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One Year of Pediatric Ophthalmology and Strabismus Research in Review

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Abstract

Purpose: To highlight recent advances in amblyopia and strabismus.

Design: Literature review.

Methods: A literature search of articles published in the English language was performed in PubMed or MEDLINE between May 2012 and April 2013 using the terms amblyopia or strabismus. Articles deemed relevant were selected.

Results: The review highlights articles that increase our understanding of strabismus and amblyopia as well as newer treatment strategies.

Conclusions: The review highlights some new information and possible future advances in amblyopia and strabismus.

Keywords

amblyopia; strabismus; pediatric ophthalmology research

PART I: AMBLYOPIA

Amblyopia is part of the “bread and butter” of pediatric ophthalmology and strabismus and has been the subject of an increased number of publications in the last decade. The definition of amblyopia may vary slightly between individuals or different studies but is generally accepted as a bilateral reduction of visual acuity to less than age-appropriate norms or an interocular acuity difference of at least 2 lines of vision. This current review highlights some of the literature published in the past year from May 2012 to April 2013. Approximately 1 in 7 of 238 articles found in a PubMed search for amblyopia was emphasized. We did not analyze the validity or design of the individual studies presented here but merely report their findings. The articles highlighted were given preference clinical trials, clinically-relevant scientific literature, larger case series, and case reports of particular significance.

With the many high functioning monocular patients from various different etiologies in our population, one can question why amblyopia is studied so frequently. After all, we tell our monocular patients that they can lead a perfectly normal life. However, do these patients actually have a limitation in visual function? Why invest in multicenter trials and extra visits to the eye care professional to detect and treat amblyopia if it is not important? Treating amblyopia does improve vision and stereopsis in almost half of patients with refractive or strabismic amblyopia, but does this have an effect on daily life?¹ There is information on the functional impact of amblyopia, which suggests an impact on self-esteem, quality of life, educational level, and career choice.²⁻⁵ However, the conclusions do not always agree. For example, this year, the Dunedin Multidisciplinary Health and Development Study in New Zealand revisited this topic with a prospective cohort study of 1037 children now followed up to age 32 years old. In this population, 3.5% had amblyopia, with no statistically significant functional impact on motor development, self-esteem, or socioeconomic status of amblyopic individuals.⁶ This raises the issue of cost-effectiveness for the treatment of unilateral vision loss.⁷ Not surprisingly, these findings of no functional impact were met with skepticism and disagreement by many pediatric ophthalmologists and strabismologists, and their conclusions will be summarized later. With the advent of modern technology, including 3-dimensional media, which requires a higher level of binocular function, the impact on daily life may change. More studies are likely in the coming years, but larger samples and more rigorous controls of confounding variables will be costly and difficult to organize.

Neurological and Anatomical Changes in Amblyopia

In previous studies by Niechwiej-Szwedo et al, neurological differences have been observed in patients with amblyopia. Pattern electrinoctinograms (ERGs) are significantly reduced in both eyes compared with subjects without amblyopia.⁸ Amblyopic eyes have been shown to have a longer saccade latency, lower peak saccade acceleration and velocity, and decreased saccade precision, suggesting a slower processing of the afferent arm of the saccadic system.^{9,10} In patients with anisometropic amblyopia, saccade peak acceleration was decreased whereas latency and amplitude variability were decreased for the amblyopic eye, even with binocular viewing or sound-eye viewing conditions.^{9,10} In addition, eye-hand coordination in patients with severe amblyopia during visually guided reaching with the amblyopic eye was also impaired.¹¹ This year, a follow-up study was published by the same group evaluating the effect of monocular blur up to 5 hours on saccadic eye movement and found that blurring one eye did not produce the same changes in saccades. This suggests that there are unique findings in amblyopia not simply explained by decreased visual acuity.¹² Saccadic eye movements were also investigated in strabismic amblyopia, showing that patients with normal stereopsis had no deficits, whereas severe amblyopia with no stereopsis had a longer saccadic latency and decreased amplitude precision, but patients with mild amblyopia and no stereopsis had only reduced saccadic amplitude precision.¹³ Eye position stability is also affected in amblyopia, with the amblyopic eye demonstrating more eye position instability regardless of whether the subject is looking with the amblyopic, fellow eye or binocularly.^{14,15} These studies suggest that refractive and strabismic amblyopia may share some abnormalities but that sensorimotor processing of eye movements and positional stability may differ in the various types of amblyopia.

Magnetic resonance imaging (MRI) continues to be studied in amblyopia. Functional MRI has shown decreases in the striate and extrastriate cortex as well as abnormalities in the activity of areas V1 and V2.^{16,17} Similarly, functional MRI in anisometropic amblyopia showed decreased signal in areas related to visuomotor processing, whereas increases were found in somatosensory cortex, motor, and auditory areas.¹⁸ Other changes include decreased volume of the areas of the brain related to spatial vision on MRI when compared with those of subjects without amblyopia.¹⁹ This suggests that there may be compensatory changes in amblyopia.

Optical coherence tomography has become more available in recent years and has been more recently applied to the diagnosis and management of childhood eye conditions. Studies of unilateral amblyopic individuals with either anisometropia or strabismus showed thickening of the fovea of the amblyopic eye with optical coherence tomography.^{8,20,21} Another study measured the retinal nerve fiber layer thickness and the macular thickness with esotropic amblyopia and found no differences compared with their fellow eye.²² This agreed with another study where the macula was found to be thicker in anisometropic amblyopic eyes but not in eyes with strabismic amblyopia.²³ Foveal thinning was also found in the amblyopic eye with hyperopic anisometropic amblyopia, but this was not related to the degree of anisometropia.²⁴ Amblyopic eyes from high hyperopia were shown to have a reversal of the thickening after treatment with full-time spectacle correction.²⁵ It will be interesting to see the results of subgroup analysis and changes with amblyopia therapy in the years to come.

Detection and Referral

What is the true incidence of amblyopia and its risk factors? In a meta-analysis of preschool studies reported in April, the prevalence of risk factors was approximately 21%.²⁶ The same study found the prevalence of amblyopia with vision of 20/40 and worse to be only 2.5%.²⁶ The accepted opinion of most eye care professionals is that early detection and treatment lead to better outcomes. The US Preventative Services Task Force recommends screening all children in the preschool years at least once between the ages of 3 and 5 years.²⁷ Technological advancements have made automated screening in the form of autorefractors or photoscreeners accessible to screening programs and pediatricians. Some screening devices can even detect abnormalities other than just refractive error such as visual axis opacities and strabismus.

An update from the American Association for Pediatric Ophthalmology and Strabismus Vision Screening Committee guidelines on automated preschool vision screening was published this year, raising the threshold for referral.²⁸ These recommendations maintain high sensitivity for the detection of high-magnitude refractive error and improve specificity for low-level amblyogenic risk factors in younger children. These adjustments were made because severe amblyopia is more responsive to therapy for those younger than 5 years, whereas moderate amblyopia can be responsive to therapy until the age of 7 years.²⁹ The new guidelines call for a referral with automated screening for children at all ages with greater than 8 prism diopters of manifest strabismus, a media opacity of greater than 1 mm, and refractive error guidelines for different age groups (Table 1).^{28,30} The American

Association for Pediatric Ophthalmology and Strabismus and the American Academy of Pediatrics still recommends optotype screening for children who can read linear letters and are reliable enough to perform the examination. The referral criteria with referral for visual acuity is lower than 20/30, 3 or more lines interacuity difference, or any manifest strabismus.
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Conditions Associated With Amblyopia

To echo what was seen in previous studies with a smaller number of patients, nasolacrimal duct obstruction (NLDO) has been shown to have a higher incidence of amblyopia, with 5.8% of all patients developing amblyopia.³¹ In these cases, the more hyperopic eye (by spherical equivalent) was the amblyopic eye.³¹ Patients with unilateral NLDO had a higher incidence of anisometropia, affecting 7.6% of patients with unilateral NLDO compared with 3.6% of patients with bilateral NLDO.³¹ This observation warrants cycloplegic refractions with regular follow-up for all children with NLDO.

Ptosis is another condition frequently associated with amblyopia, with 2 studies in the past year showing similar results. They observed that 8.6% to 10% of all patients with ptosis had deprivational amblyopia from occlusion of the visual axis.^{32,33} Of all patients with congenital ptosis in Olmsted County diagnosed between 1965 and 2004, 14.6% had amblyopia, with refractive and strabismic amblyopia accounting for 42% of these cases. Therefore, refractive error and strabismus are relatively common and are another risk factor that must be monitored in patients with ptosis. An interesting observation on a cohort of patients in India with a rare genetic disorder with findings of blepharophimosis, ptosis, and epicanthus inversus syndrome is associated with a very high incidence of amblyopia. They reported 60% of patients with amblyopia, with 75% being bilateral.³⁴ Forty percent of these patients also had strabismus, with amblyopia more common in this group.³⁴ Patients with neurofibromatosis type 1 with orbitotemporal plexiform neurofibromas are also at risk for amblyopia, affecting 62% of all patients.³⁵ Of the patients studied, 43% of all patients had amblyopia from occlusion of the visual axis, another 43% with anisometropia, and 10% with strabismus.³⁵ All of the patients with amblyopia had plexiform neurofibromas with volumes greater than 10 mL based on MRI.³⁵

Treatment

The Pediatric Eye Disease Investigator Group has been one of the major contributors to the standard of care for amblyopia therapy, incorporating multicenter clinical trials from academic and private-practice sites. One recommendation is to treat anisometropic amblyopia with spectacle correction before instituting patching or atropine penalization because spectacle correction alone may improve visual acuity.³⁶ In this group of patients, after correcting refractive error for at least 4 weeks, patching in moderate amblyopia with visual acuity between 20/40 and 20/100 responded to 2 hours of patching a day while severe amblyopia with vision 20/100 or worse responded to 6 hours of patching a day. In children with moderate amblyopia, atropine to the fellow eye once a day for 2 consecutive days a week is an effective therapy in children if there is no myopia in the fellow eye.³⁹ Pharmacological penalization with cycloplegia for 2 consecutive days a week is an appropriate therapy for amblyopia in many individuals. Despite the large amount of

evidence-based recommendations on the treatment of amblyopia, the implementation in clinical practice has not been fully realized by many practitioners. In Toronto, one study found that moderate amblyopia has been treated with more than the recommended 2 hours per day patching regimen, whereas severe amblyopia is on average treated with less than the recommended 6 hours a day of patching.⁴⁰

A promising amblyopia treatment may be with a dichoptic method, a binocular approach where images are presented separately to each eye. When the amblyopic eye is presented with a high-contrast image and the contrast of the fellow eye is reduced, there is an improvement in visual acuity and stereoacuity in children and adults.^{41–44} This exciting potential therapy for amblyopes of all ages warrants a formal study comparing to conventional amblyopia therapy methods with a randomized control trial.

In children whose response to amblyopia therapy has plateaued, there are options to attempt further visual improvement. In one randomized control trial, when the vision has ceased to improve with 2 hours a day of occlusion therapy, increasing patching to 6 hours a day can continue to improve visual acuity.⁴⁵ A meta-analysis of 6 studies on the use of L-dopa for amblyopia was performed and indicated that patients with amblyopia receiving L-dopa had a greater response to occlusion therapy with no significant increase in adverse events compared with those receiving placebo.⁴⁶ The Pediatric Eye Disease Investigator Group is currently enrolling patients in a randomized clinical trial, ATS17, using L-dopa as adjunctive treatment to patching for residual amblyopia (20/50 or worse) in older children and teenagers 7 years to younger than 13 years, with recruitment likely ending in 2013.

One study within the past year in the kitten model of amblyopia brings the possibility of new investigations for amblyopia therapy into the pipeline. In a classic model of deprivational amblyopia by Wiesel and Hubel,⁴⁷ monocular eyelid closure in the juvenile kitten results in changes in the cat cortex. In a more recent study, cats with monocular amblyopia were raised in 10 days of complete darkness.⁴⁸ The cats either were dark-reared immediately after deprivation or were delayed dark-rearing until after the presumed critical period of visual development for the cat.⁴⁸ This study demonstrated prevention of the development of amblyopia for the immediate dark-reared kittens and a reversal of visual deficits for the kittens raised in delayed dark conditions.⁴⁸ These findings were correlated with a reversal of maturation of visual cortex cytoskeletal components, which is correlated with neuronal maturation.⁴⁸ The discovery of a reversal of maturation of the visual cortex with an improvement in vision is promising, and its application to patients may be considered in the future.

Gaps in Knowledge

With the belief of “an ounce of prevention is worth a pound of cure,” the mechanisms of emmetropization still need to be elucidated. Determining how emmetropization occurs in the eye could have a large impact on the prevention of high refractive errors, particularly high myopia. Interestingly, myopia is negatively correlated with parental smoking.⁴⁹ This compares with a previous study in multiethnic pediatric eye disease and Baltimore pediatric eye disease study that indicated that a history of maternal smoking during pregnancy was associated with a higher incidence of hyperopia.⁵⁰ This certainly does not advocate smoking

by parents but warrants further studies on the involvement of nicotinic receptors on ocular growth and emmetropization of the eye.

Treatment of amblyopia continues to be under active investigation; however, practitioners still have many challenges treating the patient who is not adherent to amblyopia therapy. There is a paucity of literature on patient adherence to therapy and ways to improve it. There is also a lack of novel approaches for the patient who will not wear glasses or patch and is not a candidate for pharmacological penalization. With all the technological advances in recent years and the increased availability of portable media devices, there will hopefully be more successful therapies in the future.

PART II: STRABISMUS

This review includes all articles retrieved by a MEDLINE search using the keyword *strabismus* published in the past year from May 2012 to April 2013, plus articles published a few months before or after this period that were deemed particularly noteworthy or contributed to a specific theme.

Etiology of Strabismus

The classic Worth-versus-Chavasse dispute concerns whether the primary defect in infantile esotropia is the motor abnormality or the sensory abnormality. The contemporary version of this debate seems to have been reframed around the question of whether infantile strabismus originates in the brainstem or the cortex. A recent theory holds that the dissociative features of infantile strabismus—dissociated vertical deviation, dissociated horizontal deviation, latent nystagmus, and perhaps oblique muscle dysfunction—are atavistic torsional-vestibular reflexes mediated by the nuclei of the accessory optic system. If so, then an abnormality of the accessory optic system can be suspected as the proximal cause of infantile strabismus.^{51,52} The countervailing argument is that all of the manifestations of infantile strabismus can be produced experimentally by sensory manipulation of an infant primate. This results in a loss of cortical binocular response that correlates with the development of the characteristics of motor abnormalities of infantile strabismus, most of which may be explained as secondary consequences of latent nystagmus.⁵³

Meanwhile, some of the underlying electrophysiology of strabismus is beginning to be elucidated. Neurons in the supra-oculomotor area of the brainstem have been found to code for vergence angle. A recent study shows that in strabismic monkeys, their activity correlates with the angle of strabismus. Furthermore, pathological behavior of these neurons is suggested in that their neural thresholds and sensitivities are altered compared with normal animals.⁵⁴ However, it is unclear whether their abnormal behavior is the proximal cause of strabismus or a consequence of abnormalities further upstream in the brainstem or cortex.

Most theories of strabismus regard it as a neurological problem and discount any role for the extraocular muscles themselves. However, microscopic, ultrastructural, and functional abnormalities have been described in extraocular muscles of patients with strabismus. Now, a study shows that a considerable number of genes are significantly up-regulated or down-regulated in extraocular muscles from patients with strabismus relative to normal controls.

The authors suggest that these abnormalities of gene expression may reflect an imbalance in a trophic regulatory system that mediates muscle plasticity that could be the underlying defect in some forms of strabismus.⁵⁵

The small horizontal and vertical deviations that develop in older patients seem to be one type of strabismus for which the cause lies with the extraocular muscles and their attachments. An MRI study of older patients, with a condition termed the *sagging eye syndrome* by the authors, showed rupture of the lateral rectus–superior rectus ligament in the majority of cases. When the resulting inferior displacement of the lateral rectus muscle was symmetric, it was associated with divergence insufficiency pattern esotropia. Vertical deviations were associated asymmetrical displacement. The authors conclude that common involutional changes of the orbital connective tissue are responsible for many of the cases of acquired diplopia in older adults.⁵⁶

Many pediatric eye disorders, including a few strabismus disorders, are turning out to have a genetic cause. In a classical twin study of 1462 twin pairs, it was found that esodeviation has a 64% heritability that is independent of the heritability of refractive errors. This suggests that it may be possible to find specific genes that contribute to the development of esodeviations. Exodeviation, however, was not found to have a corresponding genetic contribution.⁵⁷

Epidemiology

The prevalence of strabismus in a Brazilian population is 1.4%, which is somewhat low compared with previous studies of white or African-American populations.⁵⁸ In contrast, the diagnosis of strabismus in an older population from Medicare claims data is 0.68%, and surgery is performed in only 0.016%. Whites are approximately 2.5 times more likely to have a surgery for their strabismus than African Americans.⁵⁹

Pseudoesotropia

Pseudoesotropia is the appearance of esotropia, usually caused by prominent epicanthal folds, which prompts a significant number of clinic visits for infants and toddlers when parents or pediatricians mistake it for true strabismus. Parental observation of strabismus was found to have a positive predictive value of 78% in a study of Korean children. As might be expected for an Asian population, parental identification of exotropia was more accurate than identification of esotropia.⁶⁰

Once a child is diagnosed with pseudoesotropia, the usual practice is to reassure the parents that there is no pathological finding and dismiss the child from further examination. Adding to previous evidence, several studies raise questions as to whether children with pseudoesotropia may actually merit further follow-up. In one study of 201 children diagnosed with pseudoesotropia before 3 years of age, 20 were later found to have strabismus (mostly esotropia) and 5 developed significant refractive errors causing mild amblyopia.⁶¹ A much smaller study also found that 6/31 children diagnosed with pseudoesotropia before 5 years of age were later found to have esotropia.⁶² A third study found that 15.7% of children diagnosed with pseudoesotropia before 3 years of age

subsequently developed accommodative esotropia; these were almost exclusively children with hyperopia greater than + 1.50 D at their initial presentation.⁶³

Of course, no one would expect that having a normal examination result at one point in time would protect against subsequent development of strabismus or refractive errors. Indeed, if the goal is to provide follow-up for any child at risk for developing strabismus or amblyopia, then all children would need repeated examinations. In each instance, however, the authors make the case that the incidence of strabismus observed in children previously examined for pseudoesotropia is higher than expected and that these children are more in need of continued examinations than the general population. The problem is that these are retrospective studies in which children who did not return for follow-up examinations were excluded. One would expect that those in whom the parents subsequently noticed definite strabismus would be more likely to return for examination, which makes it difficult to assess what the actual incidence of strabismus is in these cohorts.

Esotropia

Acquired esotropia in children (Franceschetti type) without an obvious cause—significant hyperopia, cranial nerve palsy, or other neuropathology—is a relatively uncommon condition. It usually develops suddenly and is initially often accompanied by diplopia. In a large series of these patients, it was found that surgical treatment results in satisfactory alignment in more than 90% and that most of these recover normal stereoacuity.⁶⁴

Divergence insufficiency pattern esotropia is an acquired condition affecting mostly older adults. It is characterized by esotropia and diplopia with distance fixation but little or no deviation at near. Based on an assumption that lateral rectus muscle surgery preferentially affects distance alignment, the historic recommendation has been to perform lateral rectus resections for this condition. A current study confirms several previous reports that medial rectus recessions are equally effective and do not result in secondary exotropia at near. However, the authors found that they needed larger medial rectus recessions than would be typically done for the same amount of esotropia.⁶⁵

A case of acquired exercise-induced esotropia in a teenager was successfully treated with medial rectus recession. A unilateral 4-mm recession corrected the 45° esotropia that developed during exercise without producing secondary exophoria. The author hypothesizes that altering the afferent innervation from the medial rectus tendon—as in the tenotomy and reattachment procedure for nystagmus—is responsible for the result.⁶⁶

Surgical correction of esotropia in children with developmental delay is thought to be less predictable and more prone to overcorrections over time. These issues were addressed in a recent study that is remarkable for its relatively long (>5 years) average follow-up time. The authors found that with slightly reduced medial rectus recession amounts, the success rate after initial surgery is 37.5%; however, most children obtain satisfactory results after additional procedures.⁶⁷ The relatively low initial success rate and the tendency to overcorrection do not seem to be a reason to deny these children an opportunity to have straight eyes.

Single medial rectus recession has been advocated by some as treatment of smaller-angle esotropia. A recent study comparing unilateral medial rectus recession for esotropia 15 to 35 PD to bilateral medial rectus recession for esotropia 30 to 70 PD found that the correction of esotropia per millimeter of recession rate of successful alignment were similar. The authors further found that large unilateral recessions did not produce convergence insufficiency or lateral incomitance of greater than 5 PD.⁶⁸

The ocular alignment when a patient is under anesthesia has been a subject of study for many years and, in some cases, advocated as a factor in surgical planning. A recent study used the esotropia remaining in an anesthetized patient as a proxy for medial rectus contracture in an effort to separate factors that contribute to esotropia, considering the additional esotropia when the patient is awake to be tonic convergence. The authors conclude that tonic convergence plays the greater role in partially accommodative esotropia and anatomic contracture is more important in basic nonaccommodative esotropia.⁶⁹ It is unclear whether this is consistent with the general belief that larger recessions are needed in partially accommodative esotropia. The authors suggest that surgery should be delayed in partially accommodative esotropia because the tonic convergence causes more variable alignment but is more urgent in nonaccommodative esotropia to prevent progression of medial rectus contracture.

Exotropia

Of all strabismus conditions, exotropia seems to have generated the most research interest during the last year. As expected, much of the research focuses on surgical treatment and outcomes. A multicenter group organized to study exotropia in the United Kingdom has begun to produce data. In an observational study of a cohort of patients with intermittent exotropia, they found that during a 2-year follow-up period, only 17% were managed surgically. The surgical group had the only clinically significant improvement in the angle or the control of their deviation; however, deterioration to constant exotropia was rare in patients who did not receive surgery. The surgical patients had worse initial control scores and may have been the ones more likely to deteriorate, had they not been operated on, but 21% developed persistent secondary esotropia after surgery.⁷⁰

When looking specifically at children treated surgically for intermittent exotropia, a poor outcome caused by persistent or recurrent exotropia was found in 20% and persistent overcorrection in 15%. The surgical dose was similar in the overcorrected and undercorrected patients. No relationship was found between an initial overcorrection and good outcome. Taken together, these findings suggest that the success rate cannot be improved by refinement of factors that are readily controlled by the surgeon such as the surgical dose.⁷¹ Perhaps, one reason for this is the variability of the preoperative measurements on which the surgical dose is based. In children with intermittent exotropia, test-retest reliability for angles greater than 20 PD was 7.2 PD at distance and 12.8 PD at near.⁷²

Two retrospective reports examined factors associated with poor outcomes after surgery for intermittent exotropia. One study found that predisposing factors for consecutive esotropia were high myopia, amblyopia, lateral incomitance, preoperative angle of deviation at

distance of 25 to 40 PD, difference between near and distance deviation of greater than 10 PD, tenacious proximal fusion and unilateral lateral rectus muscle recession, or medial rectus resection.⁷³ Although early surgery is advocated by some to prevent deterioration of fusion and solidification of sensory adaptations to the exotropia, another study found that older age at the time of surgery was associated with a lower recurrence rate.⁷⁴

The choice of procedure for surgical treatment of intermittent exotropia has been a running debate, with some surgeons preferring a unilateral recess-resect procedure for “basic” exotropia (in which the deviation is similar at distance and near) and others preferring bilateral lateral rectus recession. A study comparing these 2 procedures found that both groups had similar success rates initially; however, survival analysis showed a higher rate of deterioration and a lower long-term success rate with the recess-resect procedure.⁷⁵ This study does not address the issue of choosing a procedure to treat exotropia in general based on the pattern of distance-near incomitance, but basic exotropia—the subject of this report—is the subtype of exotropia for which the recess-resect procedure has often been advocated.

Hyperopia and accommodation have long been known to play a role in esotropia, but a number of recent studies now examine their importance in exotropia. In a series of children with exotropia and high hyperopia, spectacle correction of the hyperopia resulted in a paradoxical improvement of the exotropia. The authors speculate that amblyopia, frequently bilateral, prevents these patients from accommodating well. Spectacle correction treats amblyopia and reduces image blur to improve control of the exotropia. These patients also had a high prevalence of developmental delay and unexpectedly poor stereopsis for patients with intermittent exotropia.⁷⁶

Accommodation is driven by the convergence response to disparity, blur, and proximity. Patients with intermittent exotropia lose the disparity-driven component as their deviation decompensates and suppression develops. The remaining cues for accommodation are not as effective, and decompensated patients underaccommodate by more than 2 D at a distance of 33 cm. This underscores the importance of preventing patients with intermittent exotropia from decompensating at near.⁷⁷ Comparing convergence-to-accommodation and accommodation-to-convergence ratios in exotropic patients shows that they use binocular disparity rather than blur as their main cue to target distance. The authors of this study conclude that convergence is primarily used to control exotropia at near and accommodation is secondary. So minus lens, treatment of exotropia serves only to correct the overaccommodation driven by convergence rather than to induce blur-driven accommodation and accommodative convergence.⁷⁸

The degree of control of intermittent exotropia is often cited as an important factor in deciding whether surgical treatment is needed. Because this is difficult to assess reliably, a number of studies have examined other more quantifiable tests as a proxy for control of the deviation. Binocular interaction (better, worse, or same visual acuity under binocular compared with monocular viewing) was found to be associated with the accommodative response during binocular vision and the size of exodeviation. This suggests that binocular interaction, especially inhibition, may be an indicator of diminishing fusional control.⁷⁹ Most children with intermittent exotropia have normal fusional divergence at near, but there

is a bimodal distribution with nearly half of the children having reduced fusional divergence at distance. The authors speculate that fusional divergence may indicate how robust fusion is and have prognostic significance.⁸⁰

Fundus torsion, as judged from disc-foveal angle in fundus photographs, showed intorsion or extorsion more frequently in patients with intermittent exotropia than in normal controls. The size of the disc-foveal angle correlated with the amount exotropia and stereothreshold. The authors conclude that fundus torsion may be an indicator of the severity of declining fusion in patients with intermittent exotropia.⁸¹

Intermittent exotropia is believed by some to be a different disease from infantile exotropia, which is thought to be analogous to infantile esotropia. Two studies sought to contrast the features of these 2 entities. A retrospective study of patients with exotropia diagnosed before 1 year of age found that 25% wound up with good stereopsis, whereas 75% had poor stereopsis and other features associated with infantile strabismus such as inferior oblique overaction and dissociated vertical deviation. The authors assume that the groups with good and poor stereopsis are different conditions, although they did not differ in preoperative deviation, postoperative deviation, or rate of reoperation. The poor stereopsis may be partially explained by greater preoperative constancy of deviation in that group, although the difference between groups was not statistically significant in this small sample.⁸² Another study found that postoperative exodrift is similar in infantile and intermittent exotropia and, in contrast to the Improving Outcomes in Intermittent Exotropia (IOXT) Study, an initial postoperative alignment of 0 to 10 PD esotropia may be associated with better long-term alignment.⁸³

In examining the physiology of the sensory adaptations to exotropia, it was found that dichoptic visual field mapping in exotropic human patients showed hemifield suppression of peripheral vision in each eye, as has been postulated clinically. However, foveal stimulation of the deviated eye was perceived but localized to a direction consistent with harmonious anomalous retinal correspondence.⁸⁴ Monkeys raised with surgically induced exotropia showed evidence of a similar pattern of temporal retina suppression with neuroanatomical labeling techniques.⁸⁵

Sensory strabismus is believed more likely to be an esotropia when vision is lost in infancy or early childhood and exotropia with later vision loss. A Korean study found that 74% of 53 patients with sensory strabismus had exotropia. The direction and magnitude of the strabismus were not related to age of onset or duration of vision loss.⁸⁶ Patients in whom the fixating eye was hyperopic or emmetropic were more likely to be esotropic; perhaps, the prevalence of myopia in this Asian population was a factor in the predominance of exotropia.

Duane Syndrome

In Duane syndrome type 1, the underlying pathology is thought to be agenesis of the abducens nerve; however, at least 2 patients with Duane syndrome type 2 do have MRI evidence of an abducens nerve on the affected side.⁸⁷ Another article offers the provocative

speculation that fetal thromboembolic events are the etiology for several conditions with a left side and female predominance, including Duane syndrome.⁸⁸

Surgery to correct the head turn associated with Duane syndrome has traditionally been ipsilateral medial rectus recession in esotropic cases and ipsilateral lateral rectus recession in exotropic cases. Recently, a number of authors are promoting transposition surgery as the primary treatment of Duane syndrome. In response to this, 2 recent studies reaffirm that very satisfactory results can still be obtained from single rectus muscle recession.^{89,90}

Similarly, cases of bilateral esotropic Duane syndrome can be satisfactorily treated with bilateral medial rectus recession.⁹¹ The Y-splitting procedure of the lateral rectus muscle is an established procedure for treating the upshoot and downshoot in adduction, and a recent study shows that Y-split along with lateral rectus recession is effective in exotropic Duane syndrome.⁹²

A recent study shows good results with another old concept in the treatment of Duane syndrome—bilateral medial rectus recession for unilateral esotropic Duane syndrome.⁹³ The idea behind bilateral surgery is that weakening the contralateral medial rectus muscle provides additional help with the head turn by decreasing innervation to the ipsilateral medial rectus muscle, similar to so-called *innervational* surgery in sixth nerve palsy. However, this rationale is questionable in Duane syndrome because decreased innervation to the ipsilateral medial rectus muscle also decreases the anomalous innervation to the ipsilateral lateral rectus muscle. Without control cases of unilateral surgery for comparison and results that are only comparable with those of unilateral surgery in other reports,^{89,90} it is unclear whether adding the contralateral surgery contributes to the result.

Inactivation of the lateral rectus muscle in conjunction with vertical rectus muscle transposition has been previously advocated as a treatment of Duane syndrome (mostly type 1); however, a recent report describes the use of a lateral rectus muscle inactivation procedure alone. In a case of Duane syndrome with a large exotropia, upshoot, and retraction, suturing the lateral rectus muscle to the lateral canthal tendon eliminated the abnormal head posture and other manifestations of Duane syndrome while retaining surprisingly good horizontal ductions.⁹⁴

Superior Oblique Palsy

When incomitance is a prominent feature of superior oblique palsy, the challenge for surgical correction is to adequately correct the hypertropia in side gaze without overcorrecting the smaller hypertropia in primary position. In a study of superior oblique patients with less than 10 PD of hypertropia in primary position, graded inferior oblique recession reduced the mean hypertropia in contralateral gaze from 16 to 2 PD. There were 2 overcorrections in primary position, and only 1 required further surgery.⁹⁵ However, in another study, combining superior oblique tuck with inferior oblique recession for larger primary gaze hypertropia results in a high incidence of postoperative Brown syndrome. The authors recommend inferior oblique recession alone in most cases.⁹⁶

A different 2-muscle procedure for larger deviations can give satisfactory results in patients with indications of ipsilateral superior rectus restriction. A series of 3 patients with unilateral congenital superior oblique palsy underwent ipsilateral superior rectus and inferior oblique recessions. All patients had satisfactory correction of the hypertropia and abnormal head position with minimal supraduction defect. Good results were obtained despite the fact that all patients had a lax ipsilateral superior oblique tendon, which is considered by some to indicate the need for a superior oblique tuck.⁹⁷ After inferior oblique weakening alone, ipsilateral superior rectus recession is also effective for correcting the residual hypertropia and head tilt.⁹⁸

The 2 most common etiologies in a neuro-ophthalmology clinic series of superior oblique palsies were found to be microvascular and decompensated congenital. The associated horizontal deviations were specifically evaluated and, contrary to the expected finding, exodeviations were much more common than esodeviations in decompensated superior oblique palsy. In contrast, microvascular patients had similar prevalence of esodeviations, horizontal orthophoria, and exodeviations.⁹⁹

The surgical dose for lateral rectus recessions when exotropia accompanies presumed superior oblique palsy is the subject of another study. Most reports have shown that the amount of horizontal rectus muscle surgery does not need to be altered when done concurrently with inferior oblique weakening procedures. It was found in this study that reducing the usual amount of lateral rectus recession by 1 to 2 mm gave good results,¹⁰⁰ although it is not clear that the results would have been worse, had the usual amount of recession been done.

Thyroid Eye Disease

Many surgeons favor adjustable suture techniques for restrictive strabismus such as thyroid eye disease. Adjustable sutures for thyroid disease have recently fallen into disfavor by some, in large part because of the high rate of overcorrection with inferior rectus recessions. A current study reports excellent alignment (fusing in primary and reading positions without prism) after adjustable suture recessions but reiterates the need to anticipate the postoperative drift by initially adjusting for undercorrection with inferior rectus recessions.¹⁰¹

Because there is usually some degree of bilateral inferior rectus restriction in thyroid eye disease, some surgeons routinely do bilateral inferior rectus recessions. This was found to shift the range of vertical ductions upward but can create intorsion in down gaze.¹⁰² This is an expected result from the unopposed intorsion effect of the superior oblique muscles after the inferior rectus muscles have been weakened. However, it seems that actual tightness of the superior oblique muscles can be the cause of intorsion in some cases of thyroid eye disease. This can be diagnosed by traction testing after detachment of the restricted rectus muscles. When discovered, recession of the tight superior oblique muscles can prevent symptomatic intorsion or A-pattern exotropia. Preoperative findings of minimal extorsion, or frank intorsion, in the presence of a tight inferior rectus muscles can be a sign of masked superior oblique muscle tightness.¹⁰³

Orbital Trauma

In a large series of patients with diplopia after reconstructive surgery for orbital fractures, the strabismus patterns fell into four groups—inferior rectus paresis, inferior rectus restriction, presumed inferior oblique involvement, and combined inferior rectus paresis and restriction. A majority of patients had sufficient spontaneous improvement that they did not need further treatment. Most of the remainder had surgical treatment that varied depending on the pattern of strabismus.¹⁰⁴ Although inferior rectus muscle flap tear is believed by some to be a common cause of motility disturbances after orbit floor fracture, none were found in this series. However, a flap tear variant is described in a case report in which avulsion of the temporal portion of the inferior rectus muscle and its entrapment in the maxillary sinus was thought to be responsible for persistent hypertropia after orbital floor fracture repair.¹⁰⁵

A number of mechanisms were found in a series of patients with inferior rectus paresis or underaction, almost half of whom had a history of orbital fracture. Causes found at surgery included posterior muscle slippage, stretched scar, flap tear, missing muscle tissue, extensive muscle adhesions, or unidentifiable muscle. All patients had fundus intorsion, and most had subjective torsion and a negative head tilt test. The mechanism could not be determined from these clinical findings, and orbital imaging was able to do so in only 40% of cases.¹⁰⁶

New Surgical Techniques

Small-angle strabismus can be a particularly vexing problem in adults. Several weakening procedures, mostly variants of a partial rectus muscle tenotomy, have been devised to deal with this. Now, a strengthening procedure has also been described. It consists of plicating just the central portion of a rectus muscle, can be performed with topical anesthesia, and can successfully correct small deviations.¹⁰⁷

Suturing the muscle to sclera is the step in a strabismus procedure from which some of the most serious complications—endophthalmitis and retinal detachment—can arise. Hang-back recessions are advocated by some as a way to minimize the risk from a scleral needle pass, but there is concern about whether the muscle will reliably adhere to the sclera at the desired location. Gluing instead of suturing the muscle to the sclera avoids a scleral needle pass and has been studied experimentally, but is the muscle attachment secure enough to prevent lost muscles? Now, an animal study explores the combination of both techniques. Rabbit superior rectus muscles were recessed with a hang-back technique, and the muscle was stabilized at its desired insertion site with fibrin glue. Although this did not completely eliminate attachment of the muscle anterior or posterior to the desired scleral location, it was less of a problem than in a control group that received hang-back recessions alone.¹⁰⁸

Scarring is another common problem in strabismus surgery. Steroids and antimetabolites have been studied as a way to modulate scar formation, with limited success. A new class of agent, an anti-transforming growth factor β agent, pirfenidone, has been studied in a rabbit model. It was concluded that inflammation and fibrosis can be reduced by subconjunctival injection of this agent at the time of strabismus surgery.¹⁰⁹

Oblique Muscle Surgery

A variety of superior oblique muscle weakening procedures have been described over the years. The most popular methods currently, aside from simple tenotomy, are probably suture spacers and silicone band expanders. These 2 procedures were compared in a retrospective study of patients with Brown syndrome or A-pattern strabismus. Both procedures were equally effective in improving ductions in Brown syndrome or normalizing superior oblique action in A-pattern strabismus; however, silicone band expanders were associated with longer operating time and one incident of orbital inflammation that necessitated removal of the implant.¹¹⁰

Z-tenotomy (not to be confused with a previously described Z-lengthening) has been proposed as new superior oblique weakening procedure. This is performed with a monopolar electrode microdissection needle to precisely control the amount of tenotomy. It effectively normalizes superior oblique overaction and corrects A-pattern strabismus.¹¹¹ However, the 2 incisions always overlap to some degree, leaving no tendon fibers in tact for their entire length. This may be functionally equivalent to a complete tenotomy; without a comparison group, it is not possible to say whether Z-tenotomy is less likely to cause iatrogenic superior oblique palsy.

Anterior transposition is now a standard procedure for inferior oblique overaction. One recent study reviewed the results of graded inferior oblique anteriorization in patients with V-pattern strabismus and inferior oblique overaction. The inferior oblique muscle was transposed more or less anteriorly along the temporal border of the inferior rectus muscle, depending on the severity of the overaction and the size of the V pattern. This treatment effectively corrected the V pattern and the inferior oblique overaction without limiting elevation (anti-elevator syndrome); however, with multiple regression, it does not seem that the amount of anteriorization is an independent outcome predictor, so it is unclear whether grading the procedure contributes to a successful outcome.¹¹²

Transposition Procedures

Transposition procedures can be used to substitute force from adjacent muscles to compensate for a palsied muscle. Fulltendon transpositions for abducens palsy or esotropic Duane syndrome can be associated with troublesome secondary vertical deviations. Away to avoid this complication is suggested by a study in which torsion is monitored intraoperatively through marking pen dots placed on the eye. The authors feel that intraoperative torsion is a proxy for postoperative vertical deviations and can be used as a guide to adjust the tension on the transposed muscles.¹¹³

Another problem with full-tendon transpositions is that a lot of the anterior ciliary artery blood supply to the anterior segment is sacrificed. Partial-tendon transpositions sacrifice half as many vessels but are not as effective. A new study confirms previous reports that partial-tendon transpositions (augmented Hummelsheim procedure) with resection of the transposed muscle combined with medial rectus muscle recession can provide satisfactory correction of abducens palsy.¹¹⁴

A radically new transposition procedure that does not sacrifice 2 of the vertical rectus muscle ciliary vessels has also been shown to be effective. Instead of transposing both vertical rectus muscles toward the lateral rectus muscle, only the superior rectus muscle is transposed. This single-muscle transposition is augmented with a posterior suture, and the medial rectus muscle is also recessed. This reduced the primary position esotropia, abduction defect, and head turn in 17 patients with abducens palsy or esotropic Duane syndrome. What is most surprising about this unbalanced procedure is that it resulted in only 2 vertical deviations and no symptomatic intorsion.¹¹⁵

Another use for transposition surgery is in monocular elevation deficiency (Knapp procedure). In a prospective study of 36 patients with monocular elevation deficiency, 22 had inferior rectus recession, 10 of whom were followed by a Knapp procedure and 12 had a Knapp procedure alone. This strategy of recessing the inferior rectus muscle when it is restricted and performing a Knapp procedure when it is not or with persistent hypotropia after inferior rectus recession corrected almost all patients to within 10 PD of hypotropia. Only 3 patients developed consecutive hypertropia.¹¹⁶

Adjustable Suture

More than 35 years after being popularized, there is still debate over the value of the adjustable suture technique for strabismus surgery. Two new retrospective studies show better results overall with adjustable sutures than without. Further analysis suggests that certain subgroups behave differently; however, the types of patients who benefit most are different in each study. In one study, adjustable suture improved outcomes most in adults undergoing reoperation for childhood strabismus; curiously, patients with thyroid eye disease did not seem to benefit at all.¹¹⁷ In the second study, exotropic patients undergoing primary surgery—but not reoperation—benefited most.¹¹⁸ Given the heterogeneity of strabismus problems to which adjustable sutures are applied and the dependence on surgeon judgment—what immediate postoperative alignment to adjust to with adjustable sutures and how much surgery to do when an adjustable suture is not used—the utility of adjustable sutures will be difficult to show convincingly without a prospective, randomized study.

Another group has taken a different approach to assessing the value of adjustable suture. Rather than comparing patients with and without adjustable sutures, they looked at subgroups among 89 patients undergoing reoperations for horizontal strabismus with an adjustable suture technique. Those who were adjusted postoperatively were compared with those who were already at their target angle and tied off without an adjustment. There was no statistically significant difference in the success rates of the 2 groups at 6 weeks or 1 year postoperatively, although there was a trend for the adjusted patients to do better, especially at 6 weeks (81% compared with 64%). The assumption is that adjusted patients would have had worse results, had they not been adjusted to an immediate postoperative target angle similar to that in the unadjusted patients. From this, the authors conclude that adjustable sutures, at least for the 60% of patients who were adjusted, produced superior results to what would have been obtained without adjustable sutures.¹¹⁹

Posterior Fixation

Posterior fixation suture procedures are popular in some parts of the world for treatment of esotropia, although the rationale for their use in this setting is not as clear as for incomitant strabismus. For large-angle infantile esotropia, they have been shown—when performed in conjunction with bilateral medial rectus recessions—to produce results that are comparable with historical success rates for medial rectus recessions alone.¹²⁰ This leaves the question of whether posterior fixation itself does anything, or can the results be attributed entirely to the effect of medial rectus recession? This is partially addressed in one of the few studies to look at posterior fixation alone, in which patients with a high AC/A ratio treated with posterior fixation were compared with those treated with both medial rectus recession and posterior fixation. These were not comparable groups in that both distance and near deviations were much smaller in those selected for posterior fixation alone; nonetheless, it reduced distance-near incomitance by essentially the same amount as combined posterior fixation and medial rectus recession.¹²¹

Recent orbital imaging studies have called into question the historically accepted mechanism by which posterior fixation sutures are thought to act. Rather than reducing the torque by reducing a muscle's effective lever arm in its field of action, it may be that posterior fixation simply restricts the muscle's ability to telescope through its muscle pulley sleeve. From this concept, an elegant alternative to the posterior fixation suture was devised; it seems likely that suturing the muscle belly to its pulley sleeve will limit movement in the same way. A current study replicates previous work showing that pulley fixation sutures combined with (augmented) medial rectus recessions produce good results and reduce distance-near incomitance in esotropia patients with convergence excess or high AC/A ratio.¹²² It also seems that this result holds up over time.¹²³ However, without a control group, it is unclear how much pulley fixation contributed to the results, given that medial rectus recession alone is known to reduce distance-near incomitance.

Botulinum Toxin

As primary treatment of infantile esotropia, botulinum toxin injections can produce long-term results that are fairly comparable with those from a bilateral medial rectus recession; however, multiple injections (mean, 1.4) are being compared with only one incisional surgery.¹²⁴ Superior rectus muscle botulinum toxin injection can also be used as a primary treatment of vertical strabismus, although indications are relatively uncommon and ptosis is a frequent temporary complication.¹²⁵

Perhaps, a different use for botulinum toxin is to augment incisional surgery. Botulinum toxin with 7-mm medial rectus recessions leads to a successful long-term result in 74% of infants with large-angle esotropia greater than 60 PD.¹²⁶ This is only comparable with previous reports of large medial rectus recessions with shorter follow-up, but the rate of secondary exotropia is, if anything, paradoxically lower. Botulinum toxin has also been used to augment recess-resect procedures for chronic parietic strabismus with large-angle deviations.¹²⁷ However, a randomized study of recess-resect procedures for large-angle strabismus failed to find any additional benefit from botulinum toxin injection.¹²⁸

Unexpected Surgical Outcomes

Shifting the insertion of rectus muscles has been used to treat A and V patterns and to treat cyclotropia. Regardless of which application a rectus muscle shift is used for, it affects both the pattern and torsion. A recently reported series of patients developed symptomatic cyclotropia after shift for a pattern or a symptomatic pattern after shift for torsion. The contrary effect of rectus muscle shift on pattern and torsion was more likely to be symptomatic in fusing patients and those with Graves eye disease.¹²⁹

Surgical errors are currently receiving a lot of scrutiny in all surgical specialties. In ophthalmology, which is second only to neurosurgery in error rate, Universal Protocol as well as a specific checklist for intraocular lens (IOL) procedures have been implemented in an effort to reduce these errors but may not be very helpful for the types of errors that occur in strabismus surgery. A survey of self-reported surgical errors gives an incidence of 1 for every 2506 strabismus surgeries. Wrong procedure—especially esotropia surgery for exotropia or exotropia surgery for esotropia—and wrong muscle surgery were the most common errors. The authors of this study offer some strabismus surgery-specific modifications of the preoperative protocol that may reduce the error rate.¹³⁰

Variation in the insertion location of extraocular muscles is thought by some to contribute to the variability of surgical outcomes. A study of Chinese patients with strabismus and controls found that they did not differ from each other but had significantly shorter limbus-insertion distances than those reported for Western populations. The authors suggest that surgical tables developed for Western patients with strabismus may not be appropriate for Asian patients.¹³¹ The ultrasound biomicroscope (UBM) provides a means of assessing the muscle insertion location preoperatively for unoperated muscles and, perhaps more importantly, in reoperations. In a comparison study, the newer Sonomed UBM was found to localize muscle insertions more accurately than the older Humphrey UBM.¹³²

Resident Training

A structured questionnaire was administered to residents in study to evaluate the adequacy of a CD-ROM lesson, practice animal surgery followed by supervised human strabismus surgery. All first-year residents and 70% of second-year residents had some difficulty remembering the surgical steps. Approximately half of the residents felt that the training had fully prepared them to perform strabismus surgery.¹³³ In 2 other studies, checklist tools were devised using content experts to establish face and content validity. These tools are intended for documentation of residents' training progress and the effectiveness of the training experience.^{134,135}

Functional Associations of Strabismus

Strabismus has been implicated in a number behavioral disorders. Young adults with a history of congenital esotropia were found to be 2.6 times more likely to develop psychiatric illness than birth- and sex-matched controls.¹³⁶ This association did not seem to be explained by prematurity and mirrors a previous study in which mental health disorders were found to be associated with exotropia. In another study, most patients with intermittent exotropia (8/9) with attention-deficit hyperactivity disorder (ADHD) had improvement in

parent-reported ADHD symptoms 1 year after surgery as assessed by ADHD RS-IV questionnaire.¹³⁷

In reading tasks, strabismic children were found to have worse binocular coordination than controls during and after saccades as well as longer fixation times. Patients with strabismus with fusion were intermediate between those without fusion and controls. The authors speculate that poor binocular saccade coordination could impair reading capabilities; however, the study provided no evidence that reading actually is impaired in the strabismic subjects.¹³⁸ In another study of saccadic performance, it was found that the saccade latency does not improve in patients with strabismic amblyopia under binocular conditions, as is seen in normal individuals.¹³⁹

Vergence is known to affect postural stability, with better control in normal individuals when fixating on a near target. In patients with strabismus, the fixation depth at which postural stability is best is near for convergent strabismus and distant for divergent strabismus.¹³⁹ Another study found that strabismic (mostly esotropic) children did not show the expected improvement in postural control with near fixation. These authors found that postural control improved after surgical correction of the strabismus but was actually worse with preoperative prism adaptation.¹⁴⁰

Susceptibility to motion sickness correlated significantly with the magnitude of vertical heterophoria in a nonclinical population. A vertical phoria less than or greater than 0.75 PD best discriminated between subjects with low versus high motion sickness symptom scores. However, because these findings could not be fully confirmed by inducing or correcting vertical heterophoria with prism, it is not clear whether there is a causal relationship between vertical heterophoria and motion sickness.¹⁴¹

A variety of factors in emmetropization are currently under active investigation. Now, a recent Pediatric Eye Disease Investigator Group study suggests that ocular alignment may play a role as well. The refractive status of children who were 3 to younger than 7 years old at the time of enrollment in a previous study was compared with that at 10 years of age. Hyperopia tended to decrease in both eyes, but the nondominant eye had a greater decrease than the dominant eye. The decrease in the dominant eye was independent of ocular alignment, but in the nondominant eye, the greatest decrease occurred in orthotropic patients, the least in patients with a deviation of greater than 8 PD, and microtropic patients were intermediate.¹⁴²

Quality of Life

With the reality of limited health care funding, there is interest in where expenditure of resources can produce the greatest benefit. Quality-of-life studies are an increasingly important methodology for trying to answer these questions. During the past year, this has been a particularly active area of investigation with regard to strabismus. Although there are some global dimensions, it is important to develop and validate quality-of-life instruments that are applicable to specific pathology. Two studies seek to do this for a questionnaire applicable to adult strabismus^{143,144} and a third for intermittent exotropia in children.¹⁴⁵

When applied to adult strabismus, it was found that patients who are successfully aligned surgically show a significant improvement in their psychosocial and functional scales 6 weeks postoperatively. There was continued improvement from 6 weeks to 1 year after surgery in those patients who remained aligned, demonstrating that the quality-of-life improvement is long lasting. The authors propose that quality-of-life measures be included in assessment of outcomes in clinical trials.¹⁴⁶

Although most quality-of-life studies have concentrated on surgical treatment of strabismus, there is now a study that shows that maintenance of ocular alignment with long-term botulinum toxin treatment also results in quality-of-life benefits. A quality-of-life questionnaire was administered to strabismus patients who had undergone more than 25 injections, and it was found that their mean score compared favorably with normal controls, whereas patients with untreated strabismus have previously been shown to have lower scores.¹⁴⁷

Time tradeoff is another method of measuring the value of surgical intervention. A study comparing various ophthalmic procedures found that the mean value of the quality-adjusted life years was 2.181 for bilateral and 1.424 for unilateral cataracts, 1.132 for strabismus, and 0.870 for glaucoma.¹⁴⁸ However, another study comparing surgical outcomes for 5 ophthalmic diseases showed that the improvement on a quality-of-life questionnaire was comparable for cataract surgery and surgery for incomitant strabismus.¹⁴⁹

Summary

Several areas of investigation during the past year stand out as being particularly significant contributions to strabismology. For many years, discourse on the etiology of most types of strabismus has largely been theoretical and philosophical. Some of the most exciting research of the past year finally identifies specific, possibly causative, abnormalities in brainstem neurons,⁵⁴ the extraocular muscles themselves,⁵⁵ and orbital connective tissue.^{56,65} The surgical procedure innovation that has generated the most excitement is the superior rectus transposition which, if others find comparable results, may find widespread application in sixth nerve palsy and perhaps Duane syndrome.¹¹⁵ The prospective studies from the United Kingdom are a promising start to putting the investigation of exotropia on rigorous footing.^{70,71}

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TABLE 1.
American Association for Pediatric Ophthalmology and Strabismus Referral Thresholds With Automated Screening

Age	Astigmatism	Myopia	Hyperopia	Anisometropia
	2013 recommendations ²⁸			
1–2.5 y	>2.0 D	>3.5 D	>4.5 D	>2.5 D
>2.5–4 y	>2.0 D	>3.0 D	>4.0 D	>2.0 D
>4 y	>1.5 D	>1.5 D	>3.5 D	>1.5 D
	2003 recommendations ³⁰			
	>1.5 D at 90 or 180 degrees	>3.0 D	>3.5 D	>1.5 D
	>1.0 D oblique axis			