade of glaucomatous damage seen on stereophotographs in black and white children. Further study will help quantify the value of OCT in the diagnosis and management of paediatric glaucoma.

Comment: prospective observational case series, $n=222$. This study showed that RNFL and macular thickness declined with increasing glaucoma damage. This study also showed racial differences in correlation of optic nerve head damage grade and RNFL and macular thicknesses. Black children with grade 0 ONH had similar RNFL and macular thicknesses as those with Grade 1 ONH damage.

Latanaprost in pediatric glaucoma- pediatric exposure over a decade. Black AC, Jones S, Yanovitch TL, et al. J AAPOS 2009;13:558-562.Dec

Latanaprost lowers IOP by increasing uveoscleral outflow. This consecutive chart review of 115 pediatric subjects treated with Latanaprost by a single provider over 12 years looked at side effects of treatment as well as effectiveness. An evaluation of efficacy of the medication in this study was severely compromised because IOP measurements were not obtainable in many of the younger study patients. Also many of the patients were on more than 1 glaucoma medication. The study did find that 35% of patients showed an IOP reduction $\geq 15\%$. Congenital glaucoma patients had a very poor response rate while juvenile open angle glaucoma patients showed the best results. All patients who took Latanaprost longer than 6 months developed lash growth. Two subjects had to discontinue Latanaprost because of conjunctival hyperemia or irritation. One subject discontinued Latanaprost because of hypertrichosis. No patients developed iris cysts, cystoid macular edema, uveitis or HSV reactivation.

Ou Y, Yu F, Law SK, Coleman AL, Caprioli J. Outcomes of Ahmed glaucoma valve implantation in children with primary congenital glaucoma. Arch Ophthalmol. 2009 Nov;127(11):1436-41.

This paper evaluates the long-term efficacy of intraocular pressure reduction and complications of Ahmed glaucoma valve (AGV) implantation in children with primary congenital glaucoma. The paper reviews medical records of patients with primary congenital glaucoma who underwent AGV implantation with a minimum follow-up of 6 months. The authors use as their primary outcome measure a term called "cumulative probability of success," which they defined as intraocular pressure greater than 5 mm Hg and less than 23 mm Hg and at least a 15% reduction from the preoperative intraocular pressure, without serious complications, additional glaucoma surgery, or loss of light perception.

Thirty eyes of 19 children with primary congenital glaucoma who underwent AGV implantation with a minimum follow-up of 6 months were included. The children had a mean (SD) age of 1.8 (2.6) years, a mean (SD) preoperative intraocular pressure of 28.4 (6.7) mm Hg, and a mean (SD) follow-up time of 57.6 (48.0) months. The cumulative probability of success was 63% in 1 year and 33% in 5 years. After a second AGV implantation, the cumulative probability of success was 86% in 1 and 2 years and 69% in 5 years. Hispanic ethnicity ($P = .02$) and being female ($P = .005$) were associated with increased risk of failure. 20% of eyes required tube revision. The authors conclude that thirty-three percent of AGV implantations in children with primary congenital glaucoma were successful after 5 years of follow-up. With the implantation of a second AGV, the 5-year success rate increased to 69%.

[Hargadon DD](#), [Wood J](#), [Twelker JD](#), [Harvey EM](#), [Dobson V](#). Recognition acuity, grating acuity, contrast sensitivity, and visual fields in 6-year-old children. [Arch Ophthalmol](#). 2010 Jan;128(1):70-4.

This manuscript measures the monocular distance visual acuity (VA), grating VA, contrast sensitivity, and visual field extent in 59 healthy full-term children aged 5.8 to 6.3 years who had no ocular abnormalities and no myopia of 1.00 diopter (D) or greater, hyperopia of 4.00 D or greater, astigmatism of 1.50 D or greater, or anisometropia of 1.50 D or greater spherical equivalent or cylinder, as evaluated by a standard eye examination with cycloplegic refraction. The results provide additional normative monocular data on visual function in 6-year-old children and indicate that their thresholds are less than those of adults for distance

recognition VA, grating VA, and contrast sensitivity, but similar to those of adults for white-sphere kinetic perimetry.

In summary, right and left eye values did not differ significantly. Mean values for the right eye were 0.040 logMAR (SD, 0.075 log units) for Early Treatment Diabetic Retinopathy Study VA, 24.5 cycles per degree (SD, 0.3 octaves) for grating acuity, and 1.63 (SD, 0.12 log units) for contrast sensitivity. Mean visual field extent for the inferonasal, superonasal, superotemporal, and inferotemporal meridians was 59.1 degrees (SD, 9.7 degrees), 57.8 degrees (SD, 9.6 degrees), 71.2 degrees (SD, 12.3 degrees), and 100.4 degrees (SD, 6.6 degrees), respectively.

This manuscript points out the importance of using age-based normative data rather than adult normative data in assessment of visual function in young children

XXII. CONGENITAL INFECTION

XXIII. PEDIATRICS

Incidence, Ocular Manifestations, and Survival in Children with Neuroblastoma: A Population-Based Study.

[Smith SJ](#), [Diehl NN](#), [Smith BD](#), [Mohney BG](#).

[Am J Ophthalmol](#). 2010 Feb 9. [Epub ahead of print]

PURPOSE: To determine the incidence, ophthalmic manifestations, and survival among children with neuroblastoma in a defined population.

METHODS: The medical records of all pediatric (<19 years) residents of Olmsted County, Minnesota, diagnosed with neuroblastoma from January 1, 1969, through December 31, 2008, were retrospectively reviewed.

RESULTS: Fourteen children were diagnosed with neuroblastoma as residents of Olmstead County, Minnesota, during the 40-year period, yielding an age- and gender-adjusted incidence of 11.8 (95% confidence interval [CI]: 5.6-18.0) per million patients <15 years of age. The calculated incidence for patients presenting before the age of 5 in this cohort was 1 in 5970 children (95% CI: 3920-12 580 children). The mean age at diagnosis for the 14 study patients was 22.5 months (range, 10.4-42.6 months). Six of the 14 (43%; 95% CI: 18%-71%) had ocular manifestations, including orbital metastasis in 6 (100%), proptosis and ecchymosis in 4 (67%), ptosis in 2 (33%), and strabismus in 1 (17%). The Kaplan-Meier rate of survival for all 14 children was 57% at 1 year (95% CI: 36%-90%) and 50% at 5 years (95% CI: 30%-84%), while the 6 with eye findings had a survival rate of 17% at 9 months (95% CI: 3%-100%).

CONCLUSIONS: The incidence of neuroblastoma in this population was 11.8 per million patients <15 years, with ophthalmic involvement observed in 6 of the 14 study patients (43%). Orbital metastasis in the 6 children in this cohort was associated with poor prognosis.

Ophthalmic Abnormalities in Children with Down Syndrome.

Creavin AL, Brown RD.

JPOS 2009 Mar-Apr;46:76-82.

A comprehensive review of the available literature was performed to determine the common ophthalmic disorders in children aged 0-16 years with Down syndrome. Refractive error (esp. hyperopia) and strabismus (esp. esotropia) were common findings. Other frequent findings included poor visual acuity, nystagmus, blepharitis, and less frequently, cataract, and glaucoma. The high prevalence of ophthalmic disorders in children with Down syndrome demonstrated by all studies highlights the need for these children to undergo an ophthalmic assessment. One study showed that non-specialist examination of children with Down syndrome may miss up to 20% of ophthalmic disorders. These results support pediatric ophthalmic monitoring in combination with an ophthalmologic screening program, rather than in place of one

XXIV. INFANTILE DISEASES

Ophthalmological abnormalities in children with congenital disorders of glycosylation type I.

Morava E, Wosik HN, Sykut-Cegielska J, Adamowicz M, et al.

Br J Ophthalmol 2009 Mar; 93(3):350-354.

Background: Children with congenital disorders of glycosylation (CDG) type Ia frequently present with ocular involvement and visual loss. Little is known, however, about the occurrence of ophthalmological abnormalities in other subtypes of CDG syndrome.

Methods: We evaluated 45 children sequentially diagnosed with CDG type I for the presence of ocular abnormalities at the time of the diagnosis and during follow-up. We compared the various ophthalmic findings in the different CDG subgroups.

Results: Of the 45 patients, 22 had CDG type Ia, nine had CDG type Ic and 14 had a so-far undiagnosed biochemical background (CDG type Ix). We found ocular anomalies in 28 of the 45 children. Three had unique findings, including congenital cataract, retinal coloboma and glaucoma. A few CDG type Ia patients showed a sequential occurrence of symptoms, including retinitis pigmentosa or cataract.

Conclusions: Ophthalmic findings are frequent in CDG syndrome involving both the anterior and posterior segment of the eye. The disorder might lead to abnormal development of the lens or the retina, cause diminished vision, and alter ocular motility and intraocular pressure. We suggest routine screening and follow-up for ophthalmological anomalies in all children diagnosed with CDG syndrome to provide early treatment and adequate counseling.

Reduced grating acuity associated with retinal toxicity in children with infantile spasms on vigabatrin therapy.

Durbin S, Mirabella G, Buncic JR, Westall CA.

Invest Ophthalmol Vis Sci 2009 Aug; 50(8):4011-6.

Purpose: To determine whether visual functions are decreased in children with infantile spasms and vigabatrin-attributed retinal toxicity.

Methods: Contrast sensitivity and grating acuity were measured by using sweep visual evoked potential (VEP) testing in 42 children with infantile spasms (mean age, 29.23 ± 18.31 months). All

children had been exposed to vigabatrin (VGB) for a minimum of 1 month. These children were divided into retinal toxicity and no toxicity groupings based on 30-Hz flicker amplitude reductions on the full-field electroretinogram. A multivariate analysis of variance (MANOVA) compared visual functions between children with and without retinal toxicity.

Results: The MANOVA showed that visual function was significantly affected by VGB retinal toxicity. Further univariate analysis revealed that grating acuity was significantly reduced in children with toxicity. No differences in contrast sensitivity were found between children with toxicity and those without.

Conclusions: Reduced visual functions from VGB-attributed retinal toxicity can be detected in children with infantile spasms with the sweep VEP.

Comment: Visual field constriction has been detected in 30% to 50% of adult patients and in children who receive vigabatrin. Studies in rodents have shown that retinal insult is associated with an accumulation of VGB within retinal cells and elevated retinal GABA levels at the synapse. ERG reductions in the 30-Hz flicker amplitude have been associated with VGB retinal toxicity, and this has become an accepted method of screening in children. Recent evidence using ocular coherence tomography (OCT) demonstrates peripheral retinal nerve fiber layer thinning in patients with VGB-attributed field loss. The sweep VEP is recorded using surface electrodes rather than contact lens electrodes required for ERG testing. If vision function assessed using sweep VEP recording were found to be sensitive in the detection of retinal toxicity, the VEP marker could provide a less invasive alternative in identifying the effects of toxicity.

XXV. SYSTEMIC

Eye movement abnormalities in Joubert Syndrome.

Weiss AH, et al. Invest Ophthalmol Vis Sci 2009; 50:4669-77. (Oct 2009)

Purpose: Joubert syndrome is a genetic disorder characterized by hypoplasia of the midline cerebellum and deficiency of crossed connections between neural structures in the brain stem that control eye movements. The goal of the study was to quantify the eye movement abnormalities that occur in Joubert syndrome.

Methods: Eye movements were recorded in response to stationary stimuli and stimuli designed to elicit smooth pursuit, saccades, optokinetic nystagmus (OKN), vestibulo-ocular reflex (VOR), and vergence using video-oculography or Skalar search coils in 8 patients with Joubert syndrome. All patients underwent high-resolution magnetic resonance imaging (MRI).

Results: All patients had the highly characteristic molar tooth sign on brain MRI. Six patients had conjugate pendular ($n = 4$) or see-saw nystagmus ($n = 2$); gaze holding was stable in four patients. Smooth-pursuit gains were 0.28 to 1.19, 0.11 to 0.68, and 0.33 to 0.73 at peak stimulus velocities of 10, 20, and 30 deg/s in six patients; smooth pursuit could not be elicited in four patients. Saccade gains in five patients ranged from 0.35 to 0.91 and velocities ranged from 60.9 to 259.5 deg/s. Targeted saccades could not be elicited in five patients. Horizontal OKN gain was uniformly reduced across gratings drifted at velocities of 15, 30, and 45 deg/s. VOR gain was 0.8 or higher and phase appropriate in three of seven subjects; VOR gain was 0.3 or less and phase was indeterminate in four subjects.

Conclusions: The abnormalities in gaze-holding and eye movements are consistent with the distributed abnormalities of midline cerebellum and brain stem regions associated with Joubert syndrome.

Comment: Joubert syndrome is a genetic disorder of ciliary function characterized by cerebellar hypoplasia and defective cross connections between neural structures in the brain stem. Since these brain regions are critical components of the oculomotor system, the authors anticipated that a quantitative study of eye movements in Joubert syndrome would provide a sensitive measure of the functional abnormalities of these structures.

XXVI. VISUAL IMPAIRMENT

A population-based study of visual impairment among pre-school children in Beijing: the Beijing study of visual impairment in children.

Lu Q, Zheng Y, Sun B, Cui T, Congdon N, Hu A, Chen J, Shi J.
Am J Ophthalmol 2009 Jun; 147(6):1075-81.

Purpose: To evaluate the prevalence and causes of visual impairment among Chinese children aged 3 to 6 years in Beijing.

Methods: Presenting and pinhole visual acuity were tested using picture optotypes or, in children with pinhole vision < 6/18, a Snellen tumbling E chart. Comprehensive eye examinations and cycloplegic refraction were carried out for children with pinhole vision < 6/18 in the better-seeing eye.

Results: All examinations were completed on 17,699 children aged 3 to 6 years (95.3% of sample). Subjects with bilateral correctable low vision (presenting vision < 6/18 correctable to \geq 6/18) numbered 57 (0.322%; 95% confidence interval [CI], 0.237% to 0.403%), while 14 (0.079%; 95% CI, 0.038% to 0.120%) had bilateral uncorrectable low vision (best-corrected vision of < 6/18 and \geq 3/60), and 5 subjects (0.028%; 95% CI, 0.004% to 0.054%) were bilaterally blind (best-corrected acuity < 3/60). The etiology of 76 cases of visual impairment included: refractive error in 57 children (75%), hereditary factors (microphthalmos, congenital cataract, congenital motor nystagmus, albinism, and optic nerve disease) in 13 children (17.1 %), amblyopia in 3 children (3.95%), and cortical blindness in 1 child (1.3%). The cause of visual impairment could not be established in 2 (2.63%) children. The prevalence of visual impairment did not differ by gender, but correctable low vision was significantly ($P < .0001$) more common among urban as compared with rural children.

Conclusions: The leading causes of visual impairment among Chinese preschool-aged children are refractive error and hereditary eye diseases. A higher prevalence of refractive error is already present among urban as compared with rural children in this preschool population.

XXVII. NYSTAGMUS

Hobson F, Rowe FJ: Management of nystagmus by surgery and botulinum toxin options: a review. Br Ir Orthopt J 2009; (June) 6: 28-34.

This literature review searched articles written between 1939 and 2008, and set out to determine the success rate for botulinum toxin therapy and extraocular surgery in the management of acquired nystagmus.

Botox can be injected directly into the extraocular muscles or into the retrobulbar space. Benefits can be effective, albeit temporary. Sometimes a satisfactory improvement seen with botox can be used as a guideline for a more permanent surgical correction. It can be helpful in the presence of nystagmus with annoying subjective symptoms such as oscillopsia. Complications include ptosis, which can have the unintended benefit of creating occlusion.

If the deviation is mostly horizontal, a single injection into a horizontal muscle is applied; if the deviation has combined horizontal, vertical and torsional components, injection into the retrobulbar space may be indicated.

Acquired pendular nystagmus did better with botox than jerk nystagmus. Botox can be very valuable in selected cases.

The article summarizes all the surgical techniques that can be used when operating on patients with nystagmus. Surgery is often performed to reduce or eliminate an abnormal head posture. Specifically the best successes occur when surgery is performed to reposition a null point.
[37 references]

Br J Ophthalmol 2009;**93**:1560-1562 doi:10.1136/bjo.2009.161083

Estimating numbers of blind children for planning services: findings in Kilimanjaro, Tanzania

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Abstract

Aim: Childhood blindness is included in the VISION 2020 initiative. However, childhood blindness is rare, so there is limited population-based evidence to assist with the planning of services. We carried out a survey of childhood blindness in Kilimanjaro Region, Tanzania, to generate information needed for planning eye care services.

Methods: The study was carried out in parallel with a Rapid Assessment of Avoidable Blindness (RAAB) survey. Villages within Kilimanjaro Region were selected on a probability-proportional-to-size basis. Key informants in each village were trained to identify children with any vision problems; a visiting team assessed the children to determine visual status and arranged for further assessment as needed at hospital. The files of children at schools for the blind in the Region were reviewed to identify children in schools from the selected study villages.

Results: Among the 95 040 children in the 72 villages sampled, 13 children were identified as blind; an additional three children were found in the schools for the blind. The prevalence of blindness was 0.17 per 1000 children; the causes of blindness varied but there was no vitamin A- or measles-related corneal blindness and only one case of unoperated cataract.

Discussion: The low prevalence of blindness in children suggests that efforts at reducing childhood blindness in Kilimanjaro Region have been effective. Planners there should focus on community-based approaches to ensure that blind children have appropriate rehabilitation services and educational placements. While it remains impractical to carry out large childhood blindness surveys, this approach attached to a RAAB survey may be useful for generating information for planning services.

Comment: Large study, over 95,000 children screened. Screening attached to another survey already being done is a novel approach to gathering this type of data.

Two hypothetical nystagmus procedures: Augmented Tenotomy and Reattachment and Augmented Tendon Suture (sans tenotomy). Dell'Osso L et al. JPOS Nov-Dec 2009; 46:337-344.

The tenotomy and reattachment procedure directly affects only the enthesis of the tendon. The augmented tendon suture technique consists of placing several additional sutures in the tendon proximal to the tenotomy. Based on the hypothetical proprioceptive mechanisms for the beneficial effects of the T&R procedure, the authors hypothesize that the

ATS technique will duplicate the therapeutic effect of T&R resulting in a simpler procedure more suitable for single-session, multi-muscle surgery that may be required for improving the waveforms of nystagmus and less prone to cause complications.

Refractive errors and strabismus in children with Tuberos Sclerosis: a controlled study. Akinci A et al. JPOS Nov-Dec 2009; 46:345-348.

Twenty-three children with tuberous sclerosis and 151 control subjects were evaluated. The total prevalence of hypermetropia and amblyopia was significantly higher in patients with tuberous sclerosis. Early screening for this amblyogenic factor is indicated.

Onset and progression of with-the-rule astigmatism in children with Infantile Nystagmus Syndrome.

Wang J, et al. Invest Ophthalmol Vis Sci 2010; 51:594-601. (Jan 2010)

Purpose: The purpose of this study was to examine the onset and progression of with-the-rule (WTR) astigmatism during the first 8 years of life in children with idiopathic infantile nystagmus syndrome (INS) or INS associated with albinism and to compare their development with that of normal children. Also explored was whether early WTR astigmatism influences emmetropization in children with INS and whether there is evidence of meridional emmetropization.

Methods: Cycloplegic refractions culled from medical records were converted into power vector components: M (spherical equivalent), J0 (positive J0 indicates WTR astigmatism), and J45 (oblique astigmatism). Two diagnostic groups (idiopathic, n = 106; albinism, n = 95) were evaluated and compared with a reference normal group (n = 495). Four age subgroups were evaluated: age≤0.5 year, 0.5<age≤1 year, 1<age≤4 year, and 4<age≤8 year; in the normal group, no data were available for 4- to 8-year-olds. In addition, two longitudinal groups of children with INS (idiopathic, n = 22; albinism, n = 27) were studied.

Results: WTR astigmatism was prevalent among children with INS, even during infancy. Both the prevalence and magnitude of WTR astigmatism increased with age in both INS groups. Predicted J0 from fitted longitudinal data agreed with cross-sectional data. Spherical equivalent of children with INS demonstrated little emmetropization during the first 8 years of life.

Conclusions: Both the cross-sectional and longitudinal data showed that WTR astigmatism was common among children with INS and increased in magnitude with age during the first 8 years of life. Changes observed in meridional refractive error with age were consistent with meridional emmetropization in children with INS and WTR astigmatism.

Comment: This study is novel because it is known that WTR astigmatism has been reported frequently in school-age children and adults with INS. In normal infants, astigmatism typically decreases with age and most astigmatic infant eyes have against-the-rule (ATR) astigmatism. The authors show, through both cross-sectional and longitudinal data, that with-the-rule astigmatism is common among children with infantile nystagmus syndrome and increases in magnitude with age during the first 8 years of life.

Spectral domain optical coherence tomography for detection of foveal morphology in patients with nystagmus. Cronin TH, Hertle RW, Ishikawa H, et al. J AAPOS 2009;13:563-566.Dec

Evaluation of the retina is difficult in nystagmus patients secondary to their constant eye motion. Time domain optical coherence tomography (TD-OCT) is difficult in pediatric nystagmus patients because of the eye movement, shortened attention span and their compromised vision. Spectral domain OCT (SD-OCT) provides high-resolution 3-D macular imaging at 50x the speed of TD-OCT. This study tested 19 nystagmus patients (age 6-68 years) with SD-OCT. Two patients had latent nystagmus and 17 had infantile nystagmus syndrome (9 of whom had OCA). High-resolution macular images were

obtainable in 18 of 19 patients (95%). There was a high correlation between the clinical examination and the SD-OCT findings involving the macula. Foveal hypoplasia patients showed persistence of the outer plexiform layer, inner nuclear layer, inner plexiform layer, ganglion cell layer and nerve fiber layer in the fovea.