MANAGEMENT OF NYSTAGMUS
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INTRODUCTION
Nystagmus can present a difficult diagnostic challenge for even the most experienced clinician.
Patients with nystagmus challenge a clinician's skills in differential diagnosis, sensitive communication, and management.

DEFINITION
Nystagmus has been defined as a series of rhythmic involuntary movements of the eyes as a result of some disorder of the visual apparatus or of some neurological or labyrinthine disease.
Nystagmus is considered a disorder in the mechanisms that keep fixation stable.

PREVALENCE
Anderson in 1954 reported an incidence of 0.4% in the general patient population of 34,000, although other reports have found a lower incidence.

LEIGH AND ZEE
The pursuit, optokinetic, & vestibular systems act to maintain a steady image on the retina, and a neural network (the neural integrator) enables us to hold positions of gaze.
These neurologic systems have paired nuclei, and any lesion that creates an imbalance can cause nystagmus by making the eyes drift off target.

INTRODUCTION
To properly manage nystagmus patients, it is necessary to:
● describe the relevant characteristics
● classify the condition
● identify any possible causes and associations
● determine and implement appropriate management

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PREVALENCE

It is much more prevalent in patients who have certain ocular and/or systemic health conditions. For example:
- a large percentage of persons with albinism have nystagmus

ETIOLOGICAL CONSIDERATIONS

The clinician should attempt to describe the condition as either infantile or acquired and determine the general category of etiology, e.g., genetic, traumatic, toxic, metabolic error, developmental, visual deprivation, or a more rare type.

ETIOLOGICAL CONSIDERATIONS

Acquired forms of nystagmus require immediate diagnosis and early management of the underlying condition to reduce long-term consequences of the condition.

GENETICS

Heterogeneity makes etiology even more obscure.
- McKusick reported that isolated nystagmus may have any of 4 Mendelian modes of transmission (autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive).
- He believes that X-linked recessive transmission is the most common.

GENETICS

Autosomal dominant CN has been linked to chromosome 6p12.
- This has variable expressivity in terms of visual acuity, ocular alignment, and nystagmus waveform.
- Familial variability suggests that expression can be modified by environmental influences.

GENETICS

When nystagmus is associated with a disease or syndrome, genetic counseling may be easy.
- Isolated nystagmus presents problems due to heterogeneity.
CEMAS Classifications

1. Peripheral Vestibular Imbalance:
   Meniere, Drug toxicity
2. Central Vestibular Imbalance:
   Downbeat, Upbeat, Drug toxicity
3. Instability of Vestibular Mechanisms:
   Periodic Alternating Nystagmus
4. Disorders of Visual Fixation:
   Vision Loss, See-Saw, Drug toxicity

5. Disorders of Gaze Holding:
   Gaze Evoked, Acquired Pendular, Drug toxicity
6. Acquired Pendular Nystagmus:
   Central myelin, Oculopalatal, Whipple, Drug toxicity
7. Saccadic Intrusions and Oscillations:
   Square Wave Jerks, Macro-saccadic oscillations, opsinclonus, flutter, pulses

8. Miscellaneous Eye Movements:
   Superior Oblique Myokymia, Ocular motor neuromyotonia
9. Infantile Nystagmus Syndrome:
   Congenital, motor, sensory, idiopathic, nystagmus blockage
10. Fusion Maldevelopment Nystagmus Syndrome:
    Old “Latent, manifest latent,” nystagmus blockage
11. Spasmus Nutans Syndrome:
    Without optic pathway glioma, With optic pathway glioma

CASE HISTORY

Onset
Associations
- infections, fever, meds, trauma
Variability
- frequency, amplitude, gaze, time characteristics

Symptoms (developmental and neurological factors)
- Dizziness/nausea
- Headaches
- Local pain/numbness/tingling/weakness
- Seizures
- Tinnitus (peripheral vestibular)
- Gait irregularities
- other recent unusual symptoms

Ocular & General health history
Family history (genetic factors vs. spontaneous gene mutation)
- Go back 3 generations for nystagmus or other visual disorders
- Genetic conditions (e.g., albinism, achromatopsia and Leber’s)
**OBSERVATIONS**

* (Slit lamp, ophthalmoscopy)
  - Global (posture, head position, asymmetry)
  - Type (pendular, jerk, mixed)
  - Direction (H, V, R; fast phase of jerk)
  - Amplitude
    - small < 2°
    - moderate = 2-10°
    - large > 10°
  - Frequency
    - slow < 0.5 Hz, moderate, fast > 2 Hz

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**Nystagmus Waveforms**

Wong, page 94, section 7.1

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**OBSERVATIONS**

- Constancy
  - constant, intermittent, periodic
- Conjugacy
  - conjugate or disjunctive
- Symmetry
  - symmetrical, asymmetrical, monocular

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**Differential Diagnosis:**

**Infantile Nystagmus Syndrome**

- Infantile nystagmus (INS) includes all forms of nystagmus present at birth or noted in early infancy at the time of development of visual fixation
  - INS persists throughout life.
  - Formerly referred to as Congenital Nystagmus (CN)

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**INFANTILE NYSTAGMUS**

- Infantile nystagmus is caused by or associated with many afferent and efferent visual disorders.
- Its wide variation in severity and visual impairment depends upon its etiology.
- It may accompany primary visual defects, which has led to the assumption that the nystagmus was secondary to poor vision.
INFANTILE NYSTAGMUS

- Identifying the probable site of the lesion is desirable but frequently impossible.
- When viewing in a horizontal gaze position, some forms beat in that direction (right beating in right gaze).
  - Alexander’s Law: increases in gaze of fast phase

CEMAS Criteria for INS

- Infantile onset
- Ocular motor recordings show diagnostic (accelerating) slow phases
- Common Associated Findings:
  - Conjugate horizontal-torsional waveform
  - Progression from pendular to jerk waveform
  - Increases with fixation attempt

CEMAS Criteria for INS

- Family history often positive
- With or without associated sensory system deficits
  - Albinism, achromatopsia, congenital cataracts
- Associated strabismus or refractive error
- Decreases with convergence
- Null and neutral zones present

CEMAS Criteria for INS

- Associated head posture or head shaking
- May exhibit a "latent" component
- “Reversal” with OKN stimulus
- Periodicity to the oscillation
- Candidates on Chromosome X and 6
- May decrease with induced convergence, improved fusion, extraocular muscle surgery, contact lenses, and sedation.

CEMAS Criteria for INS

General Comments:

- Waveforms may change in early infancy, head posture usually evident by 4 years of age
- Vision prognosis dependent on integrity of sensory system.

INS Mnemonic = SLOFUN+

- S = symptoms (none)
- L = latency (positive; beats away from occluder)
- O = OKN (double fast; inversion; Cogan’s I&II)
- F = fixation (worse when forced)
- U = upgaze (stays horizontal)
- N = null point (Rt./Lt./Conv.)
- + = gone with lid closure & sleep
Differential Diagnosis: Spasmus Nutans

- Presents as a triad:
  - pendular nystagmus (H,V,R; fast v; small amp)
  - head nodding (noncompensatory & intermittent)
  - abnormal head position
- Tends to be asymmetric and variable
- Onset @ 4-18 months; lasts 2-8 years
- Remains with eye movement recordings
- Tx: Rule out pathology (CT) & monitor

CEMAS Criteria for Spasmus Nutans

- Infantile onset
- Variable conjugacy with pendular waveform
- High frequency, low amplitude oscillation
- Abnormal head posture and oscillation
- Improves ("disappears") during childhood
- Normal MRI/CT Scan of visual pathways

CEMAS Criteria for Spasmus Nutans

Common Associated Findings:

- Family history of strabismus
- May have associated strabismus & amblyopia
- May increase with convergence
- May be greater in one (aBDucting) eye
- Usually no associated sensory deficits
- Decreases with improved fusion

ACQUIRED NYSTAGMUS

Peripheral Vestibular Nystagmus

- Asymmetric lesions of the peripheral system (labyrinth or vestibular nerve) often present with abrupt onset of vertigo, nausea, vomiting, and nystagmus with associated oscillopsia
- Typically has a mixed horizontal-torsional trajectory
- Nystagmus is suppressed with visual fixation and exacerbated by head movement, hyperventilation, or Valsalva
- Associated features such as tinnitus and hearing loss can serve to further delineate causes

Differential Diagnosis: Vestibular Nystagmus

- Peripheral
  - Vestibular nystagmus (commonly viral)
  - Menieres Disease (unknown etiology)
  - Benign Paroxysmal Positional Vertigo (most common, short bouts of symptoms)
- Central
  - Downbeat (most common acquired, persistent nystagmus)
  - Upbeat (etiology = lesions, unknown etiology)
Central Vestibular Nystagmus

- Complex intercommunication between the vestibular nuclei, semicircular canals, and the vestibulocerebellum (floculus, paraflocculus, uvula, and nodulus), combined with integration of visual input from the superior colliculus and the primary visual cortex, provides relative balance that helps maintain gaze fidelity (Leigh & Zee, 2006)
- Lesions produce unwanted slow phase eye movement and oscillopsia

Downbeat Nystagmus

- Downbeat nystagmus is the tendency of the eyes to drift upwards and make a corrective saccade back downward
- Caused by a disruption to the posterior canal projections to the tegmentum of the brainstem
- If you see this direction of conjugate nystagmus in primary gaze, it should increase frequency in left or right gaze

Downbeat Nystagmus

- Possible causes:
  - Arnold-Chiari Malformation (~25%)
    - Needs suboccipital craniotomy
  - Cerebellar Degeneration (~25%)
  - Multiple Sclerosis (~10%)
  - Anti-seizure or tremor meds (~5%)
  - Idiopathic (~20%)

Upbeat Nystagmus

- Characterized by conjugate slow downward drifts and upward corrective saccades in primary gaze
- Follows Alexander’s Law (becomes more intense in direction of fast phase)
- Expect damage to the anterior canal projections at the superior cerebellar peduncle or the junction between the pons and adjacent brainstem structures

Upbeat Nystagmus

- Possible causes:
  - Cerebellar Degeneration (~20%)
  - Brainstem or cerebellar stroke (~20%)
  - Multiple Sclerosis (~15%)
  - Intercranial mass (~10%)
  - May also be caused by infection, trauma or inflammation

Torsional Nystagmus

- In torsional nystagmus, expect the upper pole of the eye to beat away from a central lesion
- Why? Disruption of the anterior AND posterior canal projections on the same side of the brain
- For example, extorsional fast phases OD indicate a left-sided lesion, usually of the pontomedullary junction
Torsional Nystagmus

Possible causes:
- Stroke (almost 40%)
- Multiple Sclerosis (~20%)
- Venous Angioma (~10%)
- Idiopathic (~20%)
- Arnold-Chiari Malformation, intercranial mass, seizures and trauma (>25%)

Differential Diagnosis:
Gaze Evoked Nystagmus

May be caused by structural insults, but the most common cause is drug intoxication

Offending agents:
- antiepileptics, anxiolytics, barbiturates & alcohol
- Drug-induced GEN is conjugate and horizontally symmetric
- Focal lesions typically present with sustained asymmetric GEN

Differential Diagnosis:
Acquired Pendular Nystagmus

APN can be monocular or binocular, conjugate or disconjugate
- Multiple Sclerosis causes ~60% (demyelination)
- Oculopupillary myoclonus or tremor causes ~30%
  - Often 2nd to brainstem lesions such as infarct, hemorrhage, trauma or tumor involving the Giulian-Mollaret triangle

APN Due to Vision Loss

- This type of acquired pendular nystagmus most often occurs with optic nerve disease, and can come and go with it in one or both eyes
  - This is how APN can be MONOCULAR
- If may appear in both eyes, but is often worse in the eye with worse BCVA due to optic nerve disease
  - Called the Heimann-Bielschowsky phenomenon

APN Due to Vision Loss

- APN is most frequently slow, pendular, and vertical, but can have subtle horizontal jerk nystagmus (unlike congenital types)
- Other possible causes are Leber’s “Congenital” Amaurosis, Rod-Cone Dystrophy and even severe amblyopia

Differential Diagnosis:
Periodic Alternating Nystagmus

- Horizontal nystagmus with slow phases that change direction every 1–2 minutes with a “null” phase in between direction changes
- Acquired forms are caused by lesions in the cerebellar flocculus & nodulus
- Other causes include congenital (albinism), Arnold-Chiari Malformation, cerebellar degeneration, MS, encephalitis and tumors
See-Saw Nystagmus

- Elevation with intorsion of one eye; simultaneous depression & extorsion of other eye
- Lesions causing seesaw nystagmus occur at the chiasm and INC in the midbrain
  - Test for bitemporal hemianopia
- Possible causes (~50% are idiopathic):
  - Pituitary adenoma (~15%)
  - TIA – infarct or hemorrhage (~10%)
  - Trauma (7%), Congenital (7%), Low Vision (5%)

Differential Diagnosis

- It has been my experience that determining etiology is often difficult, and consultation with a good neurologist or neuro-ophthalmologist can be beneficial.
  - Your observations can guide the radiology studies

TREATMENT CONSIDERATIONS

- Referrals should be made for treatment of underlying pathology if present.
- When nystagmus treatment is indicated, therapy is designed to dampen the oscillations and reduce symptoms.
- In most cases, functional (and cosmetic improvement) is sought.

Virtually all nystagmus patients should have aggressive management following a careful diagnosis.

- It is not acceptable to simply monitor these patients without treatment.
- It is possible to improve VA, ocular motor control, cosmesis, and visual comfort using sequential considerations of:
  1. Correction of refractive error with spectacles or CL's
  2. Prisms to improve fusion, induce convergence, and/or reduce a head turn
  3. Vision therapy to improve fusion capability & enhance stability of fixation
  4. Medication in some cases to dampen the nystagmus or reduce symptoms
  5. Surgery to reduce a head turn or increase foveation time
**OPTICAL MANAGEMENT**

- Best correction will improve VA and help dampen and stabilize the nystagmus.
  - Primate model found lack of emmetropization in simulations
  - Contact lenses: RGP’s are advocated to help achieve better control of the nystagmus by correcting undetected corneal astigmatism and providing tactile feedback via lid interactions with the lens.
  - Soft lenses can also be effective.

**Contact Lens Simulation**

- Electro-optical treatments
- [Image: Electro-optical_Device.png]

Source: Leigh & Zee, Electro-Optical_Device.m1v

**OPTICAL MANAGEMENT**

- Plus adds can increase clarity and reduce accommodative demand in children who are using relative distance magnification to compensate for reduced VA’s.
  - Minus adds?
  - Yoked prisms can be used to place the eyes in the null area and reduce a head turn:
    - Base direction toward head turn

**OPTICAL MANAGEMENT**

- Example: When the null area is in right gaze and the patient has a left compensatory head turn, a Base OUT prism over the left eye and an equal Base IN prism over the right eye will shift both eyes and the null area to the left toward primary position, thereby relieving the head turn
  - This is BASE LEFT prism for a left head turn

**OPTICAL MANAGEMENT**

- The head turn should reduce ~1 degree for every 2°.
- Cosmesis can be bad - Fresnel prisms can be used with higher amount of prism, but poor cosmesis and reduced VA through the prism makes this a less desireable option.
- Suggestions: pick small eye sizes in the frames and consider a 15 degree guideline (>15° = surgical referral).

**OPTICAL MANAGEMENT**

- Base Out prisms help to stimulate convergence in INS and can dampen the nystagmus and improve VA. May be a quick and simple solution, but watch for induced asthenopia.
Training Prism for Nystagmus

- You may need larger amounts of base out prism to see if it works
- These training prism come in powers up to 25Δ for about $112
- They also come in "microprism" amounts as low as 0.25Δ (same price)
- Applications for the larger amount include yoked to relieve torticollis

http://www.bernell.com/product/3096/162

VISION THERAPY

- Orthoptic Vision Therapy
- Visual Biofeedback
- Auditory Biofeedback
- Vertical Line Counting

Orthoptic Vision Therapy

- May decrease the intensity of the nystagmus as binocular vision is enhanced.
  - The first step is antisuppression and sensory fusion therapy, then enhancement of motor fusion in a natural environment is emphasized.
  - Additional horizontal vergence VT may be needed in cases of large heterophoria.

Visual Biofeedback

- Can be used to help move the null area toward primary gaze.
  - An afterimage flash generated foveally (or pleoptics) is used to give feedback when the patient attempts to stabilize their eyes on a target of progressively smaller size (finer acuity targets).
  - The head is moved toward primary position once success is achieved in the null position.

AFTER-IMAGE

- Four LED lights help the patient to stabilize their fixation on a target
- When it works, it improves BCVA
- This presumes the patient has dampening with fixation

**Auditory Biofeedback**

- Uses infrared eye movement monitors to convert the signal to an audible tone so that the patient can hear the nystagmus.
  - The old Eyetrac had a device made for this (the Eyeliner) that is no longer commercially available.
  - Permobile made a headmounted system, but the FDA did not approve it for use in the US.
  - I use Visagraph or ReadAlyzer now for this, although the feedback is visual, not auditory.
- Results are rapid, but sustaining the dampening is difficult - used primarily for spotting (like a telescope in LV).

**Intermittent Photic Stimulation**

- Uses targets in the Major Amblyoscope with detail that the patient counts while the eye is flashed monocularly at 3-4 Hz for 15-20 minutes.
  - red is thought to assist foveation
- It takes 6-8 weeks for good improvements, but it tends to be long lasting.
  - continued for ~6 weeks after initial strong improvement

**MEDICAL MANAGEMENT**

- Pharmacological Management
- Surgical Management

**Example of M.A. Slide**

**Vertical Line Counting**

- A simple procedure where the patient counts the number of vertical lines on a sheet of paper at ~40cm. The separation of the lines is decreased (or the working distance is increased) when improvement is seen.
- The results are good and it is inexpensive and easy to do at home.

**Pharmacological Management**

- The primary goal is to compensate for faulty function of the neural integrator (GABA/glycineric) & relieve oscillopsia.
- It is more commonly used for acquired nystagmus (e.g., metabolic, toxic, infectious, vascular, surgical damage).
Pharmacological Management

- Clonazepam, Diazepam, Lorazepam all produce short term relief (esp. see-saw), however it’s not good for long-term management due to side effects, i.e., sedation & liver problems
  - Potentially useful for all symptomatic nystagmus
  - Clonazepam most useful for downbeat nystagmus (add 3,4-diaminopyridine)

- Baclofen has been the most commonly prescribed medication for acquired nystagmus (PAN); the side effects and cost are often prohibitive.
  - Central Vestibular (best w/ upbeat nystagmus)
  - Acquired Pendular (not as effective)
  - Periodic Alternating (best use)

Periodic Alternating Nystagmus

- Gabapentin & Memantine are newer medications (US) that have demonstrated some promise for some types of acquired nystagmus (vertical & pendular; MS)
  - Neramexane mesylate (in clinical trials)
  - Valproate may also be prescribed
  - Memantine useful for:
    - Central Vestibular (not as good)
    - Acquired Pendular (2nd choice, add to Gabapentin)
    - Periodic Alternating (not as good)

- Gabapentin useful for:
  - Gaze Evoked (not as good)
  - Acquired Pendular (drug of choice)
  - Periodic Alternating (not as good)

- Pfizer has gotten in major legal trouble because of marketing this drug for depression (suicide)

- Scopolamine is prescribed orally for Parkinson disease and GI tract spasm
- Prescribed as a transdermal patch for motion sickness
  - Scopolamine can also be effective for relief of oscillopsia.
  - Keep the dosage down so that side effects are minimal.
  - Oral scopolamine is also used to treat APN
Pharmacological Management

- Ethyl alcohol: reportedly dampens nystagmus, especially See-Saw
- Cannabinoids like Marinol have been proposed, but this drug (THC) is only FDA approved for nausea and vomiting secondary to chemotherapy and AIDS-related weight loss

Surgical Management

- Used primarily to reduce a head turn in order to move the null area to primary position and improve VA.
  - Botulinum Toxin?
  - Guidelines suggest using only when head turn is $>15^\circ$ and the patient is $>4$ years old.

Botox for Nystagmus

- Botulinum toxin (“Botox”) can be injected directly into the EOM’s to inactivate those that are overacting
- Botox is a muscle paralyzer that is typically effective in small doses for a period of a few months
- Botox has been used to treat nerve palsies and nystagmus

Botox for Nystagmus: Fixation Pre-Treatment

Recommendations for Botox

- Patients with acquired nystagmus due to conditions such as MS or a stroke
- Patients that have failed with other treatment options
- The treatment is transient (2-6 months), therefore it works best when the nystagmus may also be transient, like with a resolving stroke or a pituitary tumor

Source: Leigh & Zee, 4th edition
Studies That Don’t Support Botox Treatment (from Tomsak et al, 1994)

- Abolished or reduced all components of the nystagmus in the treated eye in all three patients for about two to three months (three patients, ages 27-38)
- Visual acuity
  - Visual acuity improved from Jaeger 5 to Jaeger 1 in first patient
  - Visual acuity declined in second patient (Jaeger 2 to Jaeger 7)
  - Visual acuity unchanged in third patient (Jaeger 2)
- Complications
  - Keratitis recurrent problem one year after the initial injection in second patient
  - Patient who received 25 units developed complete external ophthalmoplegia and blepharoptosis
  - Other two retained some voluntary movements but developed diplopia
- Conclusion
  - None elected to repeat procedure (even if there was some visual acuity improvement)
  - Mainly due to the side effects from the procedure

Botox Clinical Pearls

- Best results from studies are patients with acquired nystagmus. Best in adults with nystagmus from neurological disease, not related with cranial nerve or infantile nystagmus, or other failed treatment
- Effects last several months, but repeat of procedure is required
- Most common side effects are ptosis, double vision, and nystagmus can be worse in non-injected eye
- Results vary from patient to patient
- More research is needed

Surgical Management

- The Anderson-Kestenbaum procedure is used in INS to equally recess and resect all four horizontal rectus muscles (or vertical rectus muscles in vertical nystagmus) to move the null position to primary gaze.
- Success is mixed, and strabismus is a confounding factor.

Effect of Kestenbaum on Torticollis

Surgical Management

There are other procedures that recess or detach all EOM’s to limit movement of the globe.

Success has been mixed - primarily poor in the US and a little better in Europe.

A relatively new procedure discussed by Dr. L. H. Dell’Osso:

- Four Muscle Tenotomy
- Cutting and reattaching the extraocular muscles changes the afferent-efferent feedback loop
- Success is measured in increased foveation time
- http://www.or-live.com/distributors/NLM/rnh.cfm?id=416

THANK YOU
