Clinical Congenital Nystagmus, Evaluation and Treatment
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infantile nystagmus syndrome, spasmus nutans, monocular nystagmus

Objectives
At the conclusion of this program, participants should be able to:
1. Evaluate the child with nystagmus more efficiently.
2. Decide when neuro-imaging and electrophysiology studies of children with nystagmus are appropriate.
3. Recognize the potential neurologic problems presenting with nystagmus in infancy.

Questions
True or False:
1. Upbeating nystagmus in infancy is usually a sign of neurologic disease.
2. Monocular nystagmus in infancy is usually a sign of spasmus nutans.
3. Sensory causes of nystagmus in infancy represent less than 50% of cases usually seen.

Considerable detail has been obtained about the underlying wave-forms of nystagmus in children because of the innovative ocular motor laboratories now being maintained in a few pediatric ophthalmology centers. There can be no doubt that measurement of eye movements may settle the issue of diagnosis in difficult cases. The most common wave-forms are jerk with increasing-velocity slow phase, and pendular, both of which may be seen in the same patient. Increasing velocity slow phases are typical for infantile nystagmus syndrome but they are not always present. The presence of accelerating slow phases does not distinguish between visual or motor factors as the underlying cause but does tend to rule out neurologic nystagmus. An additional typical feature of the infantile nystagmus syndrome is a foveation period during which there is a brief period when the eye is relatively still and directed to the object of regard. This position in which the slow phase of eye velocity is minimized is referred to as the “null zone.”

Recently the classification of Eye Movement Abnormalities and Strabismus Working Group has proposed a new classification for nystagmus as it relates to children. They have proposed that the term “infantile nystagmus syndrome” be used to encompass what was previously called “congenital nystagmus,” whether of the motor or sensory variety. Although there is some controversy concerning classification of nystagmus in infancy, it has been suggested that nystagmus with an onset before six months of age can be divided into three categories: 1) Congenital idiopathic nystagmus in which no visual or neurologic impairment can be found; 2) Sensory deficit nystagmus in which there is a visual sensory abnormality; and 3) Neurologic nystagmus associated with a neurologic disorder.

The criteria for inclusion into “nystagmus syndrome” includes infantile onset, and accelerating slow-phase wave-forms. One should note that the definition of “infantile nystagmus syndrome” is predicated on identifying the characteristic wave-forms and, without the appropriate eye movement recording equipment, this may not always be possible clinically. Nevertheless, the term “infantile nystagmus syndrome” seems more appropriate than the previously used “congenital nystagmus” for the same reasons that “infantile esotropia” has replaced “congenital esotropia.” The primary reason is that neither esotropia nor nystagmus is seen at birth in infants, but rather both have their onset in the first few weeks of life.

Despite the advancements provided by eye movement recordings and the clarity brought by a new nomenclature system, the clinician faces an age-old problem when evaluating a child with nystagmus in infancy—what is the underlying cause of the nystagmus and, in particular, can the clinician be sure that no neurologic etiology is responsible? While no clinical rules concerning nystagmus in infancy are foolproof, a number of issues regarding nystagmus in this group have been defined and the following is offered as an experiential framework for evaluating difficult cases.

First and foremost, the clinician should try to establish the age of onset of nystagmus in infants. Having said this, it is not an easy task. It is not unusual to hear a parent insist that they have not noticed any nystagmus in their child until the child was several months of age, despite the fact that the child has all the characteristic features of the infantile nystagmus syndrome whose onset is usually between six and twelve weeks of age. What accounts for this? The fact that the infantile nystagmus syndrome is a disorder that becomes more apparent with fixation and indeed could even be seen as a fixation disorder, is primarily responsible for this frequent error in historical observation. Infants in the first few months of life maintain sustained fixation for only brief periods of time and for distance fixation even less often. It is not surprising, therefore, that in some cases the parents have not noticed nystagmus until relatively late in the first year of life.
Nevertheless, a careful attempt to try to document the age of nystagmus in children is important.

Documentation of the onset of nystagmus is particularly important when discussing the question of acquired neurologic disease and its differential from the disorder known as “spasmus nutans.” Spasmus nutans syndrome is characterized by the triad of nystagmus, head nodding and anomalous head position (usually torticollis). Whereas congenital idiopathic nystagmus and sensory deficit nystagmus usually have an onset prior to six months of age, it is generally agreed that the onset of spasmus nutans is always after six months of age and usually prior to two to three years of age. While it is true that spasmus nutans is characterized by asymmetry of the nystagmus and, sometimes, frankly monocular nystagmus, if these features are seen in a child under six months of age, one should consider a neurologic origin for the nystagmus rather than spasmus nutans. Especially high on the differential list is a tumor involving the prechiasmal portion of the optic nerve.

Although for any given patient, knowing the general frequency of various forms of nystagmus in a large group of children does not necessarily help establish the diagnosis for that particular patient, it at least alerts the clinician to the general clinical problems that should not be overlooked. Or to put it another way, if one simply takes all the children who present to a pediatric ophthalmology clinic under the age of one with nystagmus and ask whether they have congenital idiopathic nystagmus, sensory deficit nystagmus or neurologic nystagmus, several large studies all agree that more than 90% of patients will fall into the category of sensory deficit nystagmus. In the vast majority of cases, sensory deficit nystagmus is associated with bilateral anterior visual pathway pathology, although occasionally binocular nystagmus is associated with monocular visual loss (especially in untreated PHPV). This is clearly not the experience of adult neuro-opthamologists evaluating adult patients with apparent infantile nystagmus syndrome where the idiopathic form is much more commonly seen. This is perhaps due to the fact that these patients often seek therapeutic options as adults. Nevertheless, the clinician dealing with children with nystagmus may often need electrophysiology (especially electroretinography) before a sensory deficit nystagmus can be ruled out and a congenital idiopathic diagnosis established. Indeed, the three major retinal causes other than retinopathy of prematurity of sensory deficit nystagmus (Leber’s congenital amaurosis, x-linked recessive congenital stationary night blindness and myopia, and cone dystrophies) all present with nystagmus and a relatively normal looking retina on ophthalmoscopy. Finally, when addressing the relative frequency of different forms of nystagmus in children, it should be emphasized that while there certainly appears to be a syndrome referred to as spasmus nutans, it is relatively uncommon and my unfortunate experience has been that long-term follow-up of children in whom this diagnosis has been made frequently reveals the diagnosis to be incorrect.

Recognizing that most of us who see children with nystagmus do not have available to us eye movement recording information, what can the clinician learn from observing the apparent direction of nystagmus and its amplitude? Infantile nystagmus syndrome is variable in its form although certain clinical features are relatively common. It is usually conjugate and most commonly horizontal in all fields of gaze. Although eye movement recordings have identified a frequent torsional component to the nystagmus, this is usually not apparent on clinical examination. Previous reports indicating that infantile nystagmus syndrome is rarely vertical are misleading. Upbeating nystagmus is not an unusual way for retinal disease to present in the first year of life. While the nystagmus is not truly purely vertical in orientation and usually has a slight oblique appearance to it, for practical purposes the direction of the nystagmus is upbeating. In these children it remains vertically oriented for up to twelve to eighteen months of age and then assumes a much more usual horizontal direction of typical sensory deficit nystagmus. Why this transient vertically oriented nystagmus occurs and why it seems to occur most frequently with retinal disease than other causes of sensory deficit nystagmus is not clear. Nevertheless, it has been my experience that upbeating nystagmus in the first year of life is much more likely to be a sensory deficit nystagmus especially associated with retinal disease than it is associated with neurologic disease or idiopathic nystagmus (although pedigrees have been described of more than one family member with vertically oriented idiopathic nystagmus).

In the past, attempts have been made to estimate the visual acuity of children with nystagmus based on the amplitude of nystagmus. These attempts have been singularly unsuccessful and by and large the size of the amplitude of nystagmus correlates relatively poorly with the underlying cause. There is, however, one major exception to this rule and that is the small amplitude, fast-frequency nystagmus that is seen so characteristically with cone disorders. Indeed, it is so typical that even clinically without eye movement recordings it usually can be identified and the differential diagnosis for this small amplitude fast-frequency nystagmus is relatively short – spasmus nutans and tumors of the afferent visual pathway being the primary other entities to consider.

The problem of identifying retinal disease in the presence of sensory deficit nystagmus needs to be re-emphasized. I frequently see patients who have had a diagnosis of congenital idiopathic nystagmus made who as
they enter school are found to have significantly reduced visual acuity and only then is electroretinography performed and the underlying retinal disease established. While one might take the position that this is not a problem since no specific therapy is available for these disorders, this overlooks the problem of appropriate genetic and educational counseling in these cases. Being able to prioritize who should undergo electroretinography is obviously an important clinical issue. Ophthalmoscopy rarely provides the necessary information to do so. On the other hand, retinoscopy is frequently quite helpful. For example, the patient who presents with a slow large amplitude nystagmoid movement, obviously poor visual function and on a cycloplegic retinoscopy has more than four diopters of hyperopia is almost certainly going to have Leber’s congenital amaurosis or one of the syndromes associated with congenital cone/rod dysfunction and systemic disease – for example Joubert’s, Senor’s or other syndromes. In contrast, the infant boy who presents with nystagmus and moderately decreased visual responsiveness and significant myopia is most likely to represent a case of congenital stationary night blindness and myopia (x-linked recessive) and less commonly blue-cone dystrophy. Of the three major causes of nystagmus associated with retinal disease other than retinopathy of prematurity, (Leber’s congenital amaurosis, x-linked congenital stationary night blindness and myopia, and congenital cone dystrophy) only congenital cone dystrophy (achromatopsia) is not associated with a significant refractive error on retinoscopy. While these retinoscopic errors and their identifications do not replace the need for electroretinography, they often are the primary piece of information that prioritizes it.

Although occult retinal disease is far more common as a problem in this age group than occult neurologic disease, it is neurologic disease that most concerns the clinician. That the infantile nystagmus syndrome may occur with brain tumors still remains underrecognized. The nystagmus may have all the clinical features of a sensory deficit nystagmus but subtle evidence of hypoplasia and/or atrophy of the optic nerve may be the only objective signs indicating a co-existing central nervous system tumor. The most common tumors that present in this fashion are optic nerve gliomas and craniopharyngiomas, both of which are congenital tumors. They are present during the intrauterine development of the optic nerve; therefore, it is not surprising that they can manifest with optic nerve hypoplasia and/or optic atrophy in association with nystagmus. Although it is true that chiasmal tumors may present in children as see-saw nystagmus, it has been my experience that it is much more common for them to present as asymmetric horizontal nystagmus and occasionally even frankly monocular nystagmus, although when monocular nystagmus is present the tumor is usually just anterior to the chiasm itself. That neurologic disease other than tumors may present with nystagmus in infancy is even less well recognized. For example, children with arrested or compensated hydrocephalus can present with what appears to be infantile nystagmus syndrome of the sensory deficit nystagmus type. There is usually obvious optic atrophy in association with it. The presence of optic atrophy and nystagmus in infancy should be seen as a strong indicator of the possibility of either raised intracranial pressure and/or intracranial tumor in infancy. In contrast, attributing optic atrophy and nystagmus to hypoxia is a dangerous paradigm. While it is clear that hypoxia may produce optic atrophy in association with severe cortex pathology, it rarely, if ever, accounts for optic atrophy in isolation. Clearly the infant who presents with nystagmus that is asymmetric, monocular or in association with optic nerve hypoplasia and/or optic atrophy should undergo magnetic resonance imaging studies.

A perplexing problem that still faces the clinician evaluating the child with nystagmus is how does one establish the diagnosis of ocular albinism in the absence of transillumination defects? Albinism in its more florid forms is an easy diagnosis to make clinically based on the presence of transillumination defects of the iris or hypopigmentation or absent pigmentation of the skin, hair and eye. However, in its milder forms involving just the ocular structures, albinism may be difficult to differentiate from congenital idiopathic nystagmus. One might argue that the difference is primarily academic since the visual prognosis is likely to be similar and the genetic inheritance patterns are relatively comparable. Nevertheless, most parents are unhappy with the vagaries implied by a diagnosis not firmly established. Moreover, it seems clear that at least in some cases, patients who have been diagnosed with congenital idiopathic nystagmus have mild forms of albinism at least when tested with hemispheric VEP studies. This quandary of how to establish precisely the diagnosis of ocular albinism in the absence of iris transillumination defects is one that pediatric ophthalmologists face frequently.

The ophthalmologist evaluating the child with nystagmus is first and foremost concerned with making certain that underlying ocular or systemic pathology is accounted for. This may require electrophysiology and neuro-imaging studies in order to be certain. Even more important, careful follow-up of children with nystagmus with periodic reevaluation of their visual acuity, the appearance of their nystagmus, retinoscopy and reevaluation of their ophthalmoscopic examination is clearly indicated. In many circumstances the appropriate underlying diagnosis can only be ascertained on the second, third or fourth examination. It is inappropriate, in my view, to attempt to authoritatively establish the cause of nystagmus in infants.
on the initial examination. Careful reevaluation should, therefore, be routine in the care of these children.

CME Answers
1. False. Upbeating nystagmus in infancy is often a sign of ocular disease, especially retinal disease. The nystagmus will usually revert to horizontally directed nystagmus within the first 12 to 14 months of age.
2. False. Monocular nystagmus in infancy may be due to spasmus nutans if the nystagmus begins after age six months, with the possibility of an afferent visual pathway tumor that must be ruled out in all cases. It can also be associated with dense unilateral vision loss.
3. False. In infancy more than 90% of all cases of nystagmus seen will be due to abnormalities of the ocular surfaces or anterior visual pathways.

References

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