#### CLINICAL PRACTICE

# Pediatric Strabismus

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

A healthy 3-year-old boy presents with a 6-month history of strabismus in his left eye. The visible inward deviation of the eye began intermittently but is now constant. His visual acuity is 20/20 in the right eye but only 20/100 in the left eye. The physical examination is otherwise normal. How should he be treated?

#### THE CLINICAL PROBLEM

As evolution proceeded, the location of the eyes within the head moved from a lateral to a frontal position. In animals for which panoramic vision is not crucial, this frontal migration resulted in increasing overlap of each eye's visual field and conferred the advantage of stereopsis (depth perception). In mammals, inputs from the two eyes converge on binocular neurons in the visual cortex, which are thought to be the neural substrate for stereopsis. Maturation of these binocular neurons is dependent on proper ocular alignment early in life.<sup>1</sup> Childhood strabismus disrupts this process and results in permanent loss of stereopsis if the eyes are not realigned early in development.

Untreated pediatric strabismus can also cause amblyopia (a decrease in bestcorrected visual acuity in an otherwise structurally healthy eye). The neuroanatomical substrate for amblyopia is a shrinkage in the size of neurons driven by the amblyopic eye in the visual cortex and lateral geniculate nucleus.<sup>2-6</sup> Although experimental studies of amblyopia have been performed primarily in kittens and nonhuman primates, similar pathologic features have been reported in humans with amblyopia caused by strabismus<sup>7</sup> or anisometropia (a difference between the eyes in the refractive error).<sup>8</sup> Perturbations in the visual system that occur after the age of 5 years do not cause amblyopia.<sup>9</sup>

Pediatric strabismus must be treated early to maximize the potential for binocular vision and decrease the risk of amblyopia. Treatment goals include good vision in each eye (no amblyopia) and straight eyes (orthotropia). Both conditions are necessary to produce stereopsis, which is a third goal.

The eyes of most children are not orthotropic at birth but, rather, are mildly exotropic (deviating outward). Neonatal misalignment typically resolves by 3 months, and any strabismus occurring after this age is abnormal.<sup>10</sup> Large-angle esotropia (greater than 15 degrees) is also abnormal in infants.<sup>10-12</sup>

Strabismus is classified according to the type and magnitude of misalignment (see Glossary). Most patients with esotropia present before school age, generally between the ages of 2 and 3 years. Most esodeviations (inwardly directed ocular deviations) are intermittent initially but within a few weeks become constant. An intermittent deviation does not preclude the development of stereopsis; however, failure to realign the eyes of children whose eyes are constantly esotropic results in lifelong abnormal depth perception. Patients with exotropia usually present between the ages of 1 and 4 years; the condition nearly always remains intermittent and is

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N Engl J Med 2007;356:1040-7. Copyright © 2007 Massachusetts Medical Society. therefore associated with good binocular vision. Vertical ocular deviations occur in children, in isolation or associated with horizontal strabismus, but are much less common and are not discussed here.

#### LATER CHILDHOOD AND ADULT STRABISMUS

New-onset strabismus in a school-aged child is unusual and warrants neurologic evaluation. Most cases of strabismus in this age group represent the recurrence of a partially treated strabismus earlier in life, which recurs because of a relative deficiency in fusion (the ability to maintain binocular vision). Such recurrences are most likely in children in whom deviations in ocular alignment have remained untreated for a prolonged period.

Adult strabismus is fundamentally different from pediatric strabismus. It does not produce amblyopia, and binocular vision can be restored when the strabismus is corrected. Most adult strabismus represents deterioration of childhood strabismus, which can occur even after decades of good ocular alignment. Diplopia may or may not be present. Recurrence is more common in adults whose childhood strabismus resulted in a lack of binocular vision and stereopsis<sup>13</sup> or who had partially treated or untreated amblyopia (since the poor acuity makes binocular vision less sustainable). These observations underscore the importance of aggressive treatment of childhood amblyopia and strabismus. Adults with recurrent childhood strabismus should be treated (typically with surgery), since correction can restore binocular vision and expand visual fields.14-16

Strabismus may also occur in adults after an insult to the ocular motor system, involving the supranuclear, prenuclear, or nuclear pathways subserving eye movements or the cranial nerves themselves. Important causes include vascular disease, inflammatory disease, infiltrative processes (including Graves' disease), myasthenia, and direct orbital trauma. Bothersome diplopia is invariably present. A detailed discussion of adult strabismus is beyond the scope of this review, but referral to a neuro-ophthalmologist or a specialist in adult strabismus is warranted in such cases.

### STRATEGIES AND EVIDENCE

#### ESODEVIATIONS

## Infantile Esotropia

Infantile esotropia occurs in the first 6 months of life, with large-angle crossing in an otherwise

Strabismus: An ocular misalignment
Tropia: A manifest (constant) ocular misalignment (as in "heterotropia")
Phoria: A latent tendency to deviate; held in control by fusion (as in "hetero- phoria")
Comitant strabismus: A similar magnitude of deviation in all gaze positions
Incomitant strabismus: A deviation of greater magnitude in one direction or at close range
Prism diopter: A measure of ocular misalignment; one prism diopter equals 1 cm of deviation at 1 m (approximately 0.5 degree)
Orthotropia: No ocular deviation (i.e., straight eyes)

Glossary

Esotropia: An inward deviation of the nonfixing eye

Exotropia: An outward deviation of the nonfixing eye

**Hypertropia:** A vertical deviation, in which the nonfixing eye is higher

Hypotropia: A vertical deviation, in which the nonfixing eye is lower

Amblyopia: A unilateral or bilateral decrease in best-corrected visual acuity in a structurally normal eye or eyes

Binocular vision: Blending of the separate images seen by each eye into one composite image

Stereopsis: Visual blending of two similar (not identical) images,	one falling
on each retina, into one with visual perception of depth	

developmentally and neurologically normal child (Fig. 1). Eye movements are full, and the child often alternates fixation (i.e., uses each eye independently for viewing). Children with constant, large-angle esodeviations of more than 20 degrees do not "outgrow" the condition.12

Treatment of infantile esotropia is surgical and involves recessing (weakening) the medial rectus muscles of each eye while the infant is under general anesthesia. Complications are infrequent. Globe perforation occurs in less than 1% of cases17-20 and usually heals without sequelae. Endophthalmitis occurs in fewer than 1 of 10,000 patients but can be devastating.<sup>20,21</sup> Similar risks are associated with all strabismus surgery.

The goal of surgery is alignment of the eyes within 8 prism diopters (4 degrees) and can be achieved initially in most patients. This smallangle deviation allows for limited binocular visual function (i.e., gross stereopsis) and an increased likelihood of stable long-term alignment ("monofixation").13,22-24 High-grade stereopsis after surgery is extremely unusual.25,26

Early surgical realignment in infantile esotropia appears to result in better outcomes than does later intervention. The duration of misalignment may be the major predictor of the outcome.<sup>22</sup> Among children with infantile esotropia who underwent surgery between 3.5 and 22 months

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**Figure 1. Infantile Esotropia.** This 10-month-old girl's esotropia with a large-angle deviation was noticed shortly after birth.

of age<sup>27</sup> (45% of whom had some postoperative stereopsis), there was a significant correlation between the duration of ocular alignment before the development of esotropia and later stereopsis.

Recurrent strabismus is common in children with infantile esotropia. Overcorrection and undercorrection of the original deviation, as well as vertical misalignments, can develop throughout life, and multiple surgeries are often required. In one follow-up study, the risk of recurrent strabismus was more than three times as high in children with no postoperative stereopsis as in those with detectable stereopsis.<sup>23</sup> It is unclear whether poor or no stereopsis and the high frequency of recurrent strabismus in such children are consequences of early ocular misalignment (and thus potentially modifiable with earlier intervention) or reflect an innate lack of central fusion.

#### Acquired Esotropia

The most common type of childhood esotropia is accommodative esotropia, which typically occurs between the ages of 2 and 3 years. Children with this condition are usually more hypermetropic (farsighted) than are children without the condition and therefore need to accommodate to see clearly. Because accommodation is linked with convergence, focusing drives the eyes inward, producing esotropia. Treatment consists of eyeglasses to correct the full hypermetropic refractive error, which is determined with the use of cyclopentolate eyedrops or another cycloplegic agent to cause temporary paralysis of accommodation (Fig. 2). Treatment with eyeglasses within 6 months after the onset of misalignment usually restores proper ocular alignment, with good stereopsis developing in the majority of children. Among children treated with eyeglasses, those with no detectable stereopsis have a much greater likelihood of eventually needing eye-muscle surgery than do those with stereopsis.<sup>28</sup> Some children with accommodative esotropia remain esotropic when viewing near objects and require bifocals to achieve orthotropia in this setting.

Children with esotropia who have no hypermetropia, or whose esotropia cannot be corrected fully with eyeglasses, should undergo strabismus surgery. Surgery does not improve the esotropia that occurs without eyeglasses but is performed to correct any residual deviation that remains after treatment with eyeglasses. A randomized, multicenter trial showed a slight improvement in postoperative alignment for patients with esotropia who, before surgery, had fusion after a week of wearing eyeglass-mounted prisms to mimic the effect of surgery (prism adaptation), as compared with patients who had surgery without prism adaptation or who did not have fusion with the prisms.<sup>29</sup> However, the benefit, although statistically significant, was modest, and this technique is not universally used.

Surgery in children with esotropia should be performed as early as possible to preserve stereopsis.<sup>28</sup> Prospective observational data indicate a significant inverse correlation between the duration of misalignment before surgery and the likelihood of postoperative stereopsis; the data also suggest that the development of stereopsis can be disrupted at least through the age of 4.6 years.<sup>27</sup> The period of susceptibility to the loss of stereopsis probably never completely closes, since adults with acquired strabismus and diplopia risk losing high-grade stereopsis slowly with an increasing duration of misalignment.<sup>30</sup>

In a prospective study of 4-year-old children with hypermetropia of +4.0 diopters or more, eyeglass correction was associated with a 50% reduction in the incidence of accommodative esotropia.<sup>31</sup> However, because accommodative esotropia develops in only 10 to 20% of such chil-



Panel A shows a 4-year-old girl with eye crossing caused by high hypermetropia (farsightedness). When eyeglasses that correct the refractive error are worn, the eyes straighten to allow binocular vision, as shown in Panel B.

dren,<sup>31,32</sup> routine eyeglass treatment would result in substantial overtreatment. Eyeglasses are usually not covered by medical insurance, maintaining compliance is difficult, and some (although not all) data have suggested that use of eyeglasses may interfere with the normal reduction in hypermetropia with age.<sup>33</sup> Also, many children with accommodative esotropia have refractive errors of less than +4.0 diopters.<sup>34</sup> A more prudent approach may be to treat only patients with risk factors for accommodative esotropia (e.g., a family history of strabismus or amblyopia in a firstdegree relative, subnormal stereopsis, or anisometropia), although the cost-effectiveness of such a strategy has not been well studied.<sup>35</sup>

#### EXODEVIATIONS

#### Infantile Exotropia

Any exotropia that occurs after the age of 4 months is abnormal<sup>10</sup> (Fig. 3). Constant exotropia is usu-

ally associated with neurologic delay, craniofacial syndromes, and structural abnormalities in an eye,<sup>36</sup> but in rare cases it occurs in otherwise healthy children.<sup>37</sup> Surgery can realign the eyes and is indicated unless extreme developmental delay precludes psychosocial interactions. However, ocular, orbital, and neurologic abnormalities often preclude the development of stereopsis, and recurrence of strabismus is more common when these conditions are present.

#### Intermittent Exotropia

Intermittent exotropia is one of the most common problems in pediatric ophthalmology. Although no appreciable deviation is present when the patient views near objects, the deviation becomes manifest when the patient views distant objects or is fatigued. A family history of the condition is common, and parents report observing the child habitually closing the nondominant eye when outdoors.

Several options are available to treat intermittent exotropia. These approaches have generally not been evaluated in randomized trials but, rather, are supported largely by data from case series. Nonsurgical treatments are intended to improve control of the deviation (i.e., reduce its frequency) but do not affect its magnitude. If the deviation occurs infrequently (for a few seconds on rare occasions when the child is daydreaming or tired), observation alone is reasonable. Intermittent exotropia typically does not resolve completely, but control can improve. Options for more frequent or consistent deviations include intermittent patching, the use of overminus eyeglasses (lenses that overcorrect myopia), vision therapy (exercises to stimulate convergence), and surgery. Response rates of 30% (for overminus eyeglasses) to about 50% (for other nonsurgical therapies) are reported in various retrospective series, but the studies are limited by selection bias, because for children with deviations that are poorly controlled or have a large magnitude and for those who do not have a response to conservative measures, there is a rapid move to surgical treatment.

Patching for 1 to 2 hours daily for several months works by preventing, rather than treating, suppression of an eye; this approach is most effective in infants, and efficacy is limited in children over the age of 3 years. The use of overminus eyeglasses stimulates accommodative con-

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vergence, which counteracts the exotropic drift. Vision therapy involves exercises to stimulate convergence (e.g., focusing on reading-distance targets for up to 30 minutes several times daily) and techniques to train the visual system to recognize the suppressed image. However, the techniques are not well described in the literature and are not typically used by ophthalmologists for managing intermittent exotropia. A recent randomized trial showed a modest benefit of intensive vision therapy in patients with a particular type of intermittent exotropia (convergence insufficiency, a deviation that is more prominent when near objects are viewed),38 but it is possible that the observed improvement was caused by other factors.39

Surgical treatment for intermittent exotropia is indicated when conservative measures do not reduce the frequency of the deviation. Surgery usually involves either weakening both lateral rectus muscles or combining a procedure that weakens a lateral rectus muscle with a procedure that strengthens the medial rectus muscle. Surgery is not a cure for intermittent exotropia; the recurrence rate is approximately 30% within 5 years.

Early establishment of constant orthotropia is not as crucial in patients with intermittent exotropia as it is in those with constant deviations, since stereopsis can still develop. However, the risk of the development of reduced stereopsis, mild amblyopia, or superimposed vertical strabismus increase with the duration of the intermittent deviation, underscoring the fact that even intermittent deviations may result in suppression of vision in the exotropic eye.

#### AMBLYOPIA

Amblyopia occurs in nearly 50% of children with esotropia but is unusual in children with intermittent exotropia. The restoration of proper ocular alignment decreases but does not eliminate the risk of amblyopia. Several multicenter, randomized trials have demonstrated that amblyopia does not resolve spontaneously and that treatment is effective, restoring visual acuity of 20/30 or better in both eyes in nearly 70% of children.<sup>40-45</sup>

Although occlusion of the fellow eye has been the traditional approach to treatment, a randomized trial showed that pharmacologic paralysis of accommodation ("penalization") with the use of atropine works nearly as well as occlusion, with a 6-month success rate of 74% with the use of atropine, as compared with 79% with occlusion.40 Atropine eyedrops blur the healthy eye at near vision and force fixation of the amblyopic eye. After 4 months of treatment, either limited occlusion (for as short a period as 2 hours a day) or the use of atropine (administered twice weekly) has an efficacy similar to that of more intensive therapy, such as patching for 6 hours a day or daily administration of atropine.41-43 A longer duration of treatment is generally needed with atropine than with patching - and a longer duration with limited patching or atropine use than with more intensive therapy — but treatment rarely exceeds 1 year. Neither treatment has serious side effects.

Amblyopia of the previously healthy eye occurs infrequently (in less than 3% of patients treated with either approach, even when intensive therapy is used) and is easily treated. Recurrence is most common during the first year after the cessation of treatment; resuming therapy is effective.<sup>46</sup> Amblyopia can be treated at least through the age of 14 years, although not as effectively as in children who are of preschool age or are in elementary school.<sup>47</sup> Amblyopia therapy should be completed before proceeding with strabismus surgery.

Table 1. Guidelines for the Management of Strabismus and Amblyopia.*				
	Age at Presentation	Management	Source of Guidelines	
Esodeviation				
Infantile	<6 Mo	Surgical realignment	AAO	
Infantile with high hypermetropia	<6 Mo	Eyeglasses with eye-muscle surgery	AAO	
Accommodative	1-4 Yr	Eyeglasses	AAO, AAPOS	
Accommodative with near-distance disparity	1-4 Yr	Bifocal eyeglasses	AAO, AAPOS	
Nonaccommodative	1-4 Yr	Surgical realignment	AAO	
Partially accommodative	1-4 Yr	Eyeglasses with eye-muscle surgery for residu- al esotropia	AAO, AAPOS	
Exodeviation				
Infantile	<6 Mo	Surgical realignment	AAO	
Intermittent	1–5 Yr	Observation, occlusion (patching), eyeglasses	AAO	
Convergence insufficiency	4 Yr or more	Prisms, eye exercises, surgery	AAO	

\* Guidelines are from the American Academy of Ophthalmology (AAO) and the American Association for Pediatric Ophthalmology and Strabismus (AAPOS).

#### BENEFITS OF STRABISMUS SURGERY

In addition to its effects on visual function, strabismus surgery has other benefits. Children begin to develop negative attitudes toward classmates with strabismus as early as the age of 6 years<sup>48</sup>; these attitudes adversely affect interpersonal relationships, self-image, schoolwork, and participation in sports and intensify in the teenage and adult years.<sup>49</sup> Surgical correction of childhood strabismus reduces these difficulties.<sup>50</sup> Straight eyes are also important in adults, since strabismus can have a negative effect on social interaction (e.g., during a job interview).<sup>51</sup>

### AREAS OF UNCERTAINTY

Factors that precipitate infantile esotropia are unknown, and data from randomized trials to guide decisions about the timing and type of surgical intervention are lacking. Surgery before the age of 6 months may increase the likelihood of the development of stereopsis. However, the deviation cannot be measured accurately in such young children and may increase during the first few months, necessitating repeated surgery. The natural history and optimal management of intermittent exotropia have also not been well studied.

#### GUIDELINES FROM PROFESSIONAL SOCIETIES

Guidelines from professional societies for the management of strabismus and amblyopia are summarized in Table 1.<sup>52-56</sup>

#### SUMMARY AND RECOMMENDATIONS

The child described in the vignette has new-onset esotropia and should receive a cycloplegic refraction. If eyeglasses are indicated because of hypermetropia, he should receive them and return in approximately 2 months for a reassessment of acuity and alignment and initiation of amblyopia treatment with the use of either atropine or patching. Although intermittent therapy is a reasonable option, I generally recommend full-time patching, since improvement is more rapid and compliance may be better. If eyeglasses are not indicated, amblyopia therapy should be started immediately. Strabismus surgery would not be indicated until the amblyopia was fully treated and only if the eyeglasses did not fully correct the esotropia.

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