Ophthalmology ROUNDS

Volume 16, Issue 4

AS PRESENTED IN THE ROUNDS OF THE DEPARTMENT OF OPHTHALMOLOGY AND VISION SCIENCES, FACULTY OF MEDICINE, UNIVERSITY OF TORONTO

Eye Turns for Everyone: Approach to Strabismus in Children

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This issue of *Ophthalmology Rounds* presents general principles of strabismus in children that would typically present to comprehensive ophthalmologists. The overall goal is to give clinicians a strategy and differential diagnosis for pediatric strabismus that will hopefully increase clinician confidence when asked to see a child with an eye turn. The issue starts with a guide on how to assess a child with strabismus. It is then divided into sections based on the type of deviation, with each section summarizing the common and serious causes.

Assessing children is a particular challenge. A 2-year-old in the emergency department is rarely the epitome of a well-mannered, cooperative patient. When examining a child with strabismus, it is often preferable to focus on what you need to know and ignore the extraneous details.

History

Two key historical features are onset and overall health. In terms of onset, it is almost always important to know when the deviation was first noticed and if there were any precipitating events; e.g., was a vertical deviation in an 8-year-old identified in the first year of life or just noticed recently after suffering trauma? The overall health of a child also plays a pivotal role in pediatric strabismus. For instance, about half of children with cerebral palsy and Down syndrome have strabismus.[1,2] Furthermore, uncommon but serious causes of strabismus such as myasthenia gravis and orbital tumours often have systemic findings that provide key hints to the diagnosis.[3]

Examination

While parents are often good at providing a reliable history, physical examination of the child is essential. The most helpful aspects of the examination focus on key clinical information; i.e., vision, alignment, motility, fundus examination, and (if you are particularly talented) a cycloplegic refraction.

Vision

Vision is an important part of every strabismus examination. If the child is unable to read letters, it may still be possible to match letters or name shapes. In preverbal children, you can still get a general assessment of vision by observing visual behaviour. A child who can fix and follow comfortably with each eye is likely to have relatively symmetric vision, as opposed to a child who cannot fixate with one eye or fusses or cries every time a particular eye is covered.

Eye Alignment

Assessing eye alignment identifies whether there is a true deviation and, if so, in which direction. Esotropia and exotropia refer to eyes that are deviated inward or outward, respectively, and hypertropia/hypotropia refer to eyes that are deviated upward and downward, respectively. Many children who present with an "eye deviation" actually have pseudostrabismus. The eyes can appear crossed inwardly (pseudoesotropia) due to a wide nasal bridge or epicanthal folds. The eyes can also appear turned outward (pseudoexotropia) due to a positive angle kappa or temporally dragged macula. The eyes can even look vertically deviated due to eyelid changes, such as ptosis or lid retraction. Although pseudostrabismus is usually benign, it is important to be aware that approximately 5% of children diagnosed with pseudostrabismus are diagnosed with strabismus later in life.[4]

The gold standard to measure eye alignment is the alternate prism cover test, in which eyes are covered alternately and prisms are used to measure the exact deviation. In an emergency setting, it is usually sufficient to check the cornea light reflex and perform a simple cover test. First, shine a light at the child and observe whether the corneal reflexes are centred and symmetric.

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Table 1. Strabismus in Children – Important Causes

Deviation	Common	Rare
Esotropia (eyes in)	• Infantile esotropia • Accommodative esotropia	• Acute acquired comitant esotropia • Cranial nerve VI palsy • Duane syndrome – type 1
Exotropia (eyes out)	• Intermittent exotropia	• Infantile exotropia • Cranial nerve III palsy
Hypertropia/hypotropia (one eye up/other eye down)	• Dissociated vertical deviation • Inferior oblique overaction	• Brown syndrome • Monocular elevation deficiency • Orbital floor fracture with inferior rectus entrapment
Any of the above (variable deviation)	• Sensory strabismus	• Myasthenia gravis • Extraconal orbital tumour – Benign: capillary hemangioma – Malignant: rhabdomyosarcoma, neuroblastoma
Anomalous head posture (eyes causing head to move)	—	• Cranial nerve IV palsy • Nystagmus

If strabismus appears to be present, cover the eye that appears to be fixating. In a child with a true deviation, the deviated eye should move to pick up fixation. Use of these tests will help to determine if there is a true deviation and the direction of deviation.

Motility (Comitant vs Incomitant)

In any child with strabismus, one of the most important characteristics is whether the deviation is comitant or incomitant. A deviation is comitant when it is approximately the same magnitude in all directions of gaze. Comitant deviations, such as infantile esotropia and intermittent exotropia, are generally more common and less serious.[5] Incomitant deviations, such as cranial nerve palsies, are less common and usually more serious.[6,7] In an emergency setting, rather than precisely measuring the deviation in all fields of gaze, check the extraocular motility. Incomitant deviations are typically caused by paresis or restriction of one or more extraocular muscles. As such, a comitant deviation is associated with full extraocular motility, while an incomitant deviation will generally be accompanied by a limitation of motility in one or both eyes.

Fundus Examination and Cycloplegic Refraction

A child with newly diagnosed strabismus should always undergo a fundus examination and ideally a cycloplegic refraction. Strabismus is frequently the first external manifestation of severe vision loss (so called "sensory strabismus"), and the fundus examination is important to rule out serious causes of vision loss such as retinoblastoma or optic nerve hypoplasia. A cycloplegic refraction (even an earnest attempt at one) can be very useful in certain types of strabismus. Parents of a child presenting with acute esotropia and diplopia frequently fear a serious cause such as a brain tumour; however, identification of a high hyperopic refractive error allows the clinician to reassure them that the child will likely need glasses and not neurosurgery.

Esotropia

Esotropia is the most common type of strabismus in childhood, making up approximately 60% of all cases.[8]

Infantile esotropia

Infantile (or congenital) esotropia is a common form of strabismus in very young children. It presents as a comitant deviation in the first 6 months of life.[9] The deviation is typically large and constant. The child usually cross fixates, which is protective against amblyopia; however, amblyopia can still occur, so assessing for a significant asymmetry in vision is important.[10] It is also crucial to check motility to rule out uncommon causes of early-onset esotropia, such as a congenital cranial nerve VI palsy or Duane syndrome. This can be done with a toy or video (parents' cellphones are a good source of engaging fixation targets). If needed, the doll's head manoeuvre can be used. To do this, move the child's head from side to side – gently but quickly – and the eyes should move in the opposite direction due to the vestibulo-ocular reflex.[11] A dilated fundus examination should always be performed to rule out structural disease that can also manifest as an early-onset comitant esotropia. For typical infantile esotropia, no workup is needed. The usual treatment is monitoring for amblyopia and nonurgent strabismus surgery.[12]

Accommodative esotropia

The other common type of esotropia in childhood is accommodative esotropia. It is one of the most common types of all childhood strabismus, comprising approximately 25% of all cases.[8] Accommodative esotropia is similar to infantile esotropia in that both are common and comitant; however, accommodative esotropia tends to present at an older age (1.5–4 years).[13] A basic cycloplegic refraction is useful to perform in cases of accommodative esotropia. Children with accommodative esotropia often have moderate to high hyperopia (typically +3 to +10 diopters).[14] In a child presenting with acute-onset esotropia, findings of comitant deviation and moderate to high

hyperopia are highly suggestive that it is accommodative in nature. Treatment usually involves eyeglasses to fully correct the hyperopia, although about 30% of children also need strabismus surgery.[14]

Acute acquired comitant esotropia

Acute acquired comitant esotropia is a less common but important type of childhood strabismus that presents suddenly with an inward eye turn. It can be intermittent or constant and may be accompanied by diplopia. Examination typically shows a comitant deviation without abnormally high hyperopia. In rare cases, acute acquired comitant esotropia can be associated with significant neurological disease, such as a posterior fossa tumour.[15] As such, it is important to assess for clinical signs of neurological pathology, such as a cranial nerve VI palsy, increased intracranial pressure, or nystagmus. Treatment is usually botulinum toxin injections or strabismus surgery.[16]

Cranial nerve VI palsy

In any child with esotropia, it is important to rule out a cranial nerve VI palsy. Cranial nerve VI palsies typically present with an abduction deficit in one of both eyes and an esotropia that is incomitant (significantly greater in the gaze toward the palsy; **Figure 1**). In these cases, checking extraocular motility and looking for lateral incomitance is crucial. Cranial nerve VI palsies in children often have a serious cause, such as an intracranial tumour, elevated intracranial pressure, trauma, or inflammation,[17] and therefore require urgent neuroimaging. Once the underlying cause is addressed, cranial nerve VI palsies are usually monitored for at least 6 months before considering strabismus surgery since many resolve spontaneously with time.[18]

Duane syndrome (type 1)

The final uncommon but important type of esotropia is Duane syndrome (or Duane retraction syndrome), a congenital disorder caused by abnormal development of the abducens nucleus and nerve.[19] There are several types of Duane syndrome, the most common of which (Duane syndrome type 1) can look very much like a cranial nerve VI palsy, with an abduction deficit and incomitant esotropia. Unlike a cranial nerve VI palsy, Duane syndrome does not require an urgent workup for a neurological cause. The differentiation can be difficult. The key feature of Duane syndrome is retraction of the eye (or eyelid narrowing) with attempted adduction. Unlike cranial nerve VI palsy, there also tends to be a relatively small deviation in primary position in Duane syndrome despite a significant abduction deficit. Duane syndrome is challenging to treat and surgery is often only attempted when there is a deviation in primary position or a significant head turn.

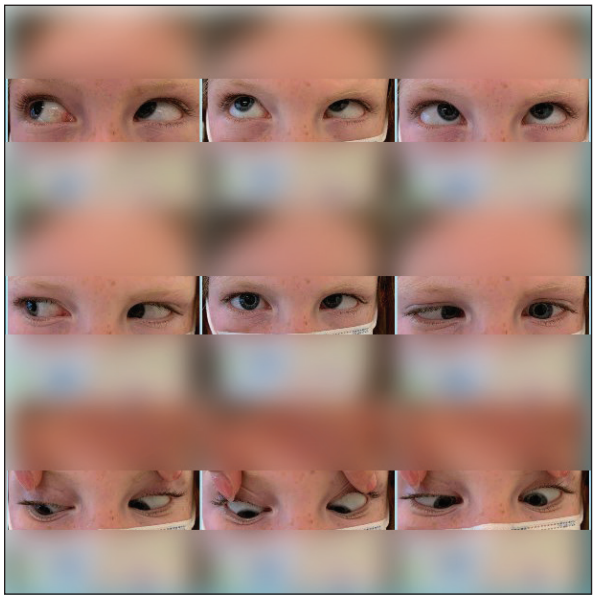
Exotropia

Exotropia is the second most common type of strabismus in childhood after esotropia.[8]

Intermittent exotropia

Intermittent exotropia, the most common form of exotropia in children by far, presents as an intermittent outward deviation of the eyes. The deviation is comitant and extraocular motility is full. There is a great deal of variability in how intermittent exotropia manifests, but it is usually worse with fatigue and illness and harder to control at distance.[20] There is no association with underlying neurological disease and neuroimaging is unnecessary in typical cases.[21] The natural history of intermittent exotropia is that most cases will remain stable and some may even improve with time.[22] If there is good control of the deviation, it is reasonable to monitor. Treatment is indicated if the deviation is worsening, impacting vision, or is a significant psychosocial concern. While many treatments have been studied, the only 2 that have convincing evidence of efficacy are alternate patching[23,24] and strabismus surgery.[25]

Figure 1. Cranial nerve VI palsy. Limitation of abduction in the left eye, causing in incomitant esotropia which is greater in left gaze.



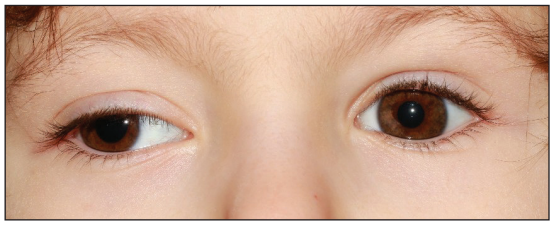
Infantile exotropia

Infantile exotropia is generally defined as a constant large-angle deviation presenting in the first 12 months of life. Infantile exotropia is not rare, but it is much less common than infantile esotropia.[26] It is important to note that many normal infants are exotropic at birth.[27] Most infants achieve normal eye alignment by the age of 4 months, so it is prudent to wait until a child is at least a few months old before diagnosing infantile exotropia. It is also important to know that there is a strong association of infantile exotropia with coexisting ocular and systemic disease, so a past medical history and full eye examination are important.[28] Similar to infantile esotropia, treatment is nonurgent strabismus surgery.[29]

Cranial nerve III palsy

Cranial nerve III palsy is a rare but serious cause of exotropia in childhood. About one-third of cases of cranial nerve III palsies in childhood are congenital, another third are due to trauma, and the remaining third are most commonly due to life-threatening neurological conditions such as tumours, aneurysms, and meningitis.[30] Fortunately for clinicians, there are usually clear signs to differentiate a cranial nerve III palsy from other types of

Figure 2. Cranial nerve III palsy. Right eye exotropia associated with ipsilateral ptosis and a dilated pupil.



exotropia, including significant limitations of extraocular motility (elevation, depression, and adduction), highly incomitant deviation, and the affected eye is usually both exotropic and hypotropic ("down and out"). There can also be ipsilateral ptosis and a dilated pupil (**Figure 2**). The workup for a cranial nerve III palsy is urgent neuroimaging (ideally magnetic resonance imaging/angiography). If eye alignment does not improve with time, surgery can be attempted, although outcomes are generally poor.[31]

Hypertropia/Hypotropia

Hypertropia is a type of eye deviation in which one eye turns upward, while hypotropia is a type of deviation in which one eye turns downward. By definition, when one eye is deviated upward, the other must be relatively deviated downward, so hypertropia and hypotropia always coexist.

Dissociated vertical deviation (DVD)/inferior oblique overaction (IOOA)

Vertical deviations are much less common than horizontal deviations in childhood.[8] As a result, the vertical deviations associated with horizontal deviations – DVD and IOOA – are two of the most common forms of vertical strabismus in children. Identification of a vertical deviation in keeping with DVD or IOOA should prompt the clinician to ask about past ocular history since there may have been a horizontal deviation that was surgically corrected and is no longer apparent on examination.

DVD is a poorly understood phenomenon in which one eye will drift upward.[32] It typically manifests when the person is not actively looking or when one eye is covered. It is associated with early-onset strabismus of any type. DVD does not impact visual development and often improves over time, so treatment is usually unnecessary; however, there are surgical options if it becomes a psychosocial issue.[33]

IOOA is another vertical deviation associated with early-onset horizontal strabismus, particularly infantile esotropia. It differs from DVD in that it causes a hypertropia only with adduction. Bilateral inferior oblique overaction can also cause a V-pattern, in which the eyes are significantly more esotropic in downgaze compared to upgaze. Like DVD, IOOA does not necessarily need to be corrected, but surgery is an option if the deviation causes a psychosocial concern or to correct a V-pattern.[34]

Brown syndrome/monocular elevation deficiency (MED)

There are 2 conditions that cause vertical deviations in upgaze: Brown syndrome and MED. The main clinical differentiating feature is that Brown syndrome causes upgaze limitation primarily in adduction, while MED causes generalized upgaze limitation. The underlying cause is also different; Brown syndrome is caused by a mechanical restriction with the superior oblique muscle and its tendon, while MED can be due to supranuclear paresis or restriction of the inferior rectus muscle.[35,36] Brown syndrome can be congenital or acquired (due to trauma, surgery, or inflammation), while MED is generally congenital. Treatment is surgical for both; however, it is only required if there is a deviation in primary position or an anomalous chin-up head posture.[37,38]

Orbital floor fracture with inferior rectus entrapment

An orbital floor fracture with entrapment of the inferior rectus muscle is an uncommon cause of vertical strabismus in children that requires urgent diagnosis and management. The cause is typically a significant trauma leading to a blowout fracture of the orbital floor.[39] The fracture is usually apparent on computed tomography scan; however, children can have a "trapdoor" fracture in which the soft bones return to their original position while still entrapping the inferior rectus muscle or associated soft tissue.[40] In any child with an orbital floor fracture, it is imperative to check for a limitation of upgaze. An entrapped inferior rectus muscle must be released with urgent surgery (ideally within hours) to prevent ischemia and long-term vertical strabismus that is challenging to treat.[41]

Any of the Above (Variable Deviation)

There are several important conditions that may present as almost any type of deviation.

Sensory strabismus

Strabismus is common in children with visual impairment in one or both eyes. This is one reason why it is important to check vision in any child with new-onset strabismus as the underlying cause can be poor vision. In sensory strabismus, the deviation is generally comitant but the direction of deviation is variable. Congenital conditions usually cause esotropia and acquired conditions usually cause exotropia.[42] Surgery is generally reserved for psychosocial issues, especially since the alignment tends to be unstable over time.[43]

Myasthenia gravis (MG)

MG is a disorder of neuromuscular transmission that typically presents with fatigable weakness.[44] While uncommon in children, MG is an important diagnostic consideration because it can manifest with any pattern of strabismus. All skeletal muscle can be impacted, so other signs can include fatigable ptosis and generalized weakness.[44] The key step in man-

agement is to recognize the signs of MG as early as possible, as untreated MG can progress to respiratory failure.[45] Treatment is primarily directed at the underlying cause (usually autoimmune).[3]

Extraconal orbital tumour

While an intraconal orbital tumour will usually push the globe forward and cause proptosis, an extraconal orbital tumour can displace the eye and present as strabismus. The most common benign orbital tumour in children is a capillary hemangioma, which usually grows rapidly in the first 6 months of life and resolves over time.[46] The most common primary malignant orbital tumour in children is rhabdomyosarcoma and the most common orbital metastasis is neuroblastoma, both of which can be rapidly progressive and potentially fatal.[47,48] If there is any suspicion for an orbital tumour in a child with strabismus, orbital imaging should be ordered, with increased urgency if there is concern for malignancy.

Anomalous Head Posture

Important eye deviations in children can manifest primarily as an anomalous head posture (i.e., eyes causing the head to move), as opposed to a clear eye misalignment.

Cranial nerve IV palsy

A cranial nerve IV palsy causes weakness of the superior oblique muscle, which produces a measurable hypertropia in the affected eye. Because the primary function of the superior oblique muscle is incyclotorsion, a cranial nerve IV palsy often presents with a head tilt (away from the side of the palsy) rather than strabismus (**Figure 3**). To differentiate a head tilt due to a cranial nerve IV palsy from other causes, such as musculoskeletal torticollis, one technique is to simply tilt the child's head in the other direction and look for a vertical deviation.

Congenital cranial nerve IV palsies are common and can present at any age.[49] It is important to differentiate a congenital palsy from an acquired palsy because a congenital palsy does not need further workup. One of the easiest ways to identify a congenital palsy is to look at photos from when the child was younger, which will usually show a subtle head tilt that was simply not noticed at the time. Acquired cranial nerve IV palsies are often due to trauma but can also be caused by intracranial neoplasms or high intracranial pressure.[18] As such, if the cranial nerve IV palsy is acquired and there is no clear cause, urgent neuroimaging should be performed. A mild palsy with minimal head tilt and no manifest strabismus does not need treatment. Children with a significant head tilt (or significant manifest hypertropia) can usually be successfully treated with surgery.[50]

Figure 3. Cranial nerve IV palsy, manifesting as a head tilt away from the eye with the palsy.

Nystagmus

While not technically a type of strabismus, nystagmus bears mentioning because it can also present as an anomalous head posture. Children with nystagmus will frequently move their head – turn, tilt, or both – to find the null position, which minimizes the nystagmus and optimizes vision. As with a cranial nerve IV palsy, one strategy to diagnose a subtle nystagmus is to move the child's head in the opposite direction of the preferred head position. This will typically move the eyes out of the null position and make the nystagmus easier to identify. Nystagmus in children has many potential causes, and a workup may be required (electroretinogram, genetic testing, and/or neuroimaging) depending on the clinical scenario.

Conclusion

Eye turns are challenging to diagnose and manage, particularly in children. It is crucial to have basic knowledge of the potential underlying causes of strabismus and how they present in order to differentiate a common form of strabismus (such as intermittent exotropia) from a potentially life-threatening form (such as a cranial nerve III palsy or MG).

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DISCLOSURE:

Dr. Wan stated that he has no disclosures to report in association with the contents of this issue.

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