Infantile Nystagmus: Current Management and Future Perspectives

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Abstract

Infantile nystagmus syndrome (INS) is a congenital or early-onset ocular disorder characterized by involuntary, rhythmic eye movements that can significantly impact visual acuity, binocular vision, and overall quality of life. This review article explores the current management strategies for INS, emphasizing a multidisciplinary approach involving ophthalmologists, optometrists, neurologists, and geneticists. The paper discusses conservative management options, including optical interventions such as spectacles, contact lenses, and prisms, alongside pharmacological treatments aimed at modulating ocular motor behavior. Furthermore, the review underscores the importance of individualized treatment plans tailored to the patient's specific visual and functional needs. By synthesizing current evidence and clinical practice guidelines, this article aims to provide a comprehensive overview of the available management lines for infantile nystagmus and identify gaps requiring further research.

Keywords: Infantile Nystagmus

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Introduction

Infantile nystagmus is a developmental nystagmus with onset during the first 6 months of life. It affects between 1 in 1000 to 1500 children, with a 2-to 3-fold male predominance. Despite the old name congenital nystagmus, the oscillations usually begin at 2-3 months of age and are rarely present at birth. The most common forms of infantile nystagmus are idiopathic infantile nystagmus (IIN) and infantile nystagmus associated with albinism or retinal diseases. **(Leigh and Zee, 2015)**

Idiopathic infantile nystagmus (IIN) is the most common type of infantile nystagmus. The onset of IIN is usually between birth and 12 weeks of age. In idiopathic infantile nystagmus no underlying eye condition or neurological problems are present. IIN is usually bilateral, conjugate, occurring in the horizontal plane with atypical frequency of 2-4Hz, and of either a pendular or a jerk waveform with a diagnostic accelerating slow phase, with the pendular type being more

common in early infancy. It may rarely appear as primarily vertical or even torsional nystagmus. **(Khanna and Dell'Osso, 2006)**

The cause of IIN is still unknown. It is suggested that infantile nystagmus follows a pathophysiological sequence of events commencing with gene mutations and their effect on cell physiology leading to disrupted development of neural function and connectivity in the afferent visual pathway and/or ocular motor system. Gene mutations could also directly affect motor and/or sensory innervation of extraocular muscles. **(Gottlob and Proudlock, 2014)**

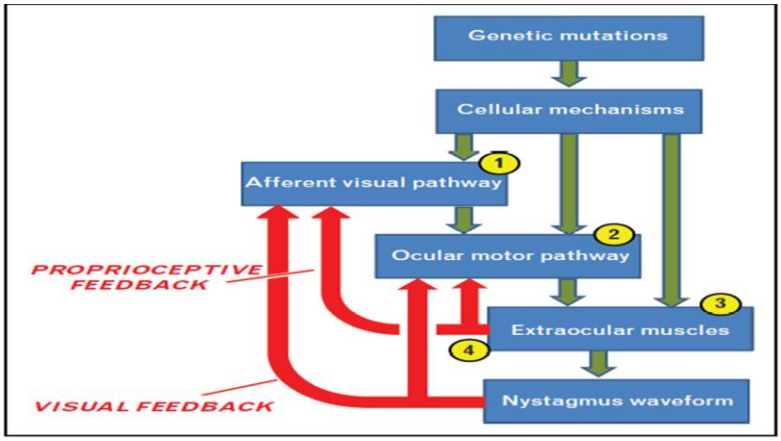
Patients with IIN can have a strong family history of nystagmus or can be singly affected. The most common mode of inheritance is due to X-linked mutations. The gene FRMD7, located at Xq26, has been identified as the major cause of hereditary X-linked nystagmus with a penetrance of 100%in males and 53%in female carriers. Individuals with mutations in the FRMD7 gene have relatively good visual acuity (better than 6/12), often possess stereopsis and show less pronounced anomalous head posture compared to individuals with IIN not caused by FRMD7 mutations. **(Tarpey et al, 2006)**

The FRMD7 gene encodes a member of the FERM domain family of proteins. These are plasma membrane–cytoskeleton coupling proteins many of which bind to actin or other cytoskeleton components. In differentiating Neuro2A cells, the FRMD7 protein co-localizes with the actin of primary neurites. FRMD7 protein expression in these cells promotes neurite outgrowth and knock-down of FRMD7 causes a reduction in average neurite length. **(Pu et al, 2012)**

Watkins et al., 2013 found an interaction between the FRMD7 protein and calcium/ calmodulin-dependent serine protein kinase (CASK). One of the functions of CASK in neurons is to link the plasma membrane to the actin cytoskeleton. They suggest that FRMD7 mutations could act by disrupting the interaction between FRMD7 and CASK needed to promote membrane extension during neurite outgrowth.

Expression of FRMD7 in the human embryo occurs in both the developing neural retina as well as in ocular motor structures such as the cerebellum and vestibulo-optokinetic system. The FRMD7 protein, therefore, could primarily influence the developing afferent or motor system. **(Pu et al, 2013)**

The medications gabapentin and memantine have been shown to influence idiopathic infantile nystagmus by reducing nystagmus intensity leading to improved visual acuity. These two medications are central nervous system inhibitors. Gabapentin probably increases synaptic concentration of the inhibitory transmitter GABA through voltage-sensitive calcium channels, whereas memantine inhibits the excitatory neurotransmitter glutamate by blocking N-methyl-D-aspartate (NMDA)-type glutamate receptors. These two transmitter systems are found in both sensory and motor systems. **(McLean et al, 2007)**



(Fig. 1) The sequence of pathophysiology that leads to infantile nystagmus; genetic mutations are known to underlie most infantile nystagmus subtypes leading to changes in cellular function, which in turn could effect: (1) the developing afferent visual pathway, (2) the developing ocular motor system, (3) extraocular muscle structure and/or motor innervation, or (4) feedback from extraocular muscle proprioceptors. (Gottlob and Proudlock, 2014)

Clinically, the nystagmus often becomes right beating on right gaze and left beating on left gaze, but remains in the horizontal plane on up, down and lateral gaze (i.e., uniplanar in all gaze positions). The nystagmus intensity (i.e., frequency× amplitude) increases with fixation effort and decreases with convergence, in darkness and during sleep. Patients rarely complain of oscillopsia. Minority of patients has an associated strabismus and some exhibit a latent component on monocular occlusion. **(Richards and Wong, 2015)**

Individuals with IIN develop a ***foveation strategy*** during visual development to improve vision. They learn how to use foveating saccades to maximize the periods when the eyes are moving slowly. These slow periods are called *foveation periods* that can be defined as the length of time during a nystagmus cycle when the eyes are more stable. This period of time corresponds to maximum afferent attention, when the patient sees more clearly. Foveation time is a better indicator of visual function than the intensity of the oscillation. Visual acuity is usually log-MAR 0.3 (6/12) or better in most patients and nystagmus usually becomes less evident with age. Strabismus is not common and good stereopsis is often present. **(Papageorgiou et al, 2014)**

Fu et al, 2011 reported that patients with IIN showed mildly reduced visual acuity before 24 months of age and a gradual maturation of visual acuity with age after 24 months, which paralleled with existing normative curves for visual acuity development.

IIN is usually associated with a null point that can be defined as the position of the gaze in which the oscillation is significantly reduced and vision is maximally improved. If the null point does not coincide with the primary gaze position, then a head position may be adopted to reduce the nystagmus. This can result in a face turn most commonly when the nystagmus is in the horizontal plane. **(Abadi and Bjerre, 2002)**

Manifest latent nystagmus

Manifest latent nystagmus (MLN), recently known as fusion maldevelopment nystagmus syndrome (FMNS) is a predominantly horizontal, jerk nystagmus that becomes more apparent when one eye is covered. The main characteristic is that, the manifest component is smaller in intensity and subclinical in size (less evident) when both eyes are open and the amplitude increases when one eye is occluded (the latent component). Other typical feature of MLN is that it changes direction. The fast phases are always towards the open eye. When the right eye is closed, it beats left, and when the left eye is closed, fast phase is right. **(Abadi et al, 2006)**

The underlying mechanism behind MLN is the disruption of binocular vision during visual development, through strabismus and amblyopia. MLN is almost always associated with congenital squint syndrome, which leads to disrupted binocular vision. Additionally, it is often associated with conditions that cause unilateral loss of vision during visual development such as cataract and optic nerve hypoplasia. Intensity decreases with age. MLN can be treated by correcting the squint. Treating the underlying amblyopia using patching therapy can also reduce the nystagmus caused by MLN. **(Mravicic et al, 2019)**

MLN can be differentiated from IN by full orthoptic examination looking for presence of early-onset manifest strabismus can provide a clue towards an MLN diagnosis. A full examination of the anterior and posterior segments of the eye can identify monocular cataract or optic nerve hypoplasia leading to MLN. Bilateral pathology may cause IN, MLN or both. Null positions and head postures are frequent in IN and much less common in MLN unless the child is cross-fixating. IN onset is often earlier (<6–12 months) than MLN. **(Dell'Osso et al, 2014)**

Albinism

Oculocutaneous albinism (OCA) is characterized by a lack of pigmentation in the eyes, skin, and hair and is caused by disruption in the production of melanin due to a number of genetic mutations. In certain forms of albinism there is no apparent lack of pigmentation in hair or skin and only the visual system is affected. This is described as ocular albinism (OA). **(Grønskov et al, 2007)**

OCA is linked to mutations in four known genes and OA in one known gene. All these mutations lead to dysfunctional melanin synthesis and storage. It is caused by mutations in the tyrosinase gene. There are two known causes of OA: (1) due to mutations in the OA1 gene which follows an X-linked recessive inheritance; or (2) autosomal-recessive ocular albinism. **(Oetting, 2002)**

OCA is associated with several changes in the eye and visual pathway, including iris transillumination, foveal hypoplasia, retinal hypopigmentation, abnormal crossing of the optic nerves at the chiasm, reorganization of the striate cortex, and nystagmus. Optical coherence tomography shows a spectrum of foveal development in albinism that frequently leads to reduced visual acuity. The optic discs can be small and dysplastic (small cupless disks or oblique cup with situs inversus). **(Lee et al, 2013)**

The nystagmus shows many similarities to that observed in IIN patients. It is usually horizontal, conjugate, with increasing slow-phase velocities and the nystagmus intensity and waveform

changing with gaze direction. These patients also typically show a null zone and often have an anomalous head posture. **(Kumar et al, 2011)**

Compared to cases of IIN associated with FRMD7 mutations, there were slight differences in nystagmus characteristics. The FRMD7-IIN patients showed a higher proportion of pendular waveform types compared with the albinos. Additionally, the nystagmus frequency was significantly lower in albinos compared with the FRMD7- IIN group. Strabismus and anomalous head posture were seen in higher proportions in the albinism group, and stereopsis was worse compared with the FRMD7-IIN group. **(Kumar et al, 2011)**

Periodic Alternating Nystagmus

Periodic Alternating Nystagmus (PAN) describes a horizontal jerk nystagmus that reverses direction every few minutes. PAN can occur as an acquired neurological nystagmus or as an aspect of IN (often raising suspicion of albinism as the underlying etiology). **(Hertle et al., 2009)**

To test for PAN, the nystagmus should be examined for a reversal in direction for at least 5 min (ideally 10) keeping the gaze in primary position to avoid reversal due to a gaze-evoked null shift. Such prolonged observations can be difficult for young or non-compliant patients. If the nystagmus beat direction (or anomalous head postures (AHP)) is different, PAN should be suspected. When associated with INS, PAN has no sinister implications but may be a contraindication for standard AHP surgery as it implies spontaneous null shifting. **(Thomas et al, 2011)**

Acquired forms of PAN arise due to instability of the vestibulo-optokinetic systems with instability of the velocity storage mechanism for vestibular eye movements, so as an adaptive mechanism for this instability a periodicity of oscillations occurs for 4 min. It has also been shown that patients with acquired PAN have abnormalities of optokinetic nystagmus, with some patients having no optokinetic nystagmus response. **(Leigh and Khanna, 2006)**

Spasmus nutans

Spasmus nutans is a rare form of infantile nystagmus characterized by a triad of nystagmus, head nodding and head torticollis. It is intermittent, fine, high-frequency (>10 Hz), pendular dissociated nystagmus with normal MRI/CT scan of visual pathways. It appears at 1-3 years of age and usually spontaneously remits in 2-8 years. **(Wizov, 2002)**

Spasmus nutans is not inherited and is more common in low socioeconomic classes. Moreover, head nodding evoques the vestibulo- ocular reflex that may dampen the spasmus nutans and thus improve vision. In other forms of nystagmus head nodding has not been found to benefit the patient and might be an associated pathological phenomenon. **(Ehrt, 2012)**

The appearance of the nystagmus alone in spasmus nutans is fairly distinct; it resembles an ocular shiver that may be as fine (low amplitude) and rapid as to be barely visible. It may be horizontal, vertical or torsional in direction. The clinical appearance of spasmus nutans differs from that of infantile nystagmus in that spasmus nutans is often asymmetrical and may actually be

monocular. It also differs in its usual time of onset; 4 months to a year in spasmus nutans versus 2 or 3 months of age in infantile nystagmus. **(Brodsky, 2016)**

Spasmus nutans is usually a benign, self-limited entity. However, MR imaging is warranted in children with spasmus nutans because children with congenital suprasellar tumors may present with an identical constellation of findings. Neurodegenerative disorders and congenital retinal dystrophies may also, on rare occasions, masquerade as spasmus nutans. The high-frequency nystagmus that characterizes achromatopsia resembles that of spasmus nutans but is conjugate rather than asymmetrical. **(Rucker and Lavin, 2021)**

Nystagmus associated with retinal diseases and low vision

In infancy many cases of nystagmus seen are due to abnormalities at numerous locations along the sensory visual pathway. In nystagmus associated to afferent diseases, it is not entirely clear whether the afferent deficits cause the nystagmus or whether the nystagmus is intrinsic to the disease. **(Gottlob, 2001)**

Nystagmus associated with retinal diseases and low vision can be horizontal or vertical or a combination of both or it can also be dissociated. The visual acuity in patients with nystagmus associated to afferent diseases is often lower than in idiopathic nystagmus due to the anatomical pathology of the eye. **(Hussain, 2016)**

Nystagmus related to afferent diseases is associated with bilateral anterior visual pathway pathology. Congenital cataracts can lead to nystagmus if not operated on early enough. Corneal opacities, developmental disorders of the optic disc and retina such as bilateral optic nerve hypoplasia, chorioretinal or optic nerve coloboma and retinopathy of prematurity (ROP) are also associated with nystagmus. Deficits of rod and cone systems, such as congenital stationary night blindness, achromatopsia and Leber's amaurosis are all associated with nystagmus. **(Lyons and Wiwatwongwana, 2013)**

Careful history-taking is important, as photophobia with poor color discrimination may indicate achromatopsia while night blindness with high myopia may suggest congenital stationary night-blindness. These congenital disorders require differentiation by clinical findings, family history, laboratory tests, radiology, and detailed electrophysiological findings under photopic and scotopic conditions. **(Papageorgiou et al, 2014)**

Nystagmus associated with neurologic diseases and syndromes

A variety of developmental and neurological syndromes are associated with nystagmus such as Down's syndrome, Noonan's syndrome and microcephaly. These are usually related to abnormalities in the brainstem and cerebellum. Space occupying lesions, cerebral palsy, periventricular leukomalacia, Chiari malformation, as well as metabolic and mitochondrial diseases are also associated with nystagmus. Also, visual pathway disease giving rise to nystagmus includes chiasmal and optic nerve glioma, craniopharyngioma, and optic nerve compression by other tumors or bone anomalies. **(Proudlock and Gottlob, 2011)**

Neurological disease should be suspected when the nystagmus is asymmetrical (dissociated) or unilateral. Acquired nystagmus is less frequent in children (17% of nystagmus patients) than in adults (40%). Many patients with neurological nystagmus also have associated neurological

symptoms or present with vertigo, nausea, and headaches due to intracranial hypertension. Ocular signs, such as relative afferent pupillary defect, papilloedema, optic atrophy and visual loss may also be present. **(Sarvananthan et al, 2009)**

Children with arrested or compensated hydrocephalus can present with sensory deficit nystagmus with associated optic atrophy. Therefore, optic atrophy and nystagmus in infancy indicate a strong possibility of either raised intracranial pressure and/or intracranial tumor in infancy. Therefore, an MRI examination should be performed in the presence of atypical nystagmus, accompanying neurological signs, developmental delay or optic atrophy. **(Salati et al, 2002)**

Clinical Evaluation of Infantile Nystagmus

The ***CEMAS*** definition of infantile nystagmus relies on waveform analysis of eye movement recordings for definitive diagnosis. However, the practicality of eye movement recording as a diagnostic requirement is limited by the availability of necessary equipment and the difficulty of oculography in infants. Furthermore, even on eye movement recordings, there is significant overlap in diagnosis. **(Richards and Wong, 2015)**

In any infant or child with abnormal eye oscillations, the nature of the movements needs to be characterized. Children in whom early onset nystagmus has been identified still face abroad differential diagnosis that includes infantile nystagmus, manifest latent nystagmus, spasmus nutans and other neurologically localizing forms of nystagmus. Even within infantile nystagmus, a wide range of underlying diagnosis must be ruled out. The clinician can navigate through this diagnostic challenge with the aid of a focused patient history, careful clinical examination and selective ancillary tests. **(Leigh and zee, 2015)**

Careful detailed history should be taken including; age of onset, history of strabismus, amblyopia, abnormal head posture, visual impairment and family history of nystagmus. Complications during pregnancy or childbirth, developmental delay or reports of ataxia or headache may indicate a neurologic cause. Family history of albinism or visual symptoms as photophobia, color blindness or night blindness suggests anterior visual pathway disease. Nystagmus onset after age 3 months and other atypical characteristics (e.g. monocular, vertical or shimmering nystagmus) suggest acquired nystagmus and heighten suspicion of optic pathway glioma. **(Buncic, 2004)**

The clinical examination begins as the child enters the room, particularly observing for signs of: photophobia, head postures (variable/ alternating/consistent) and/or head nodding as well as signs of associated systemic and neurological features. **(Self et al, 2020)**

Complete examination of all children presenting with nystagmus is essential for assessment of visual function and visual acuity throughout the critical period of visual development and also for investigation of ocular alignment and binocular vision. Cycloplegic refraction is obtained. Best corrected visual acuity (BCVA) is measured with both eyes open and monocularly, noticing the presence or absence of abnormal head posture. **(Osborne et al, 2019)**

The presence of any abnormal head posture (AHP) and its degree should be recorded for both near and distance fixation. Infantile nystagmus related AHP is noted according to the axis. It can

be anomalous horizontally (right or left head turn), vertically (chin up or down), torsionally (right or left head tilt), or in a mixed pattern **(kraft, 2012)**

Moreover, presence or absence of any involuntary head nodding should be recorded. The involuntary head nodding often seen in infantile nystagmus can be distinguished from other rhythmic head movement; if the child can voluntarily stop the head movement when asked, it is caused by the nystagmus. Also, binocular single vision is examined to evaluate sensory and motor fusion with assessment of stereoacuity when possible. Stereopsis can be measured by *Titmus test* **(Chopin et al, 2019)**

Ocular alignment has to be evaluated due to increased prevalence of strabismus in the presence of childhood nystagmus that was reported between 16 and 52%. Children with idiopathic IN are less likely to develop strabismus, whereas those with congenital retinal dystrophies or albinism are at intermediate risk, and those with bilateral optic nerve hypoplasia are at particularly high risk. **(Self et al, 2020)**

Complete ocular examination is performed with the best age-appropriate equipment available. Slit-lamp examination should be done looking for ocular signs commonly associated with nystagmus including; size of cornea (e.g. microcornea associated with coloboma), anterior segment dysgenesis, aniridia, iris transillumination seen in albinism, cataract, aphakia (congenital/acquired). **(Khanna and Dell'Osso, 2006)**

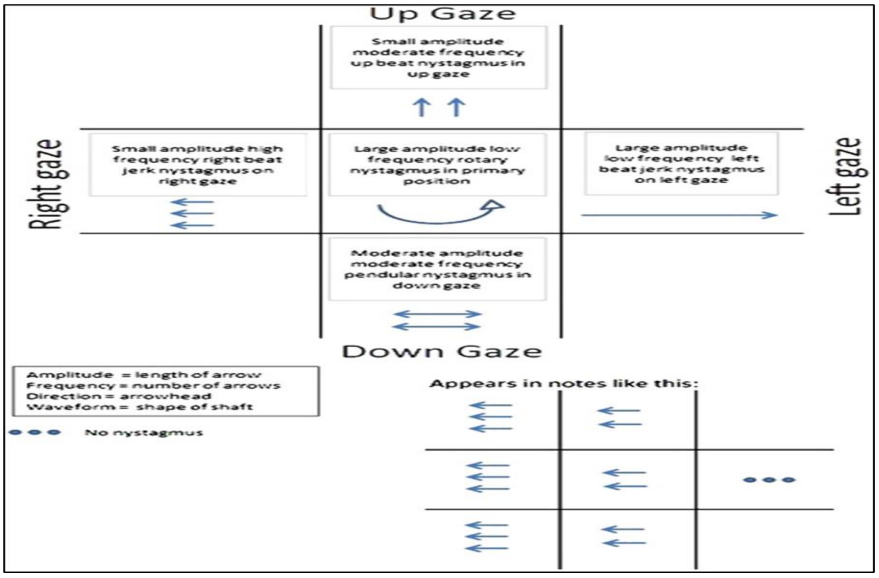
On funduscopy, special attention should be given to optic disc morphology (e.g., optic nerve hypoplasia or coloboma), signs of foveal hypoplasia (e.g., albinism or aniridia), retinal abnormalities (e.g., Leber congenital amaurosis or achromatopsia), and fundus hypopigmentation (e.g., albinism) or atrophy from congenital infection. **(Bertsch et al, 2017)**

On clinical examination, the eyes should be observed in five positions of gaze (primary, right, left, up and down) noting the nystagmus waveform (pendular or jerk), frequency (how fast), amplitude (how big), direction and plane of oscillation. Presence or absence of a null zone should be noted and recorded. **(Hertle, 2008)**

Cover- uncover test should also be done to check for latent nystagmus which is relatively common either alone or in conjunction with IN. Cover test is best performed with a +4 D to +10 D lens as an occluder to fog the vision. Occlusion with an opaque object has an undesirable effect of increasing nystagmus intensity. **(Richards and Wong, 2015)**

Typically, idiopathic infantile nystagmus (IIN) is horizontal and remains so in elevation and depression. The nystagmus often has a null region and increases in intensity, becoming jerkier farther from the null. IIN is characterized by being worse by visual attention and stress. **(Cham et al., 2021)**

Videos of head postures and nystagmus can be extremely useful in evaluation and recording. Documenting nystagmus can be achieved in a variety of ways one of them is the diagrammatic representations **(Osborne et al, 2019)**



(Fig. 2) Diagram showing recording of nystagmus amplitude, frequency, direction and waveform in 9 positions of gaze. **(Osborne et al, 2019)**

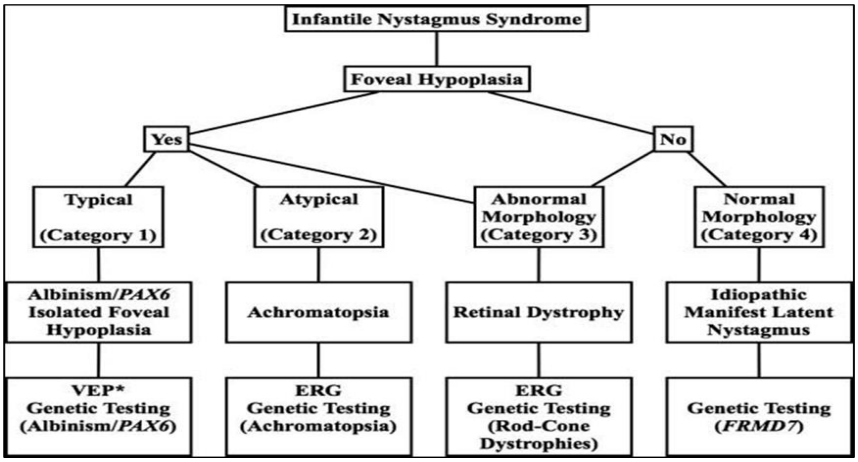
Visual electrodiagnostics are used to assess the function of the afferent visual pathway from retina to cortex. Retinal function is assessed using the electroretinogram (ERG) and the visual pathway using visual evoked potentials (VEP). They are non-invasive objective tests not requiring anesthesia, sedation or mydriasis, relatively quick to perform (30–40 min) with immediate access to results. **(McCulloch et al, 2015)**

For children with IN, in the absence of an obvious cause of vision loss or suggestion of a neurologic cause, an ERG is warranted to rule out retinal dystrophy or degeneration. The diagnostic yield of ERG in such cases is as high as 56%. If ERG returns a normal result, a brain magnetic resonance imaging (MRI) with contrast is recommended because an optic pathway glioma can masquerade as infantile-like nystagmus or spasmus nutans syndrome in rare cases. **(Buncic, 2004; Brodsky and Keating, 2014)**

In contrast, children who have a significant perinatal history suggestive of a neurologic cause, a brain MRI should be performed to rule out cortical visual impairment (CVI) e.g., periventricular leukomalacia, hypoxic ischemic encephalopathy, traumatic brain injury, infections or metabolic diseases. If the brain MRI is normal, then an ERG should be ordered. If ocular or oculocutaneous albinism is suspected, genetic testing may be offered, and a multi channel VEP that demonstrates chiasmal misrouting is sometimes helpful to support the diagnosis. **(Soong et al, 2000)**

The term idiopathic infantile nystagmus (IIN) has been used to describe infantile nystagmus where no disease has been found in the brain or retina. However, this terminology may become redundant as recent high-resolution imaging of the retina using optical coherence tomography (OCT) has shown that retinal deficits indeed exist in individuals with IIN including foveal thickening, thinning of the retinal nerve fiber layer and shortened cone outer segments. **(Lee et al, 2013)**

By identifying the presence or absence of typical or atypical foveal hypoplasia and the presence of other abnormal morphological features, it is possible to divide IN into four diagnostic categories: (1) typical foveal hypoplasia; (2) atypical foveal hypoplasia; (3) abnormal foveal morphology; and (4) normal foveal morphology Furthermore, the severity of foveal hypoplasia can be graded and this can potentially be used as a visual prognostic indicator. **(Thomas et al, 2011)**



(Fig. 3) Diagnostic use of OCT in IN. An algorithm adapted from 'potential of hand-held optical coherence tomography to determine cause of INS in children by using foveal morphology'. **(Lee et al, 2013)**

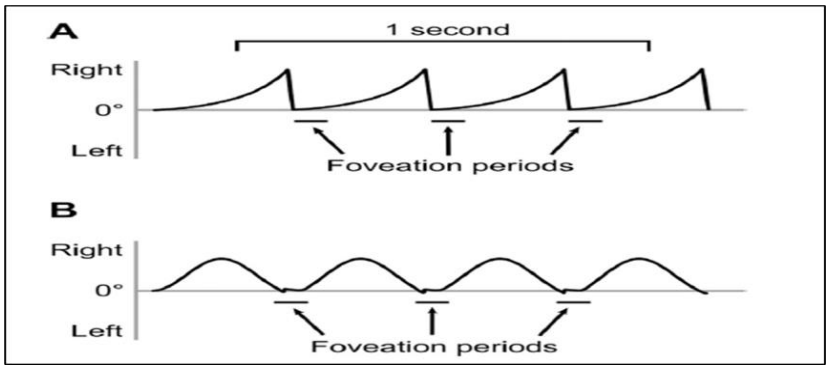
Normal foveal structural features detectable using optical coherence tomography	Illustration
(a) Extrusion of plexiform layers (b) Foveal pit (c) OS lengthening (d) ONL widening	RNFL, GCL, IPL, INL, OPL, ONL, ELM, IS/OS, RPE; (b), (a), (d), (c)

Grade of foveal hypoplasia	Structural features detected on optical coherence tomography	Present or absent	Illustration
1	(a) Extrusion of plexiform layers (b) Foveal pit – Shallow (c) OS lengthening (d) ONL widening	(a) Absent (b) Present (c) Present (d) Present	(b), (d), (c)
2	(a) Extrusion of plexiform layers (b) Foveal pit (c) OS lengthening (d) ONL widening	(a) Absent (b) Absent (c) Present (d) Present	(d), (c)
3	(a) Extrusion of plexiform layers (b) Foveal pit (c) OS lengthening (d) ONL widening	(a) Absent (b) Absent (c) Absent (d) Present	(d)
4	(a) Extrusion of plexiform layers (b) Foveal pit (c) OS lengthening (d) ONL widening	(a) Absent (b) Absent (c) Absent (d) Absent	
Atypical	(a) Extrusion of plexiform layers (b) Foveal pit – Shallow (e) IS/OS disruption	(a) Absent (b) Present (e) Present	(b), (e)

(Fig. 4) Grading foveal hypoplasia. An algorithm for grading foveal hypoplasia on the basis of OCT findings. (**Thomas et al, 2011**)

Eye movement recordings (EMRs) in IN if available, provides a means for objectively visualizing the details of eye movement that are not visible to the naked eye or occur transiently. It can also provide a permanent quantitative record for comparisons to monitor disease progression or remission. On eye movement recordings of IN pendular wave- forms are often punctuated by brief foveation periods, whereas jerk waveforms have highly characteristic increasing velocity slow phases. **(Richards and Wong, 2015)**

Routine screening for FRMD7 gene mutations has a low diagnostic yield and is not recommended as part of the workup for isolated cases of idiopathic INS. It may be considered, however, for patients with a pedigree indicating X-linked inheritance. **(Self et al, 2007)**



(Fig. 5) Schematic diagram of typical infantile nystagmus syndrome (INS) nystagmus waveforms. (A) Jerk-type INS exhibits an increasing velocity slow phase followed by a saccade in the opposite direction. (B) Pendular-type INS has slow-phase movements only, often interrupted by brief foveation periods. **(Wong, 2008)**

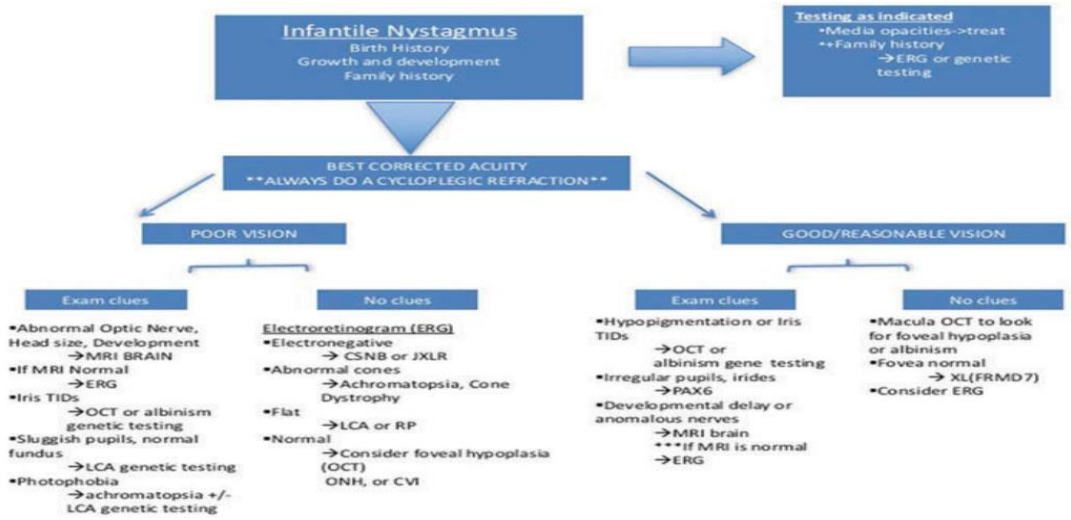
Diagnostic workflow

When seeking a diagnosis for children with nystagmus, it is important to recognize the limitations and inconsistent access to clinical equipment. Some clinical diagnostic tools are freely available (such as anterior and posterior segment examination) and some are scarcer (such as hand-held OCT, EMRs or electrodiagnostics). **(Self et al, 2020)**

Most diagnostic workflows used in practice have the aim of diagnosing for as many children as possible by relying on the most freely available diagnostic tests and seeking the most urgent diagnoses as a priority. In practice, most diagnostic workflows seek to identify which of seven common patient groups children referred with nystagmus fall into as they broadly guide subsequent management or further investigation. **(Papageorgiou and Gottlob, 2021)**

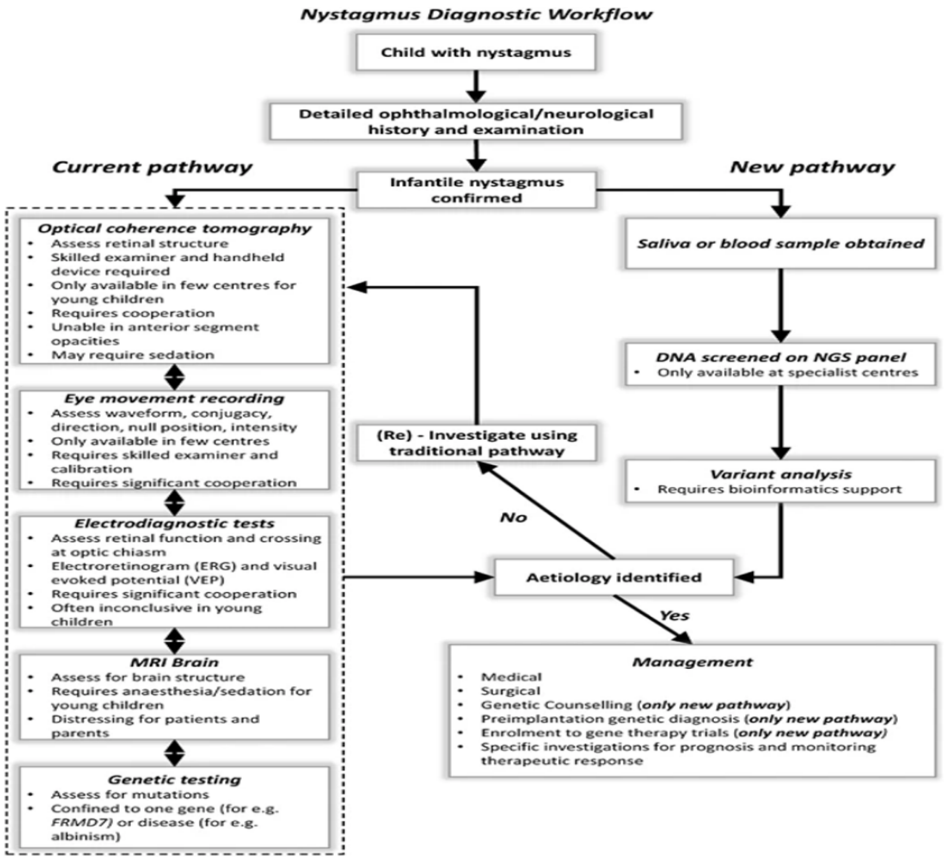
A diagnostic workflow forms the basis of clinical practice It is important to note that workflow mainly focuses on the initial route to diagnosis only, and in many cases, additional tests will be required to support clinical management and to quantify visual pathway lesions and visual prognosis in most cases. **(Bertsch et al, 2017)**

From a different point of view, IN is a genetically heterogenous disorder associated with mutations of genes expressed in the retina and brain. **Thomas et al, 2017** developed a next-generation sequencing (NGS) panel for nystagmus patients, in order to facilitate early diagnosis and enable accurate genetic counseling. This information is a first step toward individualized diagnosis for patients with atypical manifestations of INS and personalized genetic treatment



(Fig. 6) Flow chart algorithm for the workup of infantile nystagmus. **(Bertsch et al, 2017)**

[**Key: MRI**, magnetic resonance imaging; **TIDs**, transillumination defects; **OCT**, optical coherence tomography; **LCA**, Leber congenital amaurosis; **ONH**, optic nerve hypoplasia; **CVI**, cortical vision impairment; **CSNB**, congenital stationary night blindness; **JXLR**, juvenile X-linked retinoschisis; **Abnl**, abnormal; **achroma**, achromatopsia; **RP**, retinitis pigmentosa; **PAX6**, PAX6 gene, responsible for aniridia and related syndromes; **FRMD7,** FRMD7 gene, an X-linked gene associated with IIN].



(Fig. 7) Diagnostic workflow for patients with nystagmus. **(Thomas et al, 2017)**

Management of Infantile Nystagmus

The treatment of infantile nystagmus (IN) has 3 broad components; management of underlying systemic disease, treatment of associated ocular disease and symptomatic therapy for nystagmus. Underlying systemic disease such as albinism may require consultation with pediatric services. For heritable systemic and ocular conditions, referral for genetic counseling should be considered. **(Richards and Wong, 2015)**

Even in the absence of an identifiable cause, management should begin with correction of all significant refractive errors and therapy for amblyopia as needed. Although patching may elicit a latent component, this effect usually subsides with 48 hours of continuous occlusion. Patching or atropine penalization is still recommended for patients with amblyopia and IN. **(Scaramuzzi et al, 2020)**

Asymptomatic benign forms of early-onset nystagmus do not require specific treatment beyond that outlined earlier. Reassuringly, idiopathic IN and secondary IN with good visual acuity become much less obvious as the child becomes older. Further symptomatic treatment is considered in patients who demonstrate abnormal head posture or reduced visual acuity related to unstable fixation. These issues may be addressed through optical, pharmacologic, and surgical means. **(Papageorgiou et al, 2014)**

Non-surgical management of nystagmus

(A) Optical methods

1. **Glasses:**

Effort should be made to correct any underlying refractive error which will decrease the nystagmus. Retinoscopy may be difficult to perform accurately when the nystagmus amplitude is large and should be performed with the eyes in the null zone if such is present. **(Rucker, 2005)**

2. **Contact lenses:**

Contact lenses (CL) have been reported to have reduced amplitude and frequency and are helpful in high ammetropias to reduce prismatic effects of glasses. It has the optical advantage of moving synchronously with the eyes so that the visual axis coincides with the optical center of the lens at all times and shows improvement in visual acuity. There is a theory that contact lenses additionally damp nystagmus via a presumed trigeminal afferent tactile feedback mechanism. **(Biousse et al, 2004)**

3. **Over minus lenses:**

Adding concave glasses to distant correction accompanied with secondary convergence. This induced convergence diminishes amplitude and rate of nystagmus thus enhancing vision. Overcorrection with minus lenses stimulates accommodative convergence and may improve visual acuity at distance fixation by nystagmus dampening. **(Jenkins, 2017)**

1. **Prisms:**

Prisms are used for two purposes in the treatment of nystagmus: (1) to improve visual acuity and (2) to eliminate an anomalous head posture. In patients whose nystagmus is suppressed by viewing a near target, Optical Base-out prisms (7PD) may be combined with slight myopic overcorrection(–1.00 D) to exploit convergence damping in patients with intact binocular vision and thus improving visual acuity. Congenital nystagmus responds well to it. **(Khanna and Dell'Osso, 2006)**

Some patients with acquired nystagmus and in patients whose nystagmus is worse during near viewing, base-in prisms may help inducing divergence. Prisms with base opposite to preferred direction of gaze can be prescribed to correct a small amount of face turn. For example, in a patient with left head turn, the null zone is in dextroversion and a prism base-in before the right eye and base-out before the left eye will be helpful in correcting the AHP. **(Serra et al, 2006)**

The prisms are also inserted with the base opposite the preferred direction of gaze for preoperative evaluation for correction of the head turn. Thus, the results of surgery for head turn in nystagmus can be reasonably well predicted on the basis of the patient's response to prisms, and a postoperative residual head turn may be alleviated further with prisms. **(Kavitha, 2015)**

2. **Optically coupled device:**

Rushton and Cox, 1987 described an optical system that stabilizes retinal images This system consists of a high-positive-power spectacle lens (+32D) combined with a high-negative-power contact lens (-58D). The system rests on the principle that stabilization of images on the retina is achieved if the spectacle lens focuses the primary image close to the center of rotation of the eye. Such images however, are defocused, and a contact lens is required to extend back the focus onto the retina. This system achieves up to 90% stabilization of retinal images. But, it is only useful while the patient is stationary and views monocularly with limited visual field. **(Kavitha, 2015)**

(B) Electrical devices

Use of electronic devices has been advocated and is most useful in patients with pendular nystagmus. Eye movements are measured with an infrared sensor and fed to a phase-locked loop that generate a signal similar to the nystagmus but is insensitive to other eye movements, such as saccades. This electronic signal is then used to rotate Risley prisms, through which the patient views the world. When the Risley prisms rotate in synchrony with the patient's nystagmus, they nullify the visual effects of the ocular oscillations. **(Smith et al, 2004)**

Another biofeedback based device depends on that electrical stimulation or vibration over the forehead or neck may suppress congenital nystagmus, possibly by an action on the trigeminal system, which receives extra ocular proprioception. **(Thurtell and Leigh, 2010)**

(C) Acupuncture

Acupunture by insertion of needles into the sternocleidomastoid muscle has been shown to improve foveation characteristics in congenital nystagmus on a temporary basis. **(Blechschmidt et al, 2017)**

(D) Botulinum toxin

Botulinum toxin is a neurotoxin protein produced by the bacterium *Clostridium botulinum*. Injection of highly diluted doses of botulinum toxin into affected muscles temporarily prevents the release of acetylcholine from synaptic nerve terminals, blocking neuromuscular transmission, resulting in reduction in muscle activity without significant functional weakness. The length of time for which the paralysis lasts depends on the individual, but it usually lasts for 2-6 months, before it wears off. **(Nigam and Nigam 2010)**

Botulinum toxin has shown some effectiveness in the treatment of oscillopsia secondary to acquired nystagmus. The concept is that injection of botulinum toxin into either the extraocular muscles or the retrobulbar space will reduce the motility of all of the extraocular muscles and thus damp the nystagmus and improve vision in some patients. Studies of botulinum treatment for nystagmus are small retrospective case series, with a typical dosage of 20–30 units per eye. **(Wan et al, 2019)**

Limitations of this approach are the short action period (2–6 months), ptosis and diplopia, which may be more annoying to patients than visual symptoms due to the nystagmus. In some patients, the nystagmus may become worse in the non-injected eye. This is because botulinum toxin weakens all types of eye movement, not just the nystagmus. This paresis stimulates the brain to increase innervation that may worsen the nystagmus in the non-injected eye. **(Hobson and Rowe, 2009)**

(E) Drugs

The aim of pharmacologic treatment is to dampen the nystagmus and thereby improve visual symptoms without adversely affecting normal eye movements. However, drugs are not preferred because of their side effects and the need for prolonged treatment. The choice of pharmacologic agent depends on the nystagmus type. For IN, the pharmacologic agents can be used are; Gabapentin (300–600 mg, qid), Memantine (10 mg, qid), Acetazolamide (250–1000 mg, bid) or Brinzolamide 1% eye drops (1 drop, bid). **(Thurtell and Leigh, 2012)**

For idiopathic IN, oral and topical carbonic anhydrase inhibitors showed some promising results. **Thurtell et al, 2010** reported that Acetazolamide resulted in improved-foveation of IN waveforms over a broadened range of gaze angles, probably acting at more than one site. **Hertle et al, 2015**, a prospective cross over study of topical brinzolamide, showed improved wave form characteristics, but only a 0.12 log-MAR improvement in visual acuity.

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References:

1. Abadi RV and Bjerre A. Motor and sensory characteristics of infantile nystagmus. British Journal of Ophthalmology. 2002; 86:1152-1160
2. Abadi RV, Forster JE and Lloyd IC. Ocular motor outcomes after bilateral and unilateral infantile cataracts. Vision research. 2006; 46: 940-952.
3. Abadi RV. Mechanisms underlying nystagmus. Journal of the Royal Society of Medicine. 2002; 95: 231-234.
4. Abel LA. Infantile nystagmus: Current concepts in diagnosis and management. Clinical & Experimental Optometry. 2006;89:57-65

5. Bertsch M, Floyd M, Kehoe T, et al. The clinical evaluation of infantile nystagmus: What to do first and why. Ophthalmic genetics. 2017; 38: 22-33.
6. Biousse V, Tusa R, Russell B, et al. The use of contact lenses to treat visually symptomatic congenital nystagmus. J Neurol Neurosurg Psychiatry. 2004; 75:314-316.
7. Blechschmidt T, Krumsiek M and Todorova MG. The effect of acupuncture on visual function in patients with congenital and acquired nystagmus. Medicines. 2017; 4: 33.
8. Bohnsack BL, Gallina D, Thompson H, et al. Development of extraocular muscles requires early signals from periocular neural crest and the developing eye. Archives of ophthalmology .2011; 129:1030-1041.
9. Brodsky MC and Keating GF. Chiasmal glioma in spasmus nutans: a cautionary note. J Neuro ophthalmol. 2014; 34:274-275.
10. Brodsky MC. Nystagmus in Children. In: Pediatric Neuro-Ophthalmology. 2016 (pp. 383-595).Springer, New York, NY.
11. Bulling A and Gellersen H. Toward mobile eye-based human-computer interaction. IEEE Pervasive Computing. 2010;9: 8-12.
12. Buncic JR. A clinician's approach to infantile nystagmus. Am Orthop J. 2004; 54:88-94.
13. Cham KM, Abel LA, Busija L, et al. Surgical interventions for infantile nystagmus syndrome. Cochrane Database of Systematic Reviews, (2).2021 .
14. Chopin A, Chan SW, Guellai B, et al. Binocular non-stereoscopic cues can deceive clinical tests of stereopsis. Scientific reports. 2019; 9:1-10.
15. Choudhuri I., Sarvananthan, N. and Gottlob, I. Survey of management of acquired nystagmus in the United Kingdom. Eye. 2007; 21: 1194-1197.
16. Clark RA and Demer JL. Functional morphometry of horizontal rectus extraocular muscles during horizontal ocular duction. Invest Ophthalmol Vis Sci. 2012; 53:7375–7379.
17. Clark RA and Demer JL. Magnetic resonance imaging of the effects of horizontal rectus extraocular muscle surgery on pulley and globe positions and stability. Investigative ophthalmology & visual science. 2006; 47:188-194.
18. Clark RA. The role of extraocular muscle pulleys in incomitant non-paralytic strabismus. Middle East African journal of ophthalmology. 2015; 22:279.
19. Dell'Osso LF, Orge FH, Jacobs JB, et al. Fusion maldevelopment (latent/manifest latent) nystagmus syndrome: effects of four-muscle tenotomy and reattachment. Journal of Pediatric Ophthalmology & Strabismus. 2014; 51:180-188.
20. Demer JL, Oh SY, Clark RA, et al. Evidence for a pulley of the inferior oblique muscle. Investigative ophthalmology & visual science. 2003; 44:3856-3865.
21. Demer JL, Sei YO and Vadims P. "Evidence for active control of rectus extraocular muscle pulleys." Investigative Ophthalmology & Visual Science .2000; 41: 1280-1290.
22. Demer JL. Compartmentalization of extraocular muscle function. Eye. 2015; 29:157-162.
23. Eggers SD. Practical anatomy and physiology of the ocular motor system. Balance function assessment and management. 2016; 2: 17-46.
24. Ehrt O. Infantile and acquired nystagmus in childhood. European Journal of Paediatric Neurology. 2012; 16: 567-572.

25. Erkelens CJ. Coordination of smooth pursuit and saccades. Vision Research. 2006; 46: 163-170.
26. Forrester JV, Dick AD, Mc Menamin PG, et al. The Eye: Basic Sciences in Practice. 4th ed. Edinburgh: Elsevier; 2016:104–105.
27. Fu VL, Bilonick RA, Felius J, et al. Visual acuity development of children with infantile nystagmus syndrome. Investigative Ophthalmology & Visual Science. 2011; 52: 1404-1411.
28. Ghannam ASB and Yassine S. Pediatric nystagmus. International Ophthalmology Clinics. 2018; 58: 23-65.
29. Göçmen ES, Atalay Y, Kemer ÖE, et al. Anterior Segment Ischemia after Strabismus Surgery. Turkish journal of ophthalmology.2017; 47: 47-51.
30. Goldberg JH and Wichansky AM. Eye tracking in usability evaluation: A practitioner's guide. In the Mind's Eye.2003. (pp. 493-516). North-Holland.
31. Gottlob I and Proudlock FA. Aetiology of infantile nystagmus. Current opinion in neurology. 2014; 27: 83-91.
32. Gottlob I. Nystagmus. Curr Opin Ophthalmol. 2001; 12: 378-383.
33. Grønskov K, Ek J and Brondum-Nielsen K. Oculocutaneous albinism. Orphanet journal of rare diseases. 2007; 2: 1-8.
34. Guo H, Gao Z and Chen W. The biomechanical significance of pulley on binocular vision. Biomedical engineering online. 2016; 15:137.
35. Haładaj R. Normal anatomy and anomalies of the rectus extraocular muscles in human: a review of the recent data and findings. BioMed Research International. 2019; 2019.
36. Hayreh SS. Orbital vascular anatomy. Eye. 2006; 20: 1130–1144.
37. Hertle RW, Bedell HE, Dell'Osso LF, et al. A classification of eye movement abnormalities and strabismus (CEMAS). In Report of a National Eye Institute Sponsored Workshop from the committee for the Classification of Eye Movement Abnormalities and Strabismus (CEMAS) Workshop.2001:1-56.
38. Hertle RW, Felius J, Yang D, et al. Eye muscle surgery for infantile nystagmus syndrome in the first two years of life. Clinical Ophthalmology. 2009; 3:615–624.
39. Hertle RW, Yang D, Adkinson T, et al. Topical brinzolamide (Azopt) versus placebo in the treatment of infantile nystagmus syndrome (INS). British Journal of Ophthalmology. 2015; 99: 471-476.
40. Hertle RW. Nystagmus in infancy and childhood. In Seminars in ophthalmology. Taylor & Francis.23:307-317 ;2008 .
41. Hesgaard HB and Wright KW. Principles of strabismus surgery for common horizontal and vertical strabismus types. Advances in Eye Surgery. 2016; 24:249.
42. Hobson F and Rowe FJ. Management of nystagmus by surgery and botulinum toxin options: a review. British and Irish Orthoptic Journal. 2009; 6: 28–33.
43. Hughes B, Kusner LL and Kaminski HJ. Molecular architecture of the neuromuscular junction. Muscle Nerve. 2006; 33:445–61.
44. Hunfalvay M, Orr R, Murray N, et al. Evaluation of stereo acuity in professional baseball and LPGA athletes compared to non-athletes. Vision Development and Rehabilitation. 2017; 3: 34-42.

45. Hussain N. Diagnosis, assessment and management of nystagmus in childhood. Paediatrics and Child Health. 2016; 26: 31-36.
46. Jain S. Anatomy of the Extraocular Muscles. In Simplifying Strabismus. Springer, Cham; 2019:9-13.
47. Jenkins R. Nonsurgical and Orthoptic Management of Nystagmus. American Orthoptic Journal. 2017; 67:39-42.
48. Johnson MS, Christiansen SP, Rath PP, et al. Anterior ciliary circulation from the horizontal rectus muscles. Strabismus.2009; 17:45-48.
49. Kavitha KN. An approach to Nystagmus management. Sci J Med & Vis Res Foun. 2015; 33:138–140.
50. Khanna S and Dell'Osso LF. The diagnosis and treatment of infantile nystagmus syndrome (INS). The Scientific World Journal. 2006; 6, 1385-1397.
51. King WM. Binocular coordination of eye movements–Hering's Law of equal innervation or uniocular control? European Journal of Neuroscience. 2011; 33:2139-2146.
52. Kono R, Clark RA and Demer JL. Active pulleys: magnetic resonance imaging of rectus muscle paths in tertiary gazes. Investigative Ophthalmology & Visual Science. 2002; 43:2179-2188.
53. Kraft SP. Abnormal head postures: causes and management. In Pediatric Ophthalmology and Strabismus.(4th ed). CA: Elsevier, 2012: 822-836.
54. Kumar A and Saryanarayana A. clinical and ocular motor characterisation of infantile and acquired nystagmus using eye movement recordings. 2015. PhD Thesis. University of Leicester.
55. Kumar A, Shetty S, Vijayalakshmi P, et al. Improvement in visual acuity following surgery for correction of head posture in infantile nystagmus syndrome. J Pediatr Ophthalmol Strabismus. 2011; 48:341–346.
56. Lee H, Sheth V, Bibi M, et al. Potential of handheld optical coherence tomography to determine cause of infantile nystagmus in children by using foveal morphology. Ophthalmology. 2013; 120: 2714-2724.
57. Lee H, Yi HA and Kim HA. Do the paramedian tract neurons in pons take a role as a vertical neural integrator in humans?. Journal of the neurological sciences. 2012; 321: 107-110.
58. Leigh RJ and Khanna S. What can acquired nystagmus tell us about congenital forms of nystagmus?. In Seminars in Ophthalmology. Taylor & Francis. 2006; 21:83-86.
59. Leigh RJ and Zee DS. The neurology of eye movements. 2015. Contemporary Neurology.
60. Lyons CJ and Wiwatwongwana A. The optic nerve and visual pathways. Handbook of Clinical Neurology. 2013; 113:1515-1525.
61. McCulloch DL, Marmor MF, Brigell MG, et al. Erratum to: ISCEV standard for full-field clinical electroretinography. Doc Ophthalmol.2015; 131:81–83.
62. McLean R, Proudlock F, Thomas S, et al. Congenital nystagmus: randomized, controlled, double-masked trial of memantine/gabapentin. Ann Neurol. 2007; 61:130–138.
63. McLean RJ and Gottlob I. The pharmacological treatment of nystagmus: a review. Expert opinion on pharmacotherapy. 2009; 10: 1805-1816.

64. Mravicic I, Lukacevic S, Bohac M, et al. Nystagmus. In Eye Motility. 2019. IntechOpen.
65. Nakamagoe K, Iwamoto Y and Yoshida K. Evidence for brainstem structures participating in oculomotor integration. Science. 2000; 288: 857-859.
66. Nash DL, Diehl NN and Mohney BG. Incidence and Types of Pediatric Nystagmus. Am J Ophthalmol. 2017; 182:31-34.
67. Nigam PK and Nigam A. Botulinum toxin. Indian journal of dermatology. 2010; 55:8.
68. Oetting WS. New insights into ocular albinism type 1 (OA1): Mutations and polymorphisms of the OA1 gene. Human mutation. 2002; 19: 85-92.
69. Osborne D, Theodorou M, Lee H, et al. Supranuclear eye movements and nystagmus in children: a review of the literature and guide to clinical examination, interpretation of findings and age-appropriate norms. Eye. 2019; 33:261–273.
70. Papageorgiou E and Gottlob I. The challenges faced by clinicians diagnosing and treating infantile nystagmus Part I: diagnosis. Expert Review of Ophthalmology. 2021; 16: 97-112.
71. Papageorgiou E, McLean RJ and Gottlob I. Nystagmus in childhood. Pediatrics & Neonatology. 2014; 55: 341-351.
72. Pavone P, Cho SY, Praticò AD, et al. Ptosis in childhood: A clinical sign of several disorders: Case series reports and literature review. Medicine. 2018; 97.
73. Pilling RF, Thompson JR and Gottlob I. Social and visual function in nystagmus. British Journal of Ophthalmology. 2005; 89:1278-1281.
74. Proudlock FA and Gottlob I. Nystagmus. In: editors, Taylor D, Hoyt CS. Paediatric ophthalmology and strabismus. 4th ed. Kidlington, UK: Elsevier B.V.; 2011: 909-923.
75. Pu J, Lu X, Zhao G, et al. FERM domain containing protein 7 (FRMD7) upregulates the expression of neuronal cytoskeletal proteins and promotes neurite outgrowth in Neuro-2a cells. Mol Vis. 2012; 18:1428–1435.
76. Pu J, Mao Y, Lei X, et al. FERM domain containing protein 7 interacts with the Rho GDP dissociation inhibitor and specifically activates Rac1 signaling. PloS One. 2013; 8:e73108.
77. Raza SM, Quiñones-Hinojosa A and Subramanian PS. Multimodal Treatment of Orbital Tumors. In Schmidek and Sweet Operative Neurosurgical Techniques: Indications, Methods, and Results. 6th ed. Elsevier; 2012:597-602.
78. Richards MD and Wong A. Infantile nystagmus syndrome: clinical characteristics, current theories of pathogenesis, diagnosis, and management. Canadian Journal of Ophthalmology. 2015; 50, 400-408.
79. Rucker JC and Lavin PJ. Neuro-ophthalmology: ocular motor system. Bradley's Neurology in Clinical Practice E-Book. 2021; 201.
80. Rucker JC. Current treatment of nystagmus. Current treatment options in neurology. 2005; 7:69-77.
81. Rushton D and Cox N. A new optical treatment for oscillopsia. J Neurol Neurosurg Psychiatry. 1987; 50: 411-415.
82. Salati R, Borgatti R, Giammari G, et al. Oculomotor dysfunction in cerebral visual impairment following perinatal hypoxia. Developmental medicine and child neurology. 2002; 44:542-550.

83. Salmon JF. Kanski's clinical ophthalmology: a systematic approach 9th ed. Elsevier, 2020.
84. Sarvananthan N, Surendran M, Roberts EO, et al. The prevalence of nystagmus: the Leicestershire nystagmus survey. Invest Ophthalmol Vis Sci. 2009; 50:5201-5206.
85. Scaramuzzi M, Murray J, Otero-Millan J, et al. Part time patching treatment outcomes in children with amblyopia with and without fusion maldevelopment nystagmus: An eye movement study. PLoS One. 2020; 15:e0237346.
86. Schlindwein P, Schreckenberger M and Dieterich M. Visual-Motion Suppression in Congenital Pendular Nystagmus. Annals of the New York Academy of Sciences. 2009; 1164: 458-460.
87. Self JE, Dunn MJ, Erichsen JT, et al. Management of nystagmus in children: a review of the literature and current practice in UK specialist services. Eye.2020; 34: 1515–1534.
88. Self JE, Shawkat F, Malpas CT, et al. Allelic variation of the FRMD7 gene in congenital idiopathic nystagmus. Arch Ophthalmol. 2007; 125:1255-63.
89. Serra A, Dell'Osso LF, Jacobs JB, et al. Combined gaze-angle and vergence variation in infantile nystagmus: two therapies that improve the high-visual-acuity field and methods to measure it. Invest Ophthalmol Vis Sci. 2006; 47:2451–2460.
90. Skalicky SE. The Extraocular Muscles. In: Ocular and Visual Physiology.2016. Springer, Singapore.
91. Smith RM, Oommen BS and Stahl JS. Image-shifting optics for a nystagmus treatment device. J Rehabil Res Dev. 2004; 41:325-336.
92. Soong F, Levin AV and Westall CA. Comparison of techniques for detecting visually evoked potential asymmetry in albinism. J AAPOS. 2000; 4:302-310.
93. Sprenger A, Neppert B, Köster S, et al. Long-term eye movement recordings with a scleral search coil-eyelid protection device allows new applications. Journal of neuroscience methods. 2008; 170: 305-309.
94. Straube A, Leigh RJ, Bronstein A, et al. EFNS task force–therapy of nystagmus and oscillopsia. European Journal of Neurology. 2004; 11: 83-89.
95. Tarpey P, Thomas S, Sarvananthan N, et al. Mutations in FRMD7, a newly identified member of the FERM family, cause X-linked idiopathic congenital nystagmus. Nature genetics. 2006; 38: 1242-1244.
96. Thomas M, Maconachie G, Sheth V. et al. Development and clinical utility of a novel diagnostic nystagmus gene panel using targeted next-generation sequencing. Eur J Hum Genet. 2017; 25: 725–734.
97. Thomas MG, Crosier M, Lindsay S, et al. The clinical and molecular genetic features of idiopathic infantile periodic alternating nystagmus. Brain. 2011; 134: 892-902.
98. Thurtell M, Kunin M and Raphan T. Role of Muscle Pulleys in Producing Eye Position-Dependence in the Angular Vestibuloocular Reflex: A Model-Based Study. Journal of neurophysiology. 2000; 84: 639-650.
99. Thurtell MJ and Leigh RJ. Therapy for nystagmus. Journal of Neuro-Ophthalmology. 2010; 30:361-371
100. Thurtell MJ and Leigh RJ. Treatment of nystagmus. Current treatment options in neurology. 2012; 14: 60-72.

101. Thurtell MJ, Dell'osso LF, Leigh RJ, et al. Effects of acetazolamide on infantile nystagmus syndrome waveforms: comparisons to contact lenses and convergence in a well-studied subject. Open Ophthalmol J. 2010; 4:42-51.
102. Tibrewal S and Kekunnaya R. Risk of Anterior Segment Ischemia Following Simultaneous Three Rectus Muscle Surgery: Results from a Single Tertiary Care Centre. Strabismus. 2018; 26:77-83.
103. Van Der Geest JN & Frens MA. Recording eye movements with video-oculography and scleral search coils: a direct comparison of two methods. Journal of neuroscience methods. 2002; 114:185-195.
104. Wan MJ, Al-Shaker S& Hunter DG. Use of Botulinum Toxin in Ophthalmology. In: Whitcup, S.M., Hallett, M. (eds) Botulinum Toxin Therapy. Handbook of Experimental Pharmacology. Springer, Cham. 2019;263:147-160
105. Wasicky R, Ziya-Ghazvini F, Blumer R, et al. Muscle fiber types of human extraocular muscles: a histochemical and immunohistochemical study. Invest Ophthalmol Vis Sci. 2000; 41:980–90.
106. Watkins RJ, Patil R, Goult BT, et al. A novel interaction between FRMD7 and CASK: evidence for a causal role in idiopathic infantile nystagmus. Hum Mol Genet. 2013; 22:2105–2118.
107. Wilkinson MJ. Anatomy of the human orbit. Operative Techniques in Otolaryngology-Head and Neck Surgery. 2018; 29: 186-192.
108. Wizov SS. A comparative demographic and socioeconomic study of spasmus nutans and infantile nystagmus American Journal Of Ophthalmology. 2002; 133:869
109. Wong AM. Eye Movement Disorders. New York: Oxford University Press; 2008.
110. Wright KW. Exotropia. In Pediatric ophthalmology and strabismus.2006 (pp. 224-231). Springer, New York, NY.