Inheritance
X-linked, autosomal dominant & recessive pattern of inheritance has been linked with nystagmus. But X-linked is most common.¹

A survey of patients registered with CNIB (Canadian National Institute for Blind) as blind from infantile nystagmus syndrome, revealed that abnormal single gene was responsible for disorder in 33 patients, 15 caused by autosomal recessive & 15 by X-lined inheritance. In 3 cases, pedigrees were consistent with both autosomal recessive & X-linked inheritance.

Albinism, optic nerve hypoplasia, achromatopsia & Leber’s congenital amaurosis are some groups of disorders which are most frequently detected.²

Many systemic syndromes & genetic disorders, e.g. Downs syndrome associated with both infantile & acquired types of nystagmus.³

Etiopathogenesis
The theoretical neuronal mechanism of nystagmus continues to evolve and single unifying explanation is still lacking.

However, 3 major supranuclear inputs to oculomotor system are clearly important in stabilising eye movements and their dysfunction may lead to nystagmus:
1. Pursuit system
2. Vestibular system
3. Neural integrator

Pursuit system provides major inputs for fixation stability⁴. The outputs of right & left vestibular apparatus are neural discharges, each of which tends to drive eyes contralaterally. Normally right and left outputs cancel each other. Head rotation & unilateral vestibular damage alter this balance (right vestibular damage causes eye to be drifted to right & corrective saccade in left direction).

Distinguishing feature of vestibular nystagmus is that, slow phase is towards affected side with constant velocity as recorded by electronystagmography. Mostly acquired nystagmus is due to disease of vestibular system (central / peripheral).⁵

Neural integrator is theoretical neuronal system which changes resting firing rate to extraocular movements to:
1. Overcome viscoelastic forces of orbit.
2. Maintain position of eccentric gaze.

Though exact location of neural integrator is not known, much of its function resides in the nucleus prepositus hypoglossi (NPH) located just caudal to abducens nucleus.⁶

Postulated dysfunctions of neural integrator system:
1. Integrator leak
2. High gain instability

Pathophysiology of latent / manifest – latent nystagmus is different from & less well understood than infantile nystagmus.⁶ Since it is commonly associated with infantile esotropia syndrome, cause is related to documented persistence of nasotemporal motion processing asymmetry which is also characteristic of this syndrome.⁷

Classification
I. CEMAS (Classification of eye movement abnormalities & strabismus) classification of nystagmus types⁸
• Peripheral vestibular imbalance: Meniere's disease, drug toxicity
• Central vestibular imbalance: Downbeat, upbeat, drug toxicity
• Instability of vestibular mechanisms: Periodic alternating nystagmus
• Disorders of visual fixation: See –saw nystagmus, drug toxicity
• Disorders of gaze holding: Gaze evoked, acquired pendular, drug toxicity
• Acquired pendular nystagmus: Central myelin, oculo-palatal, Whipple’s disease
• Infantile nystagmus syndrome: Congenital, motor, sensory, idiopathic, nystagmus blockage.
• Fusion maldevelopment nystagmus syndrome: old “latent, manifest latent”, nystagmus blockage.
• Spasmus nutans syndrome: with / without optic pathway glioma.
• Saccadic intrusions & Oscillations: Square wave jerks, opsoclonus, flutters, macro-saccadic oscillations.
• Miscellaneous eye movements: superior oblique myokymia, ocular motor neuromyotonia.

Sensory & motor nystagmus – is the classification still valid?
Cogan has classified congenital nystagmus into sensory & motor defect nystagmus9.

The primary cause of sensory type is inadequate image formation on the fovea as a result of anterior visual pathway disease, which causes disturbance of the feedback from the fovea that interferes with the oculomotor control of the fixation mechanism. It is always bilateral, horizontal & often is of pendular type; in which eye oscillates with equal velocity in both directions, with jerky character in extreme position. Differentiation of congenital nystagmus into pendular & jerky, as proposed by Cogan, is no longer recommended.10

Motor defect nystagmus is a form of congenital nystagmus in which primary defect is in the efferent mechanisms, possibly involving the centres or pathways for conjugate oculomotor control. No ocular abnormalities are present, the amplitude & frequency may decrease or nystagmus may disappear completely in one position of gaze & visual acuity then may improve. This may cause the patient to assume an anomalous head posture to improve visual acuity with the eyes in the position of least nystagmus (null point11 / neutral zone12/privileged area13).

Cogan’s original classification of sensory & motor has been challenged by many neurologists.14
The suggestion that anomaly in the visual system in a patient with congenital nystagmus establishes a causal relationship has been disputed since both the visual disturbance & nystagmus may be present independent of each other15. Although it is true that a causal relationship cannot be established in each case, there are numerous instances, in which such a relationship seems to be overwhelmingly evident, e.g. nystagmus is frequently associated with congenital cataracts & may develop within months after the onset of congenital cataracts in a patient who previously had no nystagmus16 or it may disappear after cataract surgery followed by contact lens correction17. It can also go into remission in children with congenital aniridia after they are fitted with pinhole contact lens18,19,20.

It is difficult to deny a cause & effect relationship between the visual disturbance & nystagmus in these instances as well as in patients with motor nystagmus whose visual acuity often is clearly dependent on changes in intensity of nystagmus whose visual acuity often is clearly dependent on changes in intensity of nystagmus in different positions of gaze & may improve dramatically when nystagmus is dampened by convergence. Thus, from clinical point of view, the differentiation into sensory & motor types continues to be useful. As the study includes only patients with infantile nystagmus, we restrict further discussion only a CEMAS subtypes21,22,23.

Common types of nystagmus with onset in infancy
1. Infantile nystagmus syndrome / congenital motor:
   • Binocular, usually uniplannar, similar amplitude in both eyes, conjugate, symmetrical, jerk / pendular.
• Visual acuity is reduced in all with deficient accommodation in most of the cases, but is usually better than 6/18\textsuperscript{24}.
• Null zone is often present & the head posture is assumed to bring the eyes in null zone. The direction of the fast component characteristically reverses across the null zone.
• Same amplitude & frequency regardless of whether both eyes are open or one eye is closed.
• Worsen with increased fixation & anxiety.
• Improves with convergence, fatigue, sleep, increased fusion and extra ocular muscle surgery & contact lenses\textsuperscript{8}.
• No oscillopsia\textsuperscript{9}.
• Ocular motor recordings show diagnostic (accelerating) slow phases.
• Visual sensory defects may be associated with it. E.g. albinism, achromatopsia, congenital cataract.
• Alexander’s law: the amplitude of nystagmus increases when eye moves in the direction of fast phase (saccade).
• Pure pendular / jerk without foveation periods suggest poor prognosis.
• Inversion of optokinetic nystagmus i.e. on eliciting optokinetic nystagmus response the direction of fast component is same as that of drum & amplitude accentuated.
• Exact aetiology not known, proposed defects involving saccadic, optokinetic, smooth pursuit, fixation system & neural integrator for conjugate horizontal gaze.
• Hence final common pathway being interference with ocular motor calibration, during period of sensitivity, at which time changes cause irreversible damage.

2. Latent / Manifest – latent (Fusion Maldevelopment)
• Latent elicited only on covering dominating eye.
• Manifest which accentuates on covering dominating eye is manifest – latent.

3. Spasmus Nutans
• 3rd most common, beginning in infancy.
• Classic triad is characteristic\textsuperscript{26}.
  - High frequency, small amplitude, dysconjugate oscillations
  - Head nodding oscillations
  - Head tilt
• Less noticeable with age, very fine, rapid, pendular, asymmetric.
• Head nodding improves vision & decrease nystagmus.
• Worse in abduction, associated with amblyopia of more involved eye\textsuperscript{27}.
• May be completely benign with onset in infancy, but imaging is required if it is after 3 years, as intracranial tumour is suspected.

4. Nystagmus Blockage Syndrome
• Esotropia is a mechanism of blocking nystagmus, due to sustained convergence\textsuperscript{28}.
• On abduction amplitude increases.
• Fixing eye is preferred in adduction, so face turn is in direction of fixing eye.
Other important sub types – acquired / congenital
5. Periodic Alternating Nystagmus
- Manifests with fast phase in one direction for 90 – 120 sec, then a pause for 10- 20 sec, switches its direction to opposite side for 90 - 120 sec, which again reverses.
- With alteration, face turn also keeps altering.
- Hence abnormal head posture, direction, frequency keep on changing.
- Seen in albinism, vestibulocerebellar lesions, Friedreich ataxia, chronic otitis.
- Exclude Arnold – Chiari malformation, which also presents with periodic alternating nystagmus.

6. See – Saw
- Special pendular & torsional nystagmus.
- Eye rises & intorts as the fellow eye falls & extorts like see-saw.
- Congenital or secondary to parasellar tumour expanding within third ventricle.
- Causes parasellar lesions.

7. Upbeat
- Jerk with fast component upwards
- Converted to downbeat on convergence.
- Causes : Lesions of cerebellar vermis or medulla, post meningitis, multiple sclerosis, can occur transiently in normal infants.

8. Downbeat
- Jerk with fast component downwards
- Causes: Cervicomedullary junction lesion, alcohol, anticonvulsants.

9. Acquired
- Causes : Toxins, drugs, intracranial diseases (tumour, infarction, inflammation, degeneration).
- Hence detail systemic workup is needed: Neurological examination, imaging, chromosome analysis, pedigree, developmental milestones, electroencephalogram, visual evoked response, electroretinogram & investigations for storage disorders.

Extended nystagmus workup is not required if
1. History: Onset within 4 – 6 months of life, without developmental or genetic diseases or toxin / drug exposure, with family history of infantile nystagmus syndrome.
2. Examination: Normal visual behaviour & structural examination in both eyes with nystagmus pattern characteristic of infantile nystagmus syndrome.
   a. Extended workup required if:
      1. History: onset after 6-9months, with abnormal pregnancy, delivery, development, growth with / without toxin or drug exposure.
      2. Examination: Abnormal vision or structural examination.
      3. General: Abnormal growth & development with central nervous signs

References:


