CHAPTER 11

Nystagmus and Saccadic Intrusions and Oscillations

Louis F. Dell'Osso and Robert B. Daroff

> The day of the last hypothesis would also be the day of the last observation. . . . An hypothesis which becomes dispossessed by new facts dies an honorable death; and if it has called up for examination those truths by which it is annihilated, it deserves a moment of gratitude.
>
> Jacob Henle (1809–1885)

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See Chapter 11 for Glossary.

NYSTAGMUS

Nystagmus, the rhythmic to-and-fro oscillation of the eyes, has been regarded as enigmatic. In fact, the distinguished neuro-ophthalmologist Wilbrand once advised, "Never write on nystagmus, it will lead you nowhere."[1]

Although technologic advances have permitted quantitative insights into nystagmus analysis, the clinician should not be daunted. Many useful, often diagnostic, observations can be made by physical examination alone. Figures 11–1 and 11–2 are examples of one convenient method of diagramming nystagmus. Also, nystagmus can be further described when the globes are inspected under slit-lamp magnification, or when the fundus is viewed.

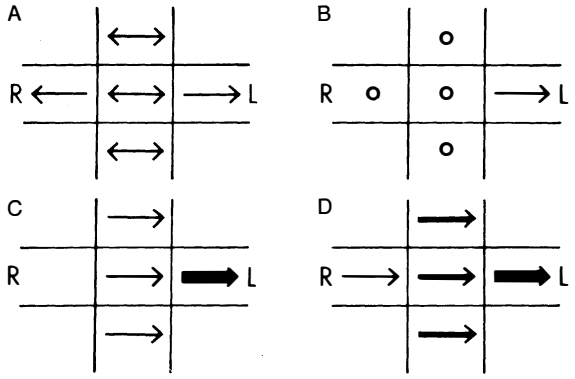

Fig. 11–1. Simple diagrammatic method for depicting nystagmus. The velocity of the nystagmus phases (*two arrowheads*) are equal (*i.e.*, pendular). Jerk nystagmus (*single arrowhead*) points in direction of fast phase. *Heavy lines* indicate more intense nystagmus. **A.** Pendular nystagmus in primary position and up or down, converting to jerk on lateral gaze. **B.** First-degree jerk nystagmus present only on left lateral gaze. **C.** Second-degree jerk nystagmus beating leftward in primary position and increasing on left gaze. **D.** Third-degree leftward jerk nystagmus.

This chapter is a coalescence of the traditional neuro-ophthalmologic approach to nystagmus diagnosis and the impact of the newer capabilities of electronic eye movement recording and mathematical "biomodeling."

Eye movement recordings have allowed definition of 47 types of nystagmus (Table 11–1) and new insights into their pathophysiology. For precise analysis, special recording techniques are necessary, such as infrared, magnetic search-coil, or video recording systems, which can faithfully reproduce the eye-movement trajectories and provide accurate information on eye position without drift or noise. For quantitative purposes, all systems should record by way of direct current, with a bandwidth of 100 Hz. The eyes should be recorded separately in horizontal, vertical, and (if possible) torsional directions, with the tracing analogs written on rectilinear graph paper. Recording should be performed during fixation of visible targets and sometimes in the dark with eyes open (see Chapter 9). For detailed quantitative analysis, the data should be digitized at 200 Hz or higher.

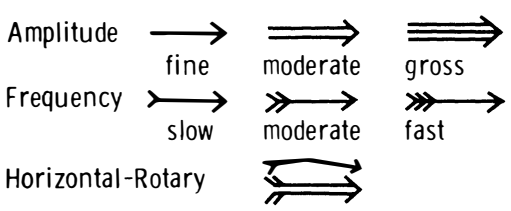

Fig. 11–2. Nystagmus diagrams can be detailed and complex if one uses these symbols.

Nystagmus has traditionally been divided into two types on the basis of the clinical impression of the waveform. Thus, if the eyes appeared to oscillate with "equal speed" in either direction, it was called "pendular" nystagmus; if movement in one direction was faster than in the other, it was called "jerk" nystagmus. True pendular nystagmus is sinusoidal, whereas jerk nystagmus has a slow phase away from the object of regard, followed by a fast (saccadic) phase toward the target. The direction of the fast component, by convention, defines the nystagmus direction. These criteria can often be assessed only by accurate recordings. Nystagmus should be described not only by its waveform and direction but also by its amplitude (A) and frequency (F), the product of which is intensity (I). The examiner should also note the positions of gaze in which the nystagmus occurs and whether the intensity changes with gaze direction. Jerk nystagmus is usually accentuated in amplitude upon gaze in the direction of the fast component, a characteristic referred to as Alexander's law.[2]

The field of gaze in which nystagmus intensity is minimal is termed the "null zone" (see Fig. 11–12). The "neutral zone" is that eye position in which a reversal of direction of jerk nystagmus occurs and in which no nystagmus, any of several bidirectional waveforms, or pendular nystagmus is present. The null and neutral zones usually overlap; however, several cases have been recorded where they do not.

Based on quantitative eye-movement recordings, we have identified three underlying defects in the slow eye movement (SEM) subsystem (see Chapter 9) that produce nystagmus:

1. *High gain instability.* In some persons, because of abnormally high gain in the SEM subsystem, a runaway (increasing velocity) movement or a pendular oscillation is evoked. In this chapter, the term *high gain* can also imply excessive delay for the gain present (*i.e.*, the control loop may have a normal gain, but an increased delay). Control theory suggests how particular changes in gain can result in either a pendular or a jerk nystagmus. Pendular nystagmus can be congenital or acquired, whereas horizontal jerk nystagmus with slow phases of increasing velocity usually is associated with congenital nystagmus; however, the latter may result from an Arnold-Chiari malformation.[3] Vertical nystagmus with an exponential slow phase of increasing velocity may be secondary to acquired cerebellar disease.[4]
2. *Vestibular tone imbalance.* The nystagmus of vestibular tone imbalance results from the imposition of asymmetric vestibular input on an inherently normal horizontal gaze generator. This asymmetric input occurs if one vestibular apparatus (labyrinths, nerve, and brain stem nuclei) functions abnormally or if both sides are asymmetrically defective. The nystag-

TABLE 11–1. Forty-seven Types of Nystagmus*

Acquired	Gaze-evoked	Pseudospontaneous
"Fixation"	Deviational	Induced
Anticipatory	Gaze-paretic	Rebound
Induced	"Neurasthenic"	Reflex
Arthrokinetic	"Seducible"	Baer's
Induced	"Setting-in"	See-saw
Somatosensory	Horizontal	Somatosensory
Associated	Induced	Induced
Induced	Provoked	Spontaneous
Stransky's	Intermittent vertical	Stepping around
Audiokinetic	Jerk	Apparent/real
Induced	Latent/manifest latent	Induced
Bartels'	Monocular "fixation"	Somatosensory
Induced	Unimacular	Torsional
Bruns'	Lateral medullary	Rotary
Centripetal	Lid	Uniocular
Cervical	Miner's†	Upbeat
Neck torsion	Occupational	Vertical
Vertebrobasilar artery insufficiency	Muscle-paretic	Vestibular
Circular/elliptic/oblique	Myasthenic	A(po)geotropic/geotropic
Alternating windmill	Optokinetic	Alternating current
Circumduction	Induced	Bechterew's
Diagonal	"Kinetic"	Caloric/caloric-after
Elliptic	"Optic"	Compensatory
Gyratory	Optomotor	Electrical/faradic/galvanic
Oblique	Panoramic	Head-shaking
Radiary	"Railway"	Induced
Congenital	Sigma	L-
"Fixation"	"Train"	Labyrinthine
Hereditary	Optokinetic after-	Perverted
Convergence	Induced	Pneumatic/compression
Convergence-evoked	Postoptokinetic	Positional/alcohol
Dissociated	Reverse postoptokinetic	Positioning
Disjunctive	Pendular	Postrotational
Downbeat	Talantropia	Pseudocaloric
Drug-induced	Periodic/aperiodic alternating	Rotational/perrotary
Barbiturate	Alternans	Secondary phase
Bow tie	Physiologic	
Induced	End-point	
Epileptic	Fatigue	
Ictal	Pursuit after-	
Flash-induced	Induced	
Flicker-induced	Pursuit-defect†	
Induced		

* Synonyms and other terms indented under either the preferred or the more inclusive designation; some nystagmus types may be acquired or congenital; quoted terms are erroneous or nonspecific.
† May not exist.

mus recording always shows a linear (straight line) slow phase, reflecting a persistent tone to drive the eyes toward the side of the relatively damaged vestibular apparatus. The slow-phase amplitude is reduced by fixation and enhanced by darkness, Frenzel (high-plus) lenses, or closing the eyes. Fixation inhibition may be related to an opposing smooth-pursuit force and requires the integrity of the cerebellar flocculus.

3. *Integrator leak.* Nystagmus caused by a "leaky integrator" occurs only in an eccentric gaze position; thus, it is gaze-evoked. The eyes are unable to maintain the eccentric position and drift back to the primary position with a decreasing velocity, reflecting a passive movement resisted by the viscous forces of orbital soft tissues. The defect may reside in the brain stem "neural integrator" or its connections (such as in the cerebellum), which mediate eye deviation. This form of gaze-evoked nystagmus is called "gaze-paretic" nystagmus (see Fig. 9–8 for an illustration of the gaze-paretic waveform).

One means of classification of nystagmus is based on whether it is a "gazed-evoked" or "gaze-modulated" type; the former category requires that there be no primary-position nystagmus. Two benign types of nystagmus (congenital and latent), physiologic types (ves-

tibular), and symptomatic types (vestibular) fall in the gaze-modulated category. Some physiologic types (endpoint) and symptomatic types (gaze-paretic) are gaze evoked. Although these concepts of a control mechanism represent useful approaches toward a more meaningful classification of nystagmus, they are far from inclusive. For practical reasons, an empirical nystagmus classification is presented that will aid the clinician in bedside and office evaluation, without the use of sophisticated recording instrumentation. This classification continues to change as our understanding of nystagmus advances.

The localizing significance of nystagmus is often a mere indication of dysfunction somewhere in the posterior fossa (*i.e.*, vestibular end-organ, brain stem, or cerebellum). However, certain nystagmus patterns are quite specific and permit reasonably accurate neuroanatomic diagnosis. When possible, the specific and nonspecific forms are separated on the basis of clinical appearance and associated signs and symptoms.

Nystagmus in Infancy

There are several types of benign nystagmus usually seen in infancy. Congenital nystagmus (CN) is the most common infantile nystagmus. Others are latent/manifest latent nystagmus (LMLN) and the pendular nystagmus of spasmus nutans.

Congenital

Congenital nystagmus is usually present at birth or noted in early infancy at the time of development of visual fixation, and it persists throughout life. Rarely, CN becomes manifest later in life,[5] so the term *congenital* should be thought of as a congenital predisposition for this particular type of ocular motor instability rather than taken literally. This form of nystagmus may accompany primary visual defects, which has led to the assumption that the nystagmus is secondary to poor vision, and that both "sensory defect" and "motor defect" types of CN exist. In fact, recordings have shown that all CN is the same with regard to waveforms and underlying mechanism, regardless of the coincidental existence of a sensory deficit. CN is the *direct* result of an ocular motor control instability that may develop with or without an accompanying sensory deficit. Thus, for those cases in which a sensory deficit exists, it can only be a subordinate factor in the development of CN, perhaps interfering with the normal calibration of a key ocular motor subsystem and thereby precipitating its instability. The common association of "pendular" CN with a sensory defect and the "jerk" form with a primary motor abnormality is both simplistic and erroneous. Studies of infants with CN show no difference in waveforms associated with the presence or absence of sensory deficits; the infants exhibited the same CN waveforms that have been recorded in children and adults.[6] Specifically, the development of foveation periods in CN waveforms begins early in infancy as acuity and fixation develop. This is clearly seen in infrared recordings of infants when they are attending to a visual task.

When oculography has been used in systematic investigations, no consistent association between wave type and the presence (or absence) of primary visual loss has been found.[7] The relationship of the visual defect to the nystagmus possibly represents simple genetic association. Although the visual problem may not be causal, it can contribute to the intensity of the nystagmus. CN represents a high-gain instability in a SEM subsystem,[8] and fixation attempt (the effort to see) is its main driving force. Poor vision will increase fixation effort and increase the intensity of the nystagmus. Moreover, a subclinical motor instability may become manifest by this exaggerated visual effort. Although the exact location of the source of the instability present in CN is unknown, we hypothesize that CN is due to a gain/delay problem in an internal (brain stem) feedback loop in the pursuit subsystem.[8] The much greater incidence of horizontal CN, compared with vertical or diagonal CN, probably reflects inherent differences in the stability of the respective pursuit subsystems (*i.e.*, the horizontal is more unstable than the vertical). Another factor in support for this hypothesis is that no oscillopsia is perceived from oscillations in pursuit velocity, not in normals and not in those with CN. Thus, no additional mechanism need be proposed to account for the absence of oscillopsia in CN; it is suppressed by the same mechanism by which normals suppress it during pursuit. The common neural integrator is *not* the site of the CN instability.[9] Several models have been proposed that attempt to explain the genesis of CN.[10–12] While each can generate some CN characteristics, they exhibit behaviors inconsistent with data from individuals with CN. Because CN appears to be activated and intensified by fixation attempt, the deficit may also be linked to the fixation subsystem (see Chapter 9). The co-existence of a high-frequency pendular oscillation with a low-frequency jerk CN (causing a dual-jerk waveform) in some subjects, and with LMLN in others, suggests that the high-frequency pendular oscillation is due to an instability at a different site. It has also been suggested that CN is caused by oscillations at two frequencies whose interactions may produce some of the known CN waveforms.[13]

Distinguishing the lower frequency pendular nystagmus from jerk nystagmus may be difficult clinically, particularly in CN. Certain forms of jerk nystagmus are invariably mislabed as pendular, or the direction is misidentified. Even with oculographic recordings, the direction of the fast phase may be misinterpreted unless velocity tracings are obtained.[14] In the absence of oculography, clinicians should describe the nystagmus care-

fully or use diagrammatic methods (Fig. 11–3; see Figs. 11–1 and 11–2). A diagonal nystagmus whose horizontal component initially looked like latent nystagmus slow phases (see below) and then developed to resemble CN slow phases was induced in monkeys by monocular visual deprivation. This deprivation took place from birth to 25 days and was followed by monocular deprivation of the other eye.[15]

Congenital nystagmus usually damps significantly with convergence. Although the exact mechanism responsible for this damping in unknown, we have long felt that it might result from an effective increase in the stiffness of the ocular motor plant brought about by the increased innervation to the antagonist medial recti. Because convergence results in a change in the muscle pulley system,[16] that may be the mechanism by which the stiffness is increased. The observations of convergence-induced damping of other types of nystagmus support this "peripheral" mechanism in preference to one relaying on an inherent property of CN. As previously mentioned, the intensity of CN is related to the fixation attempt, which probably explains why it sometimes persists with eyes open in darkness (when the subject will probably attempt to "see") and damps behind closed lids (when the subject will, unless instructed to the contrary, reduce any attempt to "see").[14] The defining criterion is fixation attempt, *not* retinal illumination or lid position. Therefore, reports of the presence or absence of CN with lid closure or darkness that lack a description of the instructions to the subject provide no useful information.

The recognition of CN is of extreme importance, particularly in the adult patient, and may obviate unnecessary neurodiagnostic procedures. The characteristics of CN are listed in Table 11–2. CN is almost always binocular and never shows more than minor amplitude dissociation between the two eyes. Clinically, the nystagmus usually appears uniplanar. Like vestibular end-organ nystagmus, horizontal nystagmus remains horizontal when the eyes are deviated vertically and does not convert to vertical nystagmus. Using new, sensitive techniques for recording torsional eye movements, we have found small but significant torsional components in the CN of subjects previously thought to have purely horizontal CN. Because the prominent horizontal movement masks the usually smaller torsional component, the latter appears to be a common characteristic of "horizontal" CN. In most patients, rightward movements were accompanied by clockwise torsion and leftward movements by counterclockwise torsion.[17] The superimposition of a latent component on an ongoing CN is discussed below.

TABLE 11–2. Characteristics of Congenital Nystagmus

Binocular with similar amplitude in both eyes
Provoked or increased by fixation attempt
Gaze-modulated, not gaze-evoked
Diminished (damped) by gaze or convergence
Usually horizontal and torsional (vertical rare)
Increasing velocity slow phases
Distinctive waveforms (foveation periods and braking saccades)
Superimposition of latent component possible
"Inversion" of the optokinetic reflex (actually, CN reversal)
Associated head oscillation or turn
No oscillopsia
Aperiodic alternation possible (Baclofen ineffective)
Abolished in sleep or inattention to visual tasks

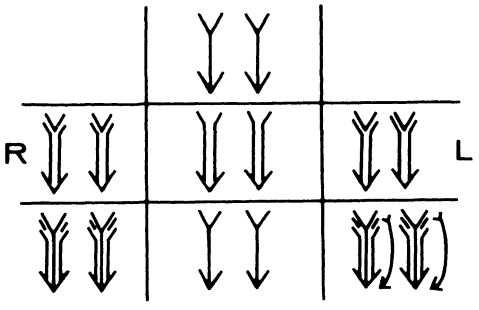

Fig. 11–3. A typical nystagmus is maximum in frequency and amplitude on eccentric and downward gaze. The nystagmus is absent during up and left gaze and up and right gaze; it is minimal during straight up or straight down gaze. In primary position the down-beating nystagmus is moderate in amplitude and slow in frequency. The frequency but not the amplitude increases on gaze right and left. On oblique downward gaze both amplitude and frequency increase, and on down and left gaze the eyes have a mixed pattern combining vertical and rotary components.

Eye movement recordings of CN occasionally show a pure pendular waveform (sinusoidal) or a saw-toothed waveform (equiamplitude linear slow phase with foveating saccade) (see Fig. 11–8) typically seen in vestibular nystagmus. These pure forms are neither frequent nor pathognomonic for CN. More often, CN manifests distinctive waveforms that have not been reported in acquired nystagmus. These waveforms are an expression of the attempts by the ocular motor control system to increase foveation time imposed on inherently unstable slow control. The CN waveforms shown in Figures 11–4 through 11–7 (other than pure pendular or jerk) have never been recorded in acquired horizontal nystagmus.[7,18] The target position is indicated by a dashed line. For pendular waveforms, the target is foveated at the peaks that are more flattened, indicating extended foveation. Extended foveation in an adult with lifelong nystagmus secondary to a congenital brain stem hamartoma, and in an adult given gabapentin for treatment of nystagmus secondary to an arteriovenous malformation,[19] supports the hypothesis that extended foveation periods in CN represent the action of a normal fixation system on the underlying CN oscillation. Figures 11–8 and 11–9 demonstrate how these waveforms serve to increase the time of foveal imaging.

The pure pendular (P) and jerk (J) waveforms in Figure 11–8 are not conducive to good acuity because

of the extremely short foveation time (instants 0 and 2 on the time axis). Although these are common acquired waveforms, when afflicted with CN, the developing nervous system "modifies" pendular and jerk nystagmus; therefore, foveation time (and thus acuity) is increased. Examples of some resultant waveforms are shown in Fig. 11–9. In pendular nystagmus with a foveating saccade waveform (P_{FS}), there is usually a substantial period of time when the target is imaged on the fovea and the eye is motionless (instant 3 on the time axis). In jerk-right nystagmus with extended foveation (JR_{EF}), the position from time 0 to 1 is when foveation takes place, and in the bidirectional jerk-left (BDJL) waveform, the position from instants 4 to 5 is conducive to good acuity. Waveform, gaze angle nulls, and convergence nulls are affected by heredity.[20] Members of the same family show higher incidences of specific combinations of waveforms or of either waveform, having only a convergence null or no convergence null (*i.e.*, having only a gaze angle null), than do members of the general CN population. Our experience has shown greater damping of CN with convergence than with gaze angle, in patients who exhibited both types of null, and this translated into acuity increases.[21] Comparison of the results of the Anderson-Kestenbaum and artificial divergence procedures also favored the artificial divergence.[22]

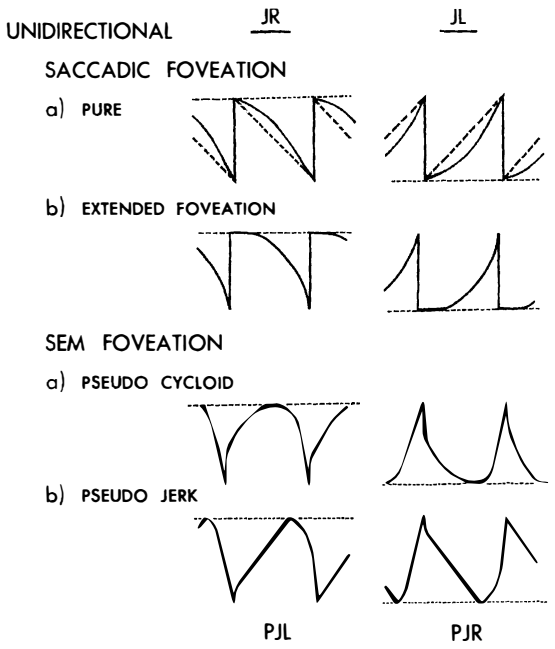

Fig. 11–5. Unidirectional types of jerk nystagmus including two with saccadic foveation (*pure* jerk and jerk with *extended foveation*) and two with slow eye movement (*SEM*) *foveation* (*pseudocycloid* and *pseudojerk*). For the pure jerk waveform, the more common increasing velocity slow phases are shown *solid,* and the rarer linear slow phases are shown *dashed.* Note small and variable saccadic amplitude in pseudocycloid waveform and further reduction in pseudojerk waveform.

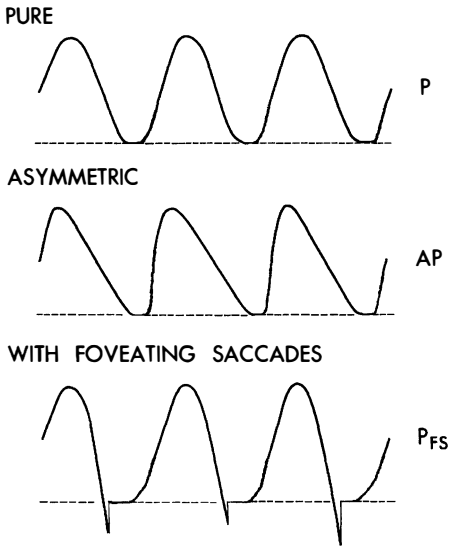

Fig. 11–4. Three types of pendular nystagmus: pure (*P*), asymmetric (*AP*), and pendular with foveating saccades (P_{FS}). Note that although foveating saccades vary in amplitude, they all return the eyes to same point (the target). Foveation takes place at the peaks that are more flattened; here shown as the leftmost peaks. In this and Figs. 11–5 through 11–7 and Fig. 11–13, *dashed lines* indicate target position (see text).

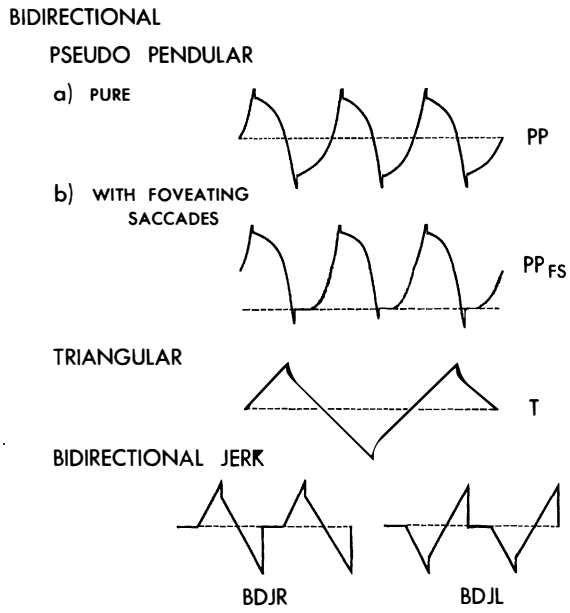

Fig. 11–6. Four types of bidirectional jerk nystagmus: pseudopendular (*PP*), pseudopendular with foveating saccades (PP_{FS}), triangular (*T*), and bidirectional jerk (*BDJ*). All saccades are in a corrective direction (*i.e.,* toward target). Foveating saccades of PP_{FS} vary in amplitude, but all achieve foveation, indicated by the flattened portions of the slow phases.

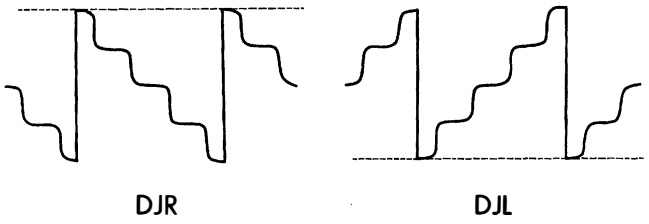

Fig. 11–7. Dual-jerk nystagmus showing sinusoidal modulation of slow eye movement off target. *DJR*, dual-jerk right; *DJL*, dual-jerk left.

Increased foveation time is *the most effective* determinant of increased acuity.[23–26] In most CN subjects, the best waveform (*i.e.*, most foveation time per cycle) is in the null region associated with a particular gaze or convergence angle, but in other subjects it is not; these latter subjects prefer the gaze or convergence angle that yields the best waveform, even if it is not the waveform with the least amplitude. We have hypothesized and tested a new type of surgery that shows promise in damping the CN of subjects that do not have either a gaze-angle or a convergence null, have a primary-position null, or do not have a static null [*i.e.*, they have asymmetric (a)periodic alternating CN].[27] The surgery consists of a simple tenotomy, dissection, and suture of the involved extraocular muscles in place, with neither recession nor resection. The various therapies available for CN, based on the presence or absence of gaze and convergence nulls, are summarized in Table 11–3. Note that for patients with both convergence and gaze-angle nulls, exploitation of the former (surgically or with

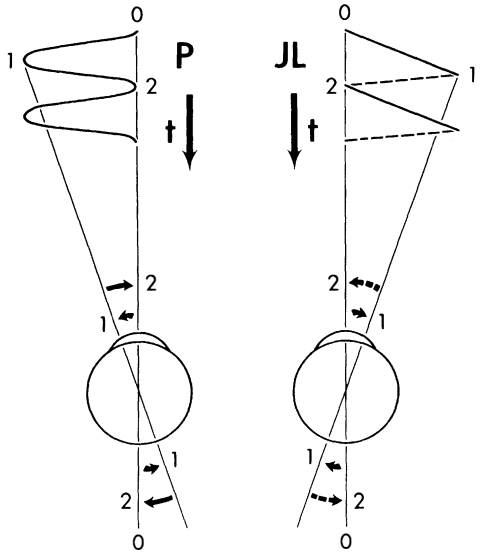

Fig. 11–8. Foveation "strategy" employed during pendular (*P*) and jerk (jerk left, [*JL*]) nystagmus. The target is only briefly foveated at points 0, 2, and so forth. *t*, time scale.

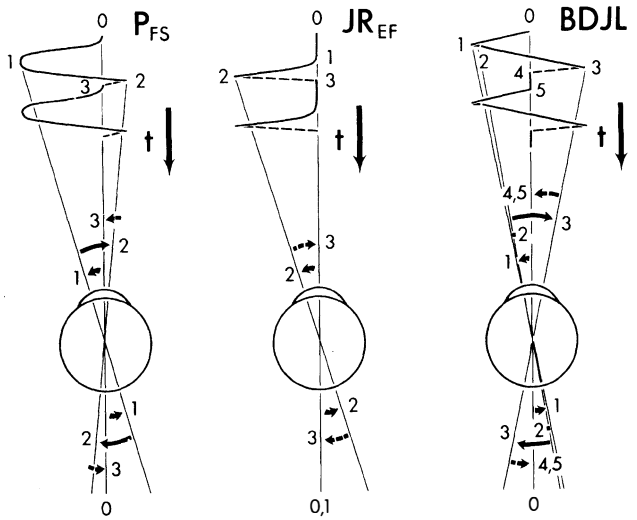

Fig. 11–9. Foveation "strategy" used during pendular nystagmus with foveating saccades (P_{FS}), jerk right with extended foveation (JR_{EF}) nystagmus, and bidirectional jerk left (*BDJL*) nystagmus. The longer the target is foveated, the better will be the good acuity. *t*, time scale.

vergence prisms) usually damps the CN and increases acuity most; it is necessary to add −1.00 S [both eyes (OU)] to vergence prisms for pre-presbyopic patients. As indicated in Table 11–3, afferent stimulation can be used in all patients, regardless of the presence of nulls, who exhibit CN damping with active stimulation (see below).

Despite a nulling of the CN, a subject may not show an increase in acuity with convergence if the resulting waveform has little foveation time per cycle, or if acuity is limited by a primary visual deficit. The fixation system of a subject with CN is able to repeatedly foveate a target within minutes of arc, almost

TABLE 11–3. Therapies for Congenital Nystagmus

If the CN nulls ONLY with gaze
Resection and recession (OU)
Version prisms
Afferent stimulation (passive or active)
If the CN nulls ONLY with convergence
Bimedial recession (artificial divergence)
Vergence prisms with −1.00 S (OU)
Afferent stimulation (passive or active)
If the CN nulls with BOTH gaze and convergence
Bimedial recession alone or combined with resection and recession
Vergence or composite prisms with −1.00 S (OU)
Afferent stimulation (passive or active)
If the CN nulls with NEITHER gaze nor convergence or is asymmetric aperiodic alternating CN
Tenotomy, dissection, and suture* (OU)
Maximal recession (OU)
Afferent stimulation (passive or active)

* This surgery is presently experimental.

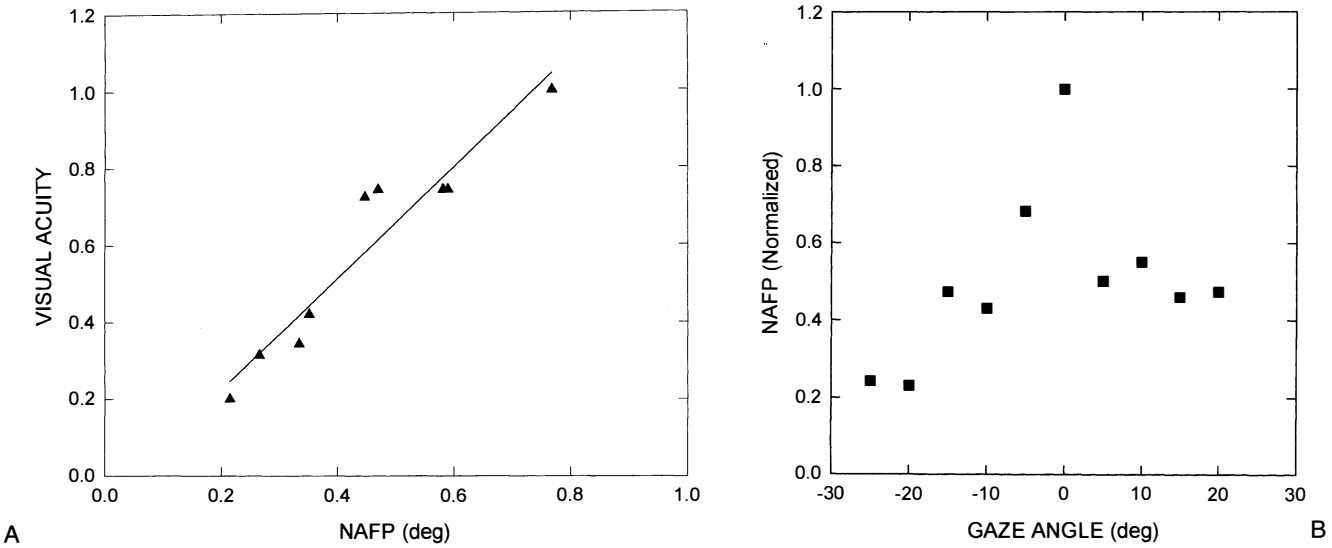

Fig. 11–10. A. The nystagmus acuity function (*NAFP*) vs. visual acuity for nine subjects with congenital nystagmus. **B.** A normalized NAFP vs. gaze angle for a subject with achiasma. (**A,** from ref. 31)

as accurately as a normal person.[21,24,28] The use of "phase-plane" analysis allows definition of a "foveation window" (±0.5° by ±4.0°/second) for the study of fixation, smooth pursuit, and the vestibulo-ocular reflex (VOR).[21,29,30] These studies demonstrate the extremely accurate fixation, pursuit, and VOR possible in subjects with CN.

The "nystagmus acuity function" (NAF) provides an objective determination of potential visual acuity from measurements of the key characteristics of the CN waveform: foveation time and the standard deviations of foveation position and velocity means (for NAF) or position mean alone (NAFP).[31] Plots of the NAF or NAFP vs. visual acuity reveal a linear relationship that allows intersubject prediction of potential visual acuity (Fig. 11–10A). The NAFs can be used both to compare potential acuity across subjects with different types of nystagmus (CN or LMLN), and to predict the acuity increase due to therapeutic intervention in a given subject. The latter is accomplished by plotting either of the NAFs vs. gaze or convergence angle. Finally, for those subjects whose foveation ability is not well developed (*i.e.*, the target image always falls within the above foveation window), the window used for its calculation can be expanded, and the expanded NAF plotted vs. gaze or convergence angle. Figure 11–10B is a plot of NAFP (normalized to the highest value) from a subject with achiasma, first seen at the Amsterdam Medical Center (see Albinism and Achiasma, below).[32] As the NAFP clearly shows, conditions for highest visual acuity occurred during gaze in primary position. Software that calculates the NAF (or expanded NAF) from eye-movement data provides a quantitative method for evaluating different therapies for their effect on potential visual acuity.

The so-called inversion of the optokinetic reflex seems to occur only with CN.[33] When optokinetic stimuli are presented to a patient with CN, a peculiar phenomenon may occur: the resulting nystagmus may be opposite in direction from what would be anticipated if the evoked optokinetic nystagmus (OKN) simply summated with the ongoing nystagmus. For example, in the presence of left-beating CN, the response to right-going optokinetic targets (a leftward fast phase) should add to the congenital left-beating nystagmus to produce enhancement of the nystagmus intensity. Instead, the nystagmus may either damp or be converted to right-beating CN. If right-going targets are presented at a gaze angle at which the nystagmus is either absent or pendular, a right-beating CN may result. Inversion of the optokinetic reflex is present in 67% of CN patients. The observation of optokinetic inversion establishes the nystagmus as CN. The phenomenon is, in reality, merely a reversal of the CN direction due to a null shift; it is not a true inversion of the optokinetic response (see discussion of "reversed pursuit," below). The basic function of the optokinetic system is to stabilize slowly moving retinal images, but this function may be interfered with by the rapidly moving retina of a CN patient. It is not surprising that the optokinetic response appears suppressed in some patients; however, the perceived circularvection is in the proper direction, and OKN dynamics appear to be normal in individuals with CN.

The head oscillations that often accompany CN increase with visual intent and have traditionally been

regarded as compensatory. For compensation to be achieved, head movements would have to be equal in amplitude and opposite in direction to the eye movements. For such a mechanism to work, the VOR would have to be totally inhibited (gain reduced to 0). Accurate objective observations of the head movements in patients with CN do not support that hypothesis.[34] Rather, the head oscillation is merely an extension of the motor instability, and the VOR functions normally to cancel the effects of head oscillation during the periods of target foveation normally present in the CN waveform.[30] The head tremor in CN can be distinguished from that in acquired disease; it is easily suppressed voluntarily in the former but not in the latter.

Point out the head tremor to the patient. If it stops, the nystagmus is CN; if it persists, both are acquired.

Patients with CN usually do not experience an illusory oscillatory movement of their environment (oscillopsia). This lack of oscillopsia in CN, and also in LMLN, suggests that both oscillations occur within an efference copy feedback loop that serves to nullify the effects of retinal-image oscillation induced by either of these instabilities.[35] Like most ocular oscillations (myoclonus being the exception), CN disappears in sleep. In two patients with CN plus an acquired nystagmus, their acquired oscillopsia seemed to be related to an inability to maintain repeatable periods of good foveation in a particular plane.[36,37] However, that inability was an epiphenomenon caused by the addition of a transitory acquired nystagmus to the ever-present CN.[35] Oscillopsia suppression in CN and other types of nystagmus appears to be accomplished by efference copy of the nystagmus signal.[35,38–41]

During fixation of stationary targets, many patients with CN have a permanent null region representing the gaze angle at which the intensity of the nystagmus is the lowest (Fig. 11–11). They often turn their heads to permit straight-ahead viewing with the eyes in the null region. Such patients benefit from appropriate prism spectacles that alleviate the necessity for the head turn and the resulting increased fixation attempt.[14,23]

Some CN patients may exhibit a "superimposed latent" component that induces null shifts toward an eye that is covered (Fig. 11–12).[42] Demonstration of such a shift and maintenance of any of the CN waveforms establish the nystagmus as congenital rather than latent (see below). Rarely, a null shift is toward the viewing eye.[14]

Some studies of CN and smooth pursuit have led to confusion between the reversal of CN direction that may occur during pursuit and "reversed pursuit." This confusion is similar to that discussed earlier for the optokinetic response. Accurate eye-movement recordings show that neither subsystem responds in a reversed manner, as should be obvious both by the absence of any symptoms of such a grave deficit and the normal abilities of CN patients in sports. Also, their perceptions of both the direction and magnitude of movements in the periphery and on the fovea are equal to those of normals. Just as the CN waveform is distorted by SEM (creating periods of extended foveation) during fixation of a stationary target, the pursuit system is able to generate pursuit movements with a direction and velocity that match those of a moving target during these same periods of the CN waveform.[29,38,43] This ensures extended foveation of the moving target and results in accurate smooth pursuit during the periods when the target image is on the fovea. Pursuit during foveation is all that is necessary for good acuity; the same conditions are met during smooth pursuit as are met during fixation of a stationary target. It has been documented that during smooth pursuit (or during optokinetic or VOR stimuli) the gaze angle at which the CN null region occurs shifts in the direction opposite to the pursuit (optokinetic grating or VOR-induced eye motion).[29,30] The amount of null shift is related to the pursuit or VOR velocity. It is this shift in the CN null angle that causes the CN reversal that has been mistakenly equated

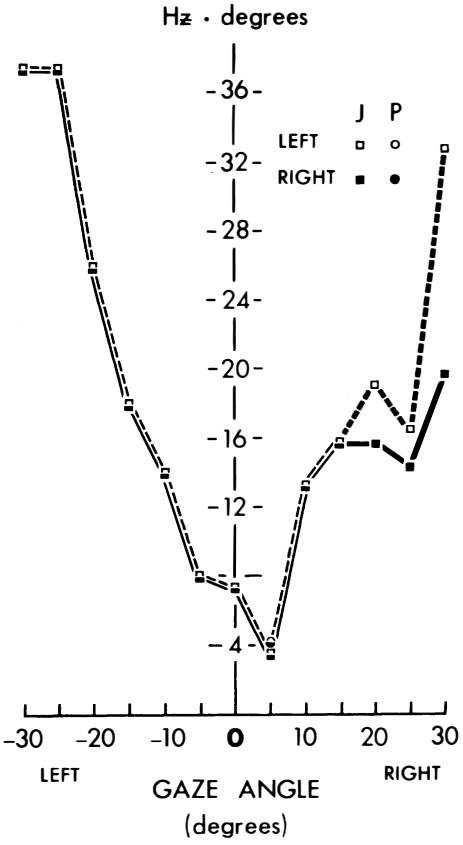

Fig. 11–11. Binocular intensity function for both pendular (*P*) and jerk (*J*) nystagmus. The null angle is at 5° right gaze.

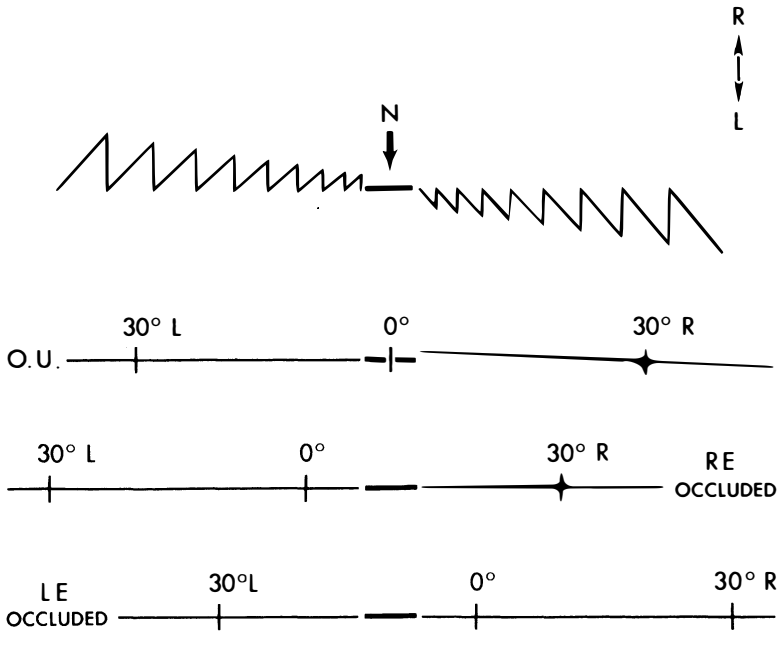

Fig. 11–12. Depiction of shifts of neutral zone or null (*N*) in congenital nystagmus. Tracing demonstrates an idealized nystagmus pattern with both eyes open (*O.U.*). Neutral zone extends over several degrees on either side of 0°. When gaze is directed laterally, nystagmus of increasing amplitude develops with fast phase in direction of gaze. Occlusion of right eye (*RE*) shifts zone to the right; at 0° there is left-beating nystagmus. Occlusion of left eye (*LE*) shifts zone to the left; at 0° there is right-beating nystagmus.

with "reversed" responses of both the optokinetic and pursuit subsystems.

In many subjects with CN, afferent stimulation of the ophthalmic division of the trigeminal nerve or of the neck may damp the nystagmus, allowing increased visual acuity.[31,44] Neck or forehead vibration prolonged foveation periods, yielding higher values of the NAF and improved visual acuity in 9 of 13 patients with CN.[31] This non-invasive and benign therapy (active afferent stimulation) may prove useful in both CN and acquired nystagmus. The use of soft contact lenses to improve the acuity of individuals with CN takes advantage of the damping effect on CN of (passive) afferent stimulation.[45–48]

> Soft contact lenses are not contraindicated in CN and can provide better acuity than spectacles in patients whose CN damps with afferent stimulation. Plano soft contact lenses can be used if no refractive correction is required.

Relatives of patients with CN may have *saccadic* instabilities,[49] and carriers of blue-cone monochromatism may have vertical (upbeat and downbeat) nystagmus and LMLN.[50]

Latent/Manifest Latent

Latent/manifest latent nystagmus (LMLN) is a jerk nystagmus with either a linear or decreasing-velocity exponential slow phase identical to that of gaze-paretic nystagmus. Occasionally, when both eyes are closed, a jerk nystagmus with a linear slow phase is present. Classically, "pure" or "true" latent nystagmus (LN) occurs only with uniocular fixation. There is no nystagmus with both eyes viewing, but when one eye is occluded, nystagmus develops in both eyes, with the fast phase toward the uncovered eye (Fig. 11–13). LN is always congenital. However, several cases of manifest latent nystagmus (MLN) associated with retrolental fibroplasia have been recorded.[51]

Early theories postulated that a unilateral retinal stimulus was the necessary condition for LN, but this concept was discounted by observations of LN in monocular fixation with a blind eye or with an acoustic stimulus in complete darkness. Similarly, the hypothesis that LN is caused by nasal-temporal asymmetries in the optokinetic reflex is not supported by evidence that subjects with LMLN are able to use retinal slip information to adapt motion-detection sensitivities[52] and are able to pursue symmetrically.[53] Also, because nasal-temporal asymmetries exist in individuals with strabismus but not LMLN,[52] this cannot be the primary causal factor in the genesis of LMLN. Asymmetries in the monocular optokinetic response of monkeys deprived of binocular input early in life may result from, rather than cause, their LN. In normal monkeys, each nucleus of the optic tract (NOT) is driven binocularly; in these monkeys, they are driven by the contralateral eye.[54] Although the resulting imbalance may provide the tonic signal that produces the LMLN slow phases (inactivation of the NOT with muscimol abolishes the LMLN), the cause of the imbalance appears to lie in higher centers.

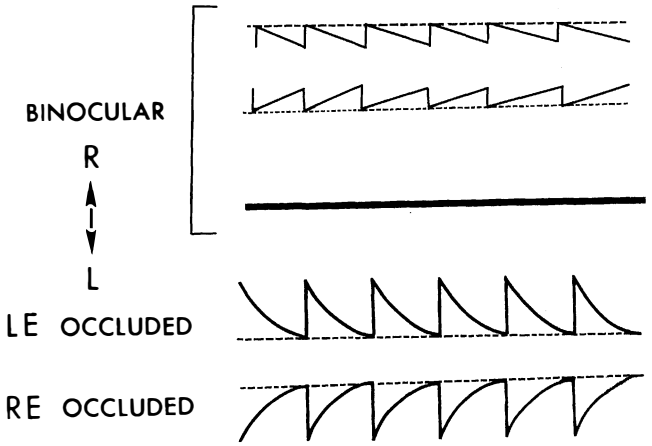

Fig. 11–13. Latent/manifest latent nystagmus. With both eyes open there is either low-amplitude manifest latent nystagmus (when only one eye is fixating) or, rarely, no nystagmus (when both eyes are fixating). Closure of either eye results in jerk nystagmus with fast phases toward the viewing (unoccluded) eye. When both eyes are open, the nystagmus fast phases are toward the fixating eye. Slow phases may be either linear (usually when both eyes are open) or decreasing-velocity exponentials (usually upon occlusion of one eye), unlike those of CN. Note that the fast phases may be foveating (for low-amplitude LMLN with linear slow phases) or defoveating (for the higher amplitude LMLN with decreasing velocity slow phases).

Our own observations have led us to relate LMLN to the cortical switching that must occur in the calculation of egocentric direction when going from binocular to monocular viewing.[51] Under binocular conditions, the gaze angle of each eye is summed with the other and divided by two to obtain the egocentric direction, referenced to the "cyclopean eye." However, with monocular viewing, egocentric direction depends only on the viewing eye, and the cortical operation of summing and dividing by two must be altered to process unchanged information from the viewing eye. The shift in egocentric direction toward the nonviewing eye causes the slow drift of the eyes in that direction. Both eyes are then corrected by a saccade in the direction of the viewing eye, which brings the eyes to the target (or, in darkness, to the intended gaze angle). This contention is supported by unilateral strabismus surgery causing central effects on egocentric localization.[55] Thus, LMLN can be generated by this inability to properly alter the cortical mathematical operation normally used to define egocentric direction.

The shift to monocular egocentric localization can also produce a mode whereby the saccadic system is used to produce defoveating saccades that momentarily carry the fixating eye past the target in a temporal direction, followed by a decelerating-velocity nasal drift back toward the target.[56] This would be equivalent to generating a pulse, but not a step, of innervation to drive the fast phases of the LMLN. Presumably, the common neural integrator is kept from integrating these defoveating pulses by the signal representing the correct eye position vis-à-vis the target.

MLN occurs in patients with strabismus who, although viewing with both eyes open, are fixing monocularly. The slow phases are of the expected decreasing exponential form, and the fast phases are always in the direction of the viewing eye.[51] The nystagmus of patients with strabismus, alternating fixation, and MLN has fast phases always in the direction of the fixating eye. Such patients are usually misdiagnosed as having CN, because the nystagmus is present with both eyes open. Recordings are required to document the decreasing exponential slow phase that delineates LMLN from CN, which has an increasing exponential slow phase. LMLN may be part of a syndrome with strabismus, alternating hyperphoria, and pendular torsional nystagmus in primary position.

Strabismus is a necessary (but not sufficient) condition for LMLN.[57] That is, all patients with LMLN have strabismus, consisting of a phoria under cover and a tropia with both eyes open, if LN or MLN is present under these respective conditions. Conversely, LMLN is not significantly associated with early-onset strabismus.[58] Rarely, on occlusion of a preferred eye, during which fixation with an amblyopic eye is forced, both eyes drift in the direction of the covered eye without corrections by fast phases. This is called "latent deviation." Early surgical correction of infantile strabismus may convert MLN to LN,[59] thereby supporting a previous hypothesis.[57]

Because the good acuity of CN patients is related to the long, postsaccadic foveation periods of many waveforms, it is difficult to explain the equally good acuity of LMLN patients, given the absence of such periods. Accurate studies of LMLN foveation have revealed a dual strategy.[56] During low-amplitude, linear-slow-phase LMLN, the saccadic fast phases foveate the target, and the low-velocity slow phases take the eye away from the target with little effect on acuity. During the higher amplitude, decreasing-velocity slow-phase MLN, the saccadic fast phases defoveate the target, allowing foveation during the low-velocity, tail ends of the slow phases (see Fig. 11–13); this ensures the best acuity possible.

Although most patients have either CN or LMLN, some have both; three unambiguous patient groups have been identified: CN, LMLN, and CN + LMLN.[20] The three groups exhibit different clinical signs and relations to strabismus; most CN patients do not have strabismus, but all LMLN patients do. Thus, CN and

LMLN are specific, easily differentiated disorders and do not, as has been suggested,[60] represent a unitary disorder with a broad spectrum of expression. Because no acquired, time-independent, primary-position jerk nystagmus reverses direction with alternate eye cover, a simple reverse-cover test can be a powerful clinical tool.

> To distinguish among benign, infantile, primary-position, jerk nystagmus, and that which is acquired and symptomatic, first verify that there is no periodic alternation in direction and then perform a reverse-cover test. If the cover test causes a reversal in the nystagmus direction consistent with LMLN, the nystagmus is benign (LMLN or CN with a latent component). If not, rule out CN (history, clinical signs (see Table 11–2), waveforms).

Nystagmus Blockage Syndrome

The nystagmus blockage syndrome (NBS) is both a poorly understood and an overdiagnosed phenomenon related to CN. As the name suggests, the nystagmus of these patients diminishes or disappears with the act of *willed esotropia* while fixating a distant target. This should not be confused with the damping of CN during convergence on a near target. There are two mechanisms by which blockage of the ongoing nystagmus can be accomplished.[61] During the willed esotropia, some CN merely damps or stops, in much the same way as with true convergence. In the second type of NBS, the CN converts to MLN with the onset of the strabismus. Normally, the substitution of the MLN slow phases for the CN waveforms that allow for better foveation would not be advantageous. However, in these few patients, the small MLN amplitude results in better acuity than the larger CN amplitude. NBS is often misdiagnosed in MLN patients with a strong Alexander's law variation of their nystagmus, which causes them to fixate with their adducting eye.[61]

Acquired

Secondary to Visual Loss

Nystagmus occurring in early childhood consequent to progressive bilateral visual loss should not be classified as CN unless CN waveforms are documented. The conceptual problems in the classification were discussed above. Usually, nystagmus secondary to visual loss cannot be distinguished from CN in a patient with coexisting primary visual abnormalities.

The nystagmus associated with rod monochromacy (complete congenital achromatopsia) is said to be distinguishable from other forms of CN on the basis of slow buildup of the slow component velocity of OKN. This occurs during monocular stimulation and directional asymmetry of OKN when the temporal-to-nasal direction is compared with the nasal-to-temporal direction.[62] Patients with blindness from birth and nystagmus may have an impaired VOR and an inability to initiate saccades voluntarily, despite the presence of quick phases of nystagmus.[63] Adults with "eye movements of the blind" exhibit features similar to those of patients with cerebellar disease.[63] Cats reared from birth in stroboscopic illumination develop low-amplitude nystagmus; this is believed to be an animal model for nystagmus secondary to visual loss.[64]

Monocular visual loss may produce monocular nystagmus, usually vertical, at any age from birth through adult life. The fact that the nystagmus is monocular and usually vertical makes it distinguishable from CN, but it may mimic spasmus nutans, particularly if there is associated head nodding.

Spasmus Nutans

Spasmus nutans is a rare constellation of ocular oscillation, head nodding, and torticollis that begins in infancy (usually between 4 and 18 months of age) and disappears in childhood (usually before 3 years of age). The nystagmus is generally bilateral (but can differ in each eye and may even be strictly monocular), and it oscillates in horizontal, torsional, or vertical directions. An instance of spasmus nutans presenting with monocular nystagmus in monozygous twins has been reported.[65] Spasmus nutans may sometimes be mimicked by tumors of the optic nerve, chiasm, or third ventricle[66]; therefore, any child with suspected spasmus nutans should have brain imaging. Retinal disease has been reported to mimic the clinical signs of spasms nutans,[67] as has a case of opsoclonus-myoclonus.[68]

The nystagmus tends to be asymmetric in the two eyes, to vary in different directions of gaze, and to be rapid and of small amplitude. The head nodding is inconstant and irregular and can be horizontal or vertical, or both. The average duration of spasmus nutans is 12 to 24 months; rarely, it lasts a number of years. Studies of quantitative head- and eye-movement recordings indicate that the head movement may, using the normal VOR, actually serve to abolish the eye movements.[69] In some patients, it may be only compensatory with suppression of the VOR.

The pendular oscillation of spasmus nutans is characterized by a variable phase difference between the oscillations of each eye.[70] These phase differences can appear from minute to minute and during the child's development. The dissociated nystagmus is usually of a higher frequency than CN, and the result can be disconjugate, conjugate, or uniocular. We hypothesize that spasmus nutans is a yoking abnormality, perhaps due to delayed

development. Recordings show that, in some cases, spasmus nutans may not disappear completely but may recede to a subclinical level; CN and LMLN do not disappear with age.

Acquired Pendular Nystagmus (Adults)

Acquired pendular nystagmus may reflect brain stem or cerebellar dysfunction, or both. It occurs in patients with vascular or demyelinating disease. In the latter, it has been regarded as a sign of cerebellar nuclear lesions. The nystagmus is multivectorial (*i.e.,* horizontal, vertical, diagonal, elliptic, or circular) and usually is associated with a head tremor. Marked dissociation between the two eyes often exists and may not correlate with differences in visual acuity from coexisting optic neuropathy.[71] Despite the dissociation, the oscillations of the two eyes are phase-locked, even when there is a difference in their frequencies.[72] Acquired pendular nystagmus has also been found in autosomal peroxisomal disorder.[73] Gabapentin was found to be effective in treating some forms of acquired pendular nystagmus.[73,74]

Rarely, acquired pendular nystagmus in the adult becomes manifest with acquired amblyopia, as mentioned above. Scopolamine has been reported to be an effective treatment,[75] but botulinum toxin is of limited efficacy in treating acquired pendular nystagmus.[76] A review of current therapeutic approaches to various types of nystagmus and saccadic oscillations, based on known physiology and pharmacology, points out the need for more precise, double-blind studies.[77]

Miner's nystagmus is a rarity limited presumably to mine workers in the United Kingdom. It is described as a small-amplitude, horizontal, and vertical nystagmus that is often more pronounced in upward gaze. The pathogenesis of this putative dysfunction is uncertain, but functional contamination with voluntary "nystagmus" is suspected; a secondary gain setting is usually present.

Except for the dissociation between the two eyes, acquired pendular nystagmus may be similar to pendular CN; both can have associated head tremor and characteristically damp with eyelid closure. Studies into the pathogenesis of acquired pendular nystagmus have ruled out delayed visual feedback and increased gain in the visually enhanced VOR as causal factors.[78]

Acquired Horizontal Jerk Nystagmus

Vestibular

We generally delimit vestibular nystagmus as being consequent to dysfunction of the vestibular end-organ, nerve, or nuclear complex within the brain stem. It is a horizontal-torsional or purely horizontal, primary-position jerk nystagmus with a linear slow phase. The nystagmus intensity increases with gaze toward the fast phase (obeying Alexander's law); it decreases and, with central lesions, may reverse directions upon gaze toward the direction of the slow phase. The symptom of vertigo usually co-exists. As might be expected, acute lesions of the cerebellar flocculus (the vestibulocerebellum) can produce a similar nystagmus (see Chapter 10). Cases of discrete cerebellar infarction are quite rare. Nystagmus may accompany episodic attacks of ataxia.[79] Evidence has been presented supporting a specific chromosomal abnormality in some cases[80] and brain stem lesions in others.[81] For practical clinical purposes, the responsible lesion in vestibular nystagmus is located in either the end-organ, nerve, or brain stem. Such localization requires an appreciation of the manifestations of end-organ dysfunction. In normal subjects, some degree of nystagmus and vertigo develops when the labyrinth (end-organ) is stimulated with warm or cold water applied to the tympanic membrane. The direction of the resulting nystagmus, in terms of the fast (jerk) phase, can be remembered by the mnemonic "COWS" (cold, opposite; warm, same). Cold water in the left ear (or warm water in the right) induces a right-beating nystagmus; cold water in the right ear (or warm water in the left) induces a left-beating nystagmus. In addition, the subject experiences vertigo and, with eye closure, past-points with an outstretched arm and falls in a consistent direction on Romberg testing. The apparent direction of the vertiginous movement, whether of the environment or self, is always in the direction of the fast phase of the nystagmus. The past-pointing and Romberg fall are always in the direction of the slow phase. For example, with cold water placed in the external canal of the left ear, the subject develops a right-beating jerk nystagmus and experiences environmental or bodily movement to the right (paradoxically appearing to move continuously in one direction).[82] With the eyes closed, the patient's attempts at pointing an outstretched finger at a target in front of him result in past-pointing to the left; on standing there is a tendency to fall to the left (in the direction of the slow phase of the nystagmus). This Romberg fall can be directionally altered by head turning: with the head turned to the left, the slow phase is directed toward the rear and the fall is backward; with the head turned to the right, the fall is forward.[83]

These manifestations of cold-water irrigation mimic the effects of a destructive lesion of the vestibular end-organ; warm-water irrigation mimics an irritative lesion. Clinically, most diseases of the end-organ create destructive effects. Irritative phenomena occur but are transient, often subclinical, and usually of interest only to the electronystagmographer. During an attack of Me-

niere's disease, there may be ipsilateral (jerk toward the affected side) nystagmus. Perhaps the most common cause of ipsilateral nystagmus secondary to end-organ disease is "recovery nystagmus."[84] Here, spontaneous nystagmus that occurs after a unilateral labyrinthine lesion may transiently reverse direction as some function is restored in the damaged end-organ. This probably reflects the compensatory "central rebalancing" of the vestibular nuclei. This compensation can also change a primary-position vestibular nystagmus (of peripheral or central etiology) to a paroxysmal positional nystagmus.[85]

A patient with unidirectional jerk nystagmus, vertigo in the direction of the fast-phase component, and past-pointing and Romberg fall in the direction of the slow component is suffering acute dysfunction of the vestibular end-organ on the side of the nystagmus *slow phase.* When the pattern of direction for the nystagmus, vertigo, past-pointing, and Romberg fall is not as just described but varies in some aspect, the symptom complex represents an abnormality of the central vestibular nuclei. Thus, in central vestibular disease, the vertigo may be in the direction of the slow phase of the nystagmus, and the past-pointing or Romberg fall may be toward the fast phase.

Other factors distinguish peripheral from central vestibular nystagmus. Pure vertical or pure torsional nystagmus is never peripheral and always represents central dysfunction. Similarly, pure horizontal nystagmus without a torsional component is suggestive of central disease.[82] Nystagmus that is reduced in intensity by visual fixation is peripheral, whereas nystagmus due to central lesions is usually not reduced, and may even be enhanced, by fixation. Peripheral vestibular nystagmus is best visualized clinically behind Frenzel lenses (+20 diopters), which eliminate the inhibiting effects of visual fixation and magnify the eyes.[86] A marked bidirectionality to the nystagmus (left-beating on left gaze, and a similarly severe right-beating nystagmus on right gaze) is almost always central. Table 11–4 presents the differential features of peripheral and central vestibular nystagmus.

Gaze-Evoked (Gaze-Paretic) Nystagmus

Gaze-evoked nystagmus is elicited by the attempt to maintain an eccentric eye position, and it is the most common form of nystagmus encountered in clinical practice. Patients recovering from a central gaze palsy show a phase in which lateral gaze movement is possible but cannot be maintained in the deviated position; that is, the eyes drift back slowly toward primary position (see Chapter 10). A corrective saccade repositions the eyes eccentrically, and repetition

TABLE 11–4. Vestibular Nystagmus

Symptom or sign	Peripheral (end-organ)	Central (nuclear)
Direction of nystagmus	Unidirectional, fast phase opposite lesion	Bidirectional or unidirectional
Pure horizontal nystagmus without torsional component	Uncommon	Common
Vertical or purely torsional nystagmus	Never present	May be present
Visual fixation	Inhibits nystagmus and vertigo	No inhibition
Severity of vertigo	Marked	Mild
Direction of spin	Toward slow phase	Variable
Direction of past-pointing	Toward slow phase	Variable
Direction of Romberg fall	Toward slow phase	Variable
Effect of head turning	Changes Romberg fall	No effect
Duration of symptoms	Finite (minutes, days, weeks) but recurrent	May be chronic
Tinnitus and/or deafness	Often present	Usually absent
Common causes	Infection (labyrinthitis), Meniere's disease, neuronitis, vascular, trauma, toxicity	Vascular, demyelinating, and neoplastic disorders

of this pattern produces nystagmus, aptly designated "gaze-paretic." This was a clinical description that was not based on oculographic findings. Information about the role of the brain stem neural integrators (see Chapter 9) led to the presumption that a defective integrator would result in the inability of the eyes to maintain an eccentric position, causing them to drift toward the center with a decreasing-velocity exponential waveform. This is indeed the waveform that defines the gaze-paretic subtype of gaze-evoked nystagmus, which is particularly prevalent in patients with cerebellar disease that especially involves the flocculus (see Chapter 10). It has been postulated that there is an inherent "leakiness" of the brain stem neural integrators, namely, a tendency to drift from a given firing level. The cerebellar flocculus normally corrects for this drift. With a floccular lesion, the leakiness and drift are unchecked, and gaze-paretic nystagmus develops. If the integrator leak is small and the time-constant long, a gaze-paretic nystagmus could have a slow phase that is linear rather than a decreasing-velocity exponential. Such nystagmus cannot be designated as gaze-paretic with any degree of certainty and may only be described as gaze-evoked.

In summary, the term *gaze-paretic nystagmus* is restricted to a subgroup of gaze-evoked nystagmus with a decreasing-velocity exponential slow phase. It is "integrator nystagmus" with a defect in the step function of neural firing frequency constituting the pathophysiologic mechanism. The same integrators are probably responsible for smooth-pursuit eye movements, which seem to be invariably abnormal in patients with gaze-paretic nystagmus.

The most common cause of pathologic, bidirectional, gaze-evoked nystagmus is sedative or anticonvulsant medication. The nystagmus fast phase is always in the direction of gaze (toward the right on right gaze, left-beating on left gaze, and upbeating on upward gaze; down gaze is usually without nystagmus). In the absence of drugs, horizontal gaze-evoked nystagmus with linear slow phases can be localized only enough to indicate brain stem or, if unilateral, labyrinthine dysfunction. Analysis of the associated neurologic signs and symptoms would be required for more precise localization.

Gaze-evoked vertical nystagmus almost always coexists with the horizontal variety. Primary-position vertical jerk nystagmus (upbeat and downbeat) is discussed below.

Special Nystagmus Types

Physiologic (End-Point)

There are three basic types of nystagmus that are regarded as normal (physiologic) phenomena:[87]

Fatigue nystagmus begins during extended maintenance of an extreme gaze position and has been found in up to 60% of normals when horizontal gaze is maximally deviated for a time exceeding 30 seconds. It may become increasingly torsional with prolonged deviation effort and may be greater in the adducting eye. Fatigue nystagmus is not a clinically important phenomenon, because routine examinations do not include the maintenance of far eccentric gaze.

Unsustained end-point nystagmus is certainly the most frequently encountered physiologic nystagmus. Its incidence and characteristics have never been studied quantitatively. All experienced clinicians recognize that a few beats of nystagmus are within perfectly normal limits at gaze deviations of 30° or more.

Sustained end-point nystagmus begins immediately upon, or within several seconds of, reaching an eccentric lateral-gaze position. It has been found in more than 60% of normal subjects with horizontal-gaze maintenance greater than 40°. Quantitative oculography reveals that physiologic nystagmus can begin with only a 20° deviation[87] and is almost universal at deviations of 40° or more.[88] The slow phase is linear, except with an extreme 40° to 50° deviation, in which a decreasing-velocity exponential may develop. The nystagmus may be different in the two eyes, but it is symmetric in the two lateral directions. The amplitude of physiologic nystagmus does not exceed 3°.[87] Thus, small-amplitude gaze-evoked nystagmus may be a normal phenomenon, provided the slow phase, with gaze angles up to 40°, is linear. The onset of end-point nystagmus is related to slow drift velocity,[89] and the reduction of drift velocity during fixation (probably by the fixation subsystem) inhibits the nystagmus. Gaze-evoked nystagmus is by necessity "pathologic" if any of three features are present: (1) asymmetry in the two directions, (2) amplitude of 4° or more, or (3) exponential slow phase within a gaze angle of less than 40°.

Dissociated

Nystagmus in which the two eyes show a significant asymmetry in either amplitude or direction is considered "dissociated." The most common type of dissociation is that observed in internuclear ophthalmoplegias; it is most marked in the abducting eye (see Chapter 10). Abduction "nystagmus," which is sometimes designated by the confusing term *ataxic nystagmus,* is not really a nystagmus. This saccadic oscillation is secondary to lesions of the medial longitudinal fasciculus, and is discussed under Saccadic Pulses/Pulse Trains later in this chapter and in Chapter 10.

The pendular nystagmus in patients with multiple sclerosis is usually dissociated. A variety of nystagmus dissociations with diverse lesions of the posterior fossa have been described (*e.g.,* asymmetric vertical nystag-

mus greater in one eye on looking up and in the other eye on looking down in a young girl with a recurrent cerebellar medulloblastoma).

Torsional

Torsional nystagmus describes a torsional movement of the globe about its anteroposterior axis; the term *rotary nystagmus* is used interchangeably. Most nystagmus consequent to vestibular end-organ dysfunction has a torsional component admixed with a major horizontal or vertical nystagmus. A purely torsional nystagmus never occurs with vestibular end-organ disease. When of small amplitude, torsional nystagmus may reflect a medullary lesion. Larger-amplitude torsional nystagmus may be congenital, but when it is acquired it often indicates diencephalic (thalamic) involvement, in which case it is the underlying pattern in see-saw nystagmus. Torsional nystagmus can be classified into two groups.[90] In group I the nystagmus is in primary position, and in group II it is gaze-evoked. The etiologies of both groups are either demyelinating, vascular, or neoplastic.

For consistency, nystagmus in the torsional plane should be defined with respect to the subject, *not* the observer. When a subject's nystagmus beats to his or her right, it is called jerk-right nystagmus; if it beats toward his or her forehead, it is upbeat (even if the subject is in the head-hanging position). Therefore, when the nystagmus fast phases bring the top of the eye toward the subject's right shoulder, it is *clockwise* nystagmus. Clinical descriptions of torsional nystagmus, made from the observer's point of view, deviate from the accepted convention that applies to both horizontal and vertical movements. Maintaining the subject-based directions reduces confusion, eases understanding of anatomic substrates, and anchors the subject's perception of oscillopsia to the direction of his nystagmus. Just as leftward horizontal slow phases cause rightward perceived world motion, clockwise torsional slow phases cause counterclockwise perceived world motion (see Circular, Elliptic, and Oblique, below).

See-Saw

See-saw nystagmus is characterized by conjugate, pendular, torsional oscillation with a superimposed disjunctive vertical vector. The intorting eye rises and the opposite, extorting eye falls. Repetition of this sequence in the alternate direction provides the see-saw effect. The torsional movements predominate in all fields of gaze, but the see-saw feature may be restricted to the primary position or, more commonly, to downward or lateral gaze. See-saw nystagmus can be of the jerk type (with one phase being slow and the other fast) with unilateral meso-diencephalic lesions.[91] Most patients with acquired see-saw nystagmus have bitemporal hemianopias consequent to large parasellar tumors expanding within the third ventricle. It is occasionally evoked transiently after blinks or saccades.[92] Upper brain stem vascular disease and severe head trauma are the next most common etiologies. Post-traumatic see-saw may be temporarily abolished by ingestion of alcohol.[93] Rarely, the nystagmus is associated with septo-optic dysplasia, an Arnold-Chiari malformation,[94] multiple sclerosis,[95] or loss of vision alone.[96] See-saw nystagmus probably reflects diencephalic (thalamic) dysfunction possibly of a pathway or pathways from the zona incerta to the interstitial nucleus of Cajal. A study of visual-vestibular interaction concluded that see-saw nystagmus resulted from a loss of retinal error signals secondary to disruption of chiasmal crossing fibers.[97]

Congenital see-saw nystagmus manifests either in constant vertical disconjugacies without a significant torsional component or in conjugate torsional nystagmus with a vertical component that can be opposite to that of the acquired variety; that is, the intorting eye falls while the extorting eye rises. Congenital see-saw nystagmus is also seen in canine and human achiasma (see Albinism and Achiasma, below). An unusual instance of congenital see-saw nystagmus in two mentally retarded adult siblings, associated with retinitis pigmentosa, had the typical vertical/torsional relationship associated with acquired see-saw.[98]

The ocular tilt reaction, described in Chapter 10, is actually one-half of a see-saw cycle.

Convergence/Convergence-Evoked

The act of convergence usually damps nystagmus, particularly the congenital type.[99] Convergence can also damp[99] or evoke[100] lid nystagmus and may damp or enhance downbeat nystagmus.[101] Upbeat nystagmus may change to downbeat with convergence.[102]

Repetitive divergence is a term describing a slow divergence movement followed by a rapid convergence to the primary position. The movements occur at irregular intervals, distinguishing this from nystagmus.[103] In the single reported instance of this phenomenon in a patient with hepatic encephalopathy, an entire cycle lasted from 4 to 10 seconds, and the interval between cycles was 1 to 15 seconds.

Nystagmus evoked by convergence must be distinguished from "convergence nystagmus." Convergence-

retraction "nystagmus" as a manifestation of the dorsal midbrain syndrome is discussed in Chapter 10; here, the initiating convergence movements are saccadic,[104] and thus not a true nystagmus. Fast divergent movements, followed by a slow convergence, associated with epileptic electroencephalographic activity, occurred in a neonate with an intraventricular hemorrhage.[105]

With the exception of pure convergence nystagmus in infants with spasmus nutans, true pendular convergence nystagmus is uncommon. It was observed in a patient with presumed progressive supranuclear palsy who had paralysis of all volitional eye movements. In retrospect, however, it is probable that the patient had central nervous system Whipple's disease, perhaps the most common cause of pendular convergence nystagmus (see Chapter 10). A study of three patients with convergence nystagmus revealed phase shifts of about 180° in both the horizontal and torsional planes with conjugate nystagmus in the vertical plane.[106] Convergence increased the nystagmus in two of the patients. The waveforms were either sinusiodal or complex sums of sinusoids, and in one patient they were cycloidal. Unlike the pseudocycloid waveform of CN, there were no initiating saccades to these cycloidal movements. Low-frequency convergence nystagmus was hypothesized to result from a visually mediated vergence instability, whereas high-frequency forms might have arisen from an instability in internal brain stem connections associated with vergence.

Nystagmus evoked by convergence is unusual and may be either conjugate or disconjugate, congenital or acquired.[107] In two cases reported, no definite clinical correlation could be made with a specific lesion. The neuropathologic examination revealed no morphologic explanation for nystagmus in the patient with congenital convergence-evoked nystagmus; the patient with the acquired form had demyelinating disease with a spastic paraparesis and no cranial nerve abnormality other than the ocular motor findings.[107] Horizontal pendular nystagmus rarely is evoked by accommodative vergence.[108] This is to be distinguished from the so-called voluntary nystagmus (discussed below), which is often best accomplished when the eyes are slightly converged.

Periodic Alternating

Periodic alternating nystagmus (PAN) is an extraordinary ocular motor phenomenon in which a persisting horizontal jerk nystagmus periodically changes directions. PAN may be congenital or acquired. The congenital variety, which may be associated with albinism,[109,110] has the slow-phase waveform of an increasing-velocity exponential and usually lacks the well-defined stereotyped periodicity seen in acquired PAN (*i.e.*, it is *asymmetric aperiodic* alternating nystagmus). The periodicity of the congenital PAN is markedly influenced by changes in gaze position, supporting the hypothesis that the PAN is a result of a temporal shift in the null zone (Fig. 11–14).[42]

Patients with CN and a varying head turn should be examined for PAN.

The usual sequence in acquired PAN consists of about 90 seconds of nystagmus beating in one direction, 10 seconds of a neutral phase in which the eyes stop or beat downward irregularly, and 90 seconds of beating in the opposite direction. This periodicity is continuous during waking hours and may prevail during sleep. Some patients demonstrate asymmetries in the timing of the two major phases, but the basic pattern for each patient is usually invariable.

In a detailed clinical and control-system study, Leigh and colleagues[111] proposed that PAN arises from (1) a defect in the brain stem neural networks that generates slow phases of vestibular and optokinetic nystagmus; (2) the action of an adaptive network that normally acts to null prolonged, inappropriate nystagmus; and (3) an inability to use retinal-error velocity information. They proposed a control system model that denied access of

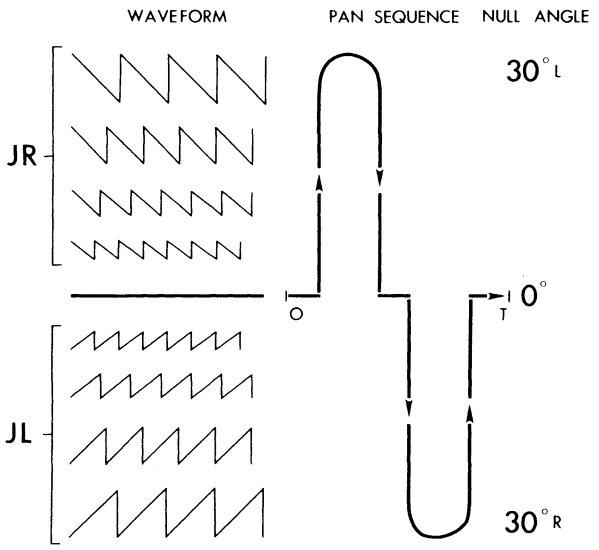

Fig. 11–14. Periodic alternating nystagmus (*PAN*) sequence is depicted in relation to waveform and null angle. Sequence reflects one PAN period (from *O* to *T*). Period begins in a neutral phase; null is at 0°. As null shifts to the left, jerk-right (*JR*) nystagmus develops and gradually increases in amplitude to maximum when null is at extreme left (*e.g.*, 30°L). Null then shifts back toward 0° and *JR* nystagmus decreases, finally stopping and forming the next neutral phase when null reaches 0°. The same sequence of null shifting to right and back accounts for jerk left (*JL*) phase. The diagram is idealized and does not reflect the asymmetries of the true clinical state. (From ref. 42.)

visual signals to the OKN-vestibular system. This model is particularly appealing because of the occasional relationship between impaired vision and PAN. Support for their hypothesis of impairment in the velocity storage element was presented by Furman and colleagues,[112] who studied four patients with PAN. PAN has been described after bilateral vitreous hemorrhages (associated with a massive subarachnoid hemorrhage) and after cataracts. It disappeared after bilateral vitrectomy and after cataract surgery. Ablation of the nodulus and ventral uvula of the cerebellum in monkeys produces PAN.[113]

Although numerous conditions have been associated with PAN, including CN, head trauma, vascular insufficiency, encephalitis, syphilis, multiple sclerosis, spinocerebellar degenerations, and posterior fossa tumors, particular attention should be directed to an abnormality of the craniocervical junction. The possibility of a lesion should be investigated with magnetic resonance imaging. PAN may coexist with downbeat nystagmus, which also suggests an abnormality in the same location.

PAN has been described as secondary to phenytoin intoxication in a patient with alcoholic cerebellar degeneration.[114] The antispasticity drug baclofen abolishes acquired PAN but has no effect on the congenital variety.[115] The drug abolished experimentally created PAN in the monkey,[113] as well as a single case of aperiodic alternating nystagmus in a patient with vertebrobasilar insufficiency.[116]

PAN may be associated with a periodic alternating skew deviation.[117] Periodic alternating gaze deviations, with and without associated alternating nystagmus or alternating head turning, are rare, related phenomena.[118] PAN should not be confused with the nystagmus occurring in the enigmatic, usually familial, acetazolamide-responsive, paroxysmal ataxia syndrome.[119]

Downbeat

Downbeat nystagmus is defined as nystagmus in primary gaze position, with the fast phase beating in a downward direction. Patients with brain stem disease or drug intoxications usually lack gaze-evoked downward nystagmus despite nystagmus in all other fields of gaze. Thus, nystagmus beating downward in the primary position is a striking phenomenon and is highly suggestive of a disorder of the craniocervical junction, such as Arnold-Chiari malformations.[120,121] Downbeat nystagmus is usually of sufficient amplitude in primary position to cause oscillopsia, and, contrary to Alexander's law,[2] it is not maximum at the extreme of downward gaze. Rather, it is usually of maximum intensity when the eyes are deviated laterally and slightly below the horizontal[121]; the nystagmus may be intermittent.

The other major cause of downbeat nystagmus is spinocerebellar degeneration. Indeed, it is difficult to ascertain from the literature whether an Arnold-Chiari malformation or spinocerebellar degeneration is the most common cause. However, because the latter is correctable, a defect of the craniocervical junction must be carefully considered in all patients with downbeat nystagmus. Downbeat nystagmus may co-exist with PAN, another type of nystagmus suggestive of an abnormality of the craniocervical junction. A variety of miscellaneous conditions have also been reported to produce downbeat nystagmus.[101,121] These include anticonvulsant, alcohol, and lithium intoxication; magnesium deficiency; B_{12} deficiency; brain stem encephalitis; alcoholic cerebellar degeneration; dolichoectasia of the ventral artery; and vertebral artery occlusion.[122] Rarely, downbeat nystagmus is secondary to upper brain stem or supratentorial disease, or it may appear as a form of congenital nystagmus. (See Schmidt[123] for an excellent clinical review of downbeat nystagmus.)

Downbeat nystagmus was regarded as the prototype of nystagmus secondary to a "pursuit defect," but studies have cast serious doubt as to whether a unidirectional pursuit defect has been established as a cause of any form of nystagmus.[120] The slow-phase waveform of downbeat nystagmus can vary from a linear, to an increasing-velocity, to a decreasing-velocity exponential in the same patient, presumably reflecting short-term gain changes by cerebellar compensation for leaky brain stem neural integrators.[4] One patient with a pseudocycloid waveform damped with convergence; this prompted treatment with base-out prism spectacles.[101] This has subsequently proved superior to retinal image stabilization as a means of reducing oscillopsia.[124] Downbeat is usually increased in intensity with head-hanging[120] as well as linear acceleration, and occasionally convergence. The mechanism of downbeat is postulated to be disruption of central vestibular pathways,[120] possibly involving specific connections from the otoliths or an asymmetry of the vertical semicircular canal gains.[125] It is associated with lesions of the caudal midline cerebellum, as opposed to the central medulla with upbeat nystagmus.[126–128]

Upbeat

Primary-position nystagmus with the fast phase beating upward rarely reflects drug intoxication. Most often, the nystagmus is acquired and indicates structural disease, usually of the brain stem.[129–131] The location of the lesions in patients with upbeat nystagmus after meningitis, Wernicke's encephalopathy, or organophosphate poisoning is uncertain. The localizing value of upbeat and other types of nystagmus has been found to be

specific in some cases but not in others.[132] Cyclosporin A therapy has also been identified as a possible cause of upbeat nystagmus.[133] With convergence, upbeat may enhance[130] or convert to downbeat.[102] The slow-phase waveform is usually linear but may be an increasing-velocity exponential.

Upbeat nystagmus has been regarded as "pursuit defect" nystagmus, but for the reasons given above in the discussion of downbeat nystagmus, a pursuit defect has not been established as an etiology. Upbeat may be enhanced[130] or suppressed[134] by head tilt. Therefore, it is conceptualized hypothetically as secondary to a disruption of central otolithic pathways; the effects of convergence on the nystagmus are presumed to reflect vergence effects on these pathways. Tobacco smoking causes upbeat nystagmus in normal human subjects in darkness, but the nystagmus is suppressed by visual fixation.[135] The mechanism is presumed to be the excitatory effects of nicotine on central vestibular pathways.

Rebound

Rebound nystagmus is either the diminution and direction change of gaze-evoked horizontal nystagmus during sustained ocular deviation or a horizontal gaze-evoked nystagmus that, on refixation to primary position, transiently beats in the opposite direction. The sign is often present in patients with cerebellar disease.[136] Rebound nystagmus is conceptualized as a smooth eye movement bias generated to oppose gaze-evoked centripetal drift of the eyes. Normal subjects may demonstrate rebound nystagmus after prolonged far lateral gaze if the lights are shut off the moment the eyes are returned to primary position; rebound nystagmus may even occur in normals during fixation in a fully lit room.[88] Rebound and centripetal nystagmus have been reported in Creutzfeldt-Jakob disease.[137]

Circular, Elliptic, and Oblique

Circular nystagmus, sometimes confusingly mislabeled as "rotary," is a form of pendular nystagmus in which the globe oscillates continuously in a fine, rapid, circular path. Unlike torsional nystagmus, in which the 12 o'clock meridian of the limbus torts laterally, this point maintains its position in circular nystagmus. The nystagmus represents the summation of simultaneous, equal-amplitude, horizontal, and vertical pendular oscillations that are 90° out of phase. Elliptic nystagmus is produced when the horizontal and vertical oscillations are 90° out of phase but are of unequal amplitude. Analysis of the vertical and horizontal pendular nystagmus movements, which summate to form circular and elliptic nystagmus, indicates that a true circular pattern is rarely sustained. More often, the nystagmus varies between elliptic and circular. This type of nystagmus is often congenital and identical in the two eyes, and the patient is otherwise free of neurologic signs. Acquired circular-elliptic nystagmus occurs in multiple sclerosis, is often dissociated in the two eyes, and almost always co-exists with truncal or extremity ataxia. Drug treatment with isoniazid may be effective.[138]

Oblique or diagonal nystagmus results when simultaneous pendular, horizontal, and vertical vectors are either in phase or 180° out of phase. The angle of the diagonal vector depends on the relative amplitudes of the horizontal and vertical components. This type is more often acquired than congenital and has the same significance as acquired circular-elliptic nystagmus. Unlike all other types of nystagmus, the oscillopsia induced by elliptical nystagmus is in the *same* direction as the slow phases.[138] Thus, if the subject's eye moves in a clockwise, circular-elliptic manner (from the subject's point of view), the direction of perceived world motion will also be clockwise.

Cervical

The literature on cervical (cord) nystagmus contains numerous examples of spontaneous or positional nystagmus allegedly secondary to lesions of the cervical spinal cord or roots.[139–141] Although this form of positional nystagmus occurs only rarely, it is claimed to support the legitimacy of dizziness in patients who have sustained whiplash injuries and are involved in litigation. For that reason, the entire concept of cervical nystagmus has become highly suspect.[140,141] We have not seen a patient with convincing cervical nystagmus.

Muscle-Paretic (Myasthenic)

A paretic eye muscle, from whatever cause, can fatigue quickly during contraction, and muscle-paretic nystagmus can be observed. This is often evident as gaze-evoked nystagmus in myasthenia gravis, in which there is usually asymmetry between the two eyes.[142] Another form of oscillation in myasthenia is "nystagmus" of the abducting eye (may be saccadic pulse trains, discussed below), co-existing with paresis of adduction; this mimics an internuclear ophthalmoplegia. Here the oscillation is not due to lateral rectus paresis, but rather to excessive innervation by increased central gain, the result of paresis of the contralateral yoke medial rectus. Cessation of both muscle-paretic and contralateral yoke nystagmus in myasthenia usually follows administration of anticholinesterase medication.

Lid

Lid nystagmus is a rhythmic, upward jerking of the upper eyelids that usually consists of the normally coordinated movements of the lids and eyes during vertical ocular nystagmus. Several types of pathologic lid nystagmus are recognized. Type I, with no specific localizing value, co-exists synchronously with vertical ocular nystagmus, but the amplitude of the lid movements exceeds significantly that of the eyes. Type II is evoked by lateral gaze and is characterized by rapid phasic twitches of the lids that are synchronous with the fast phases of horizontal ocular nystagmus. This second type may be a sign of the lateral medullary syndrome and can be inhibited by near-effort.[99] Type III lid nystagmus is provoked by ocular convergence.[100,143] In a patient with this type of nystagmus studied pathologically, a large area of subacute demyelinization in the rostral medulla was found. Lid nystagmus has been identified as a sign of midbrain disease in a subject with an astrocytoma.[144]

Epileptic

Nystagmus associated with epileptic activity includes retraction, pendular, torsional, and divergent-convergent forms.[105] At times, the pupils may constrict and dilate synchronously with the nystagmus.[145] The usual form of epileptic nystagmus is horizontal jerk with the fast phase contralateral to a posterior parietal focus, but a vertical nystagmus may be present.[146] The eyes may tonically deviate toward or away from the side of the epileptic focus.[147] The decreasing-velocity slow phases suggest that a gaze-holding failure[148] causes the slow phases, and the relationship of the ictal activity suggests activation of the saccadic system (see Chapter 10).[149]

Induced Nystagmus

Caloric

The characteristics of caloric-induced vestibular nystagmus were described above. With unilateral irrigation, the nystagmus is either horizontal, torsional, or oblique, depending on the position of the head. Bilateral simultaneous caloric stimulation produces vertical nystagmus; the direction of the fast (jerk) phase can be remembered by the mnemonic "CUWD" (pronounced "cud" and designating cold, up; warm, down).

Traditionally, caloric nystagmus was regarded as being evoked entirely by thermal convection of the endolymph. However, the fact that such nystagmus exists in the zero-gravity conditions of outer space indicates the necessity of an alternative mechanism.[150] Indeed, investigations have revealed two mechanisms responsible for the induction of caloric nystagmus.[151] In addition to the convection mechanism, a direct temperature effect on the canal's sensory apparatus was identified that was independent of head orientation. A review of the technique of quantitative bithermal caloric testing for evaluating vestibular function is provided elsewhere. Caloric and head rotation (doll's) are useful tests in the evaluation of comatose patients.[152]

Rotational

Rotating or accelerating head movements induce motion of endolymph in the semicircular canals, with a resultant jerk nystagmus. If the axis of rotation passes through the upright head, as happens with the Bárány chair, the nystagmus fast phase is in the same direction as head (or chair) rotation. After cessation of the rotation, the postrotary nystagmus is in the opposite direction. Rotational nystagmus is used in evaluating the ocular motor system in infants (see Fig. 3–2), but its primary use in recent years has been to evaluate vestibulo-ocular gain and other aspects (visual suppression of the VOR) of the vestibular system.

Positional

In patients complaining of vertigo related to shifts in position of the head or body, the possibility of positional nystagmus should be investigated. The test is performed by observing for nystagmus produced when the patient rapidly reclines from a sitting to a supine position, with the head either turned alternately to one side and then the other, or hyperextended (hanging). Two types of nystagmus, peripheral and central, can be differentiated (Table 11–5).

Peripheral positional nystagmus is associated with marked vertigo, which begins after a delay of 2 to 20 seconds. The nystagmus and vertigo eventually fatigue, usually within 1 minute. A rapid return to the sitting position causes another brief burst of nystagmus and vertigo ("rebound"). Repositioning in the provocative supine posture again induces nystagmus and vertigo, but to a lesser extent. Repetition of the shifts of posture

TABLE 11–5. Positional Nystagmus

Features	Peripheral	Central
Latency	3–40 s	None; nystagmus begins immediately
Fatigability	Yes	No
Rebound	Yes	No
Habituation	Yes	No
Intensity of vertigo	Severe	Mild
Reproducibility	Poor	Good
Directionality and waveforms	Stereotyped	Variable

ultimately results in diminution and disappearance of the nystagmus and vertigo. Characteristic of the peripheral variety is variable reproducibility: the nystagmus and vertigo may not be present every time the offending position is attained. Whereas latency, fatigability, and habituation have traditionally been regarded as the major features distinguishing peripheral from central positional nystagmus, Baloh et al[153] emphasize that the nystagmus vector is the critical determinant. Positional nystagmus with a torsional-vertical vector, with the torsional component greater in the undermost eye and the vertical component (upbeating) greater in the uppermost eye, is always peripheral, irrespective of the nature of latency, fatigability, and habituation. The torsional component increases when gaze is directed toward the down eye, and the upbeating component increases with gaze directed toward the upper eye.[153] With head-hanging (extended), a downbeating nystagmus (fast phase beating toward the chin) probably has the same significance as downbeating nystagmus with the patient upright.

Central positional nystagmus, which is invariably reproducible, begins immediately on movement to the provoking position; the nystagmus neither fatigues nor habituates, and the vertigo is usually mild. Positional nystagmus that changes direction while the head position remains fixed has been regarded as a central sign. However, direction-changing positional nystagmus occurs with peripheral disease and even in normal subjects.[154]

The peripheral variety, designated "benign paroxysmal positional vertigo" (BPPV), is indicative of labyrinthine disease, and neuroradiologic procedures are rarely indicated. The most common specific etiology is head trauma. However, no cause is found in most cases. The malady increases in prevalence with age. The traditional presumption has been that the provoking position occurred with the diseased ear undermost, and that the fast phase of nystagmus beat toward that ear. The direction of the nystagmus and the lateralization of the labyrinthopathy have been challenged.[153] Nystagmus, identical to the benign peripheral variety, may result from the slow drift produced by central vestibular compensation consequent to either peripheral or central vestibular dysfunction.[85]

The most reasonable etiology of BPPV is "canalolithiasis." The hypothesis is that otoconia detach from a utricle, congeal to form a "plug," and float freely in the endolymph of a posterior semicircular canal. Because the plug is of greater specific gravity than the endolymph, the canal becomes a gravity receptor and symptoms and signs are produced when the head is in a particular position. This concept has led to a form of "physical therapy" in which repetitive movement, or a single provocative movement, dislodges the displaced otoconia.[155] Most patients with the disorder recover spontaneously after several weeks. However, if a person has persistent symptoms and the attacks are consistently evoked with the head in the offending position, a liberatory maneuver is performed. With BPPV, in addition to positional vertigo, patients develop symptoms on arising, bending over, leaning forward, and with head movements while upright.

The central type of positional nystagmus is often associated with neoplastic, vascular, demyelinating, or degenerative disorders involving the brain stem or cerebellum.[156] Intermediate forms of positional nystagmus, such as those that fatigue and habituate but have no noticeable latency, should raise suspicions of central disease.

Testing for positional nystagmus is fairly standardized and does not require electronystagmography. We prefer self-illuminated Frenzel glasses (highly convex lenses, +20 D, which blur vision), but testing can also be performed in a completely darkened room, with the examiner periodically observing the eyes with a dim light. Routine testing for positional nystagmus in patients without the specific symptom of positional vertigo does not generally yield useful results.

The BPPV just mentioned is due to dysfunction of the posterior semicircular canals. Some patients have horizontal BPPV[157] for which a liberatory maneuver has also been described.[158] The term *positional nystagmus* is often used interchangeably with *positional vertigo* in designating a syndrome, and *positional* and *positioning* are used interchangeably to describe nystagmus.

Optokinetic

The localizing value of OKN with cerebral hemispheric lesions is discussed in Chapter 10. OKN is used for several other important functions in clinical neuro-ophthalmology. It provides evidence of at least gross levels of visual function in infants or patients with functional visual loss. As mentioned in Chapter 10, OKN in the downward direction is used to induce convergence-retraction "nystagmus," and horizontal OKN is used to demonstrate the adduction insufficiency in internuclear ophthalmoparesis. "Inversion" of OKN is diagnostic of CN. OKN can be used to diagnose oculomotor nerve misdirection, and, finally, it may be quite useful as a diagnostic test in myasthenia gravis, because the velocity of the fast phase is significantly increased after the standard edrophonium chloride (Tensilon) test.

Drug- and Toxin-Induced

Drug-induced nystagmus is a common sequela of barbiturate, tranquilizer, phenothiazine, and anticonvulsant therapy.[159] The nystagmus is generally regarded as gaze-evoked and is usually horizontal or horizontal-torsional in direction. Vertical nystagmus is often present on up-

ward gaze and only rarely on downward gaze. At times the nystagmus may be dissociated in the two eyes despite the lack of structural disease to account for the asymmetry. Although primary-position nystagmus is usually indicative of severe drug intoxication, it may appear 10 hours after the oral ingestion of only 100 mg of secobarbital.[85] In addition, this amount of secobarbital can produce positional nystagmus. As mentioned, lithium can produce downbeat nystagmus,[160,161] tobacco can induce upbeat nystagmus,[135] and severe alcohol intoxication can produce downbeat nystagmus that abates during sobriety.[162]

Unfortunately, the fact that alcohol can produce horizontal gaze-evoked nystagmus has led to a roadside sobriety test conducted by law-enforcement officers.[163] Nystagmus as an indicator of alcohol intoxication is fraught with extraordinary pitfalls: many normal individuals have physiologic end-point nystagmus; small doses of tranquilizers that wouldn't interfere with driving ability can produce nystagmus; nystagmus may be congenital or consequent to structural neurologic disease; and often a sophisticated neuro-ophthalmologist or oculographer is required to determine whether nystagmus is pathologic. It seems unreasonable that such judgments should be the domain of cursorily trained law officers, no matter how intelligent, perceptive, and well meaning they might be. As noted, meticulous history taking and drug-screening blood studies are often essential in evaluating patients with nystagmus. Toluene (glue-sniffing) can induce pendular nystagmus with both horizontal and vertical components.[164]

Special Anatomic Categories

Acoustic Neuroma

Schwannomas of the eighth nerve grow so slowly that adaptive mechanisms often obscure clinical vestibular manifestations. Vestibular nystagmus beating contralateral to the lesion may be present, particularly if fixation is eliminated. As the tumor expands to compress the brain stem, a slow, gaze-evoked ipsilateral nystagmus is often added. The combination of a small-amplitude, rapid primary-position jerk nystagmus beating contralateral to the lesion, and a slower, larger-amplitude, gaze-evoked (Bruns') nystagmus ipsilateral to the lesion also occurs with other extra-axial masses, including cerebellar tumors, compressing the brain stem. Rarely, Bruns' nystagmus is inverted.[165]

Lateral Medullary Syndrome

The lateral medullary syndrome (Wallenberg) is a distinctive constellation of signs. The nystagmus in this syndrome tends to be stereotyped. With the eyes open there is horizontal-torsional jerk nystagmus beating contralateral to the lesion; when recorded with the eyes closed, the nystagmus beats ipsilateral to the lesion. Other rare manifestations, confined to single cases, are gaze-evoked eyelid and ocular nystagmus inhibited by the near reflex[99] and horizontal gaze-evoked monocular downbeat nystagmus.

An extraordinarily dramatic eye-movement abnormality, saccadic lateropulsion, may occur with lateral medullary infarction. Eye movements as well as body and limb movements are biased toward the side of the lesion (ipsipulsion). The ocular motor abnormality is most striking during shifts of fixation; all ipsilateral saccades are too large (hypermetric), whereas those to the opposite side are too small (hypometric). Spontaneous drifts to the side of the lesion are gaze-dependent and may reflect disruptions of the gaze-holding mechanism.[166] There is also reduced capability to adjust saccadic gain in response to the dysmetria,[167] significant tilt in the subjective vertical, with ipsilateral excyclotropia,[168] and torsional nystagmus and torsipulsion.[169,170] Upward or downward refixations veer ipsilaterally along an oblique rather than a vertical line. Lateropulsion away from the side of the lesion (contrapulsion) has been described with a unilateral disorder of the rostral cerebellum.[171] Both types of lateropulsion are regarded as saccadic instabilities (Table 11–6). The gaze deviation may reflect increased inhibition of the ipsilateral vestibular nucleus, and ipsipulsion may reflect decreased excitation of contralateral premotor areas in the pontine paramedian reticular formation.[172]

Albinism and Achiasma

Ocular albinism is associated with anomalous visual projections that result in a variety of eye movement disturbances, with considerable intersubject variability. These individuals may have pendular or jerk nystagmus, absent OKN, "inverted" pursuit, or "defective" pursuit (see section on CN) when targets are projected onto the temporal half-retina.[173] Periodic alternating nystagmus may also occur.[109,110] Albinism may also exist in the *absence* of any nystagmus.[174,175]

Achiasma is a very rare condition, first recognized in dogs (circa 1974) and then in humans (circa 1992). It is associated with the combination of CN and see-saw nystagmus, the latter diagnosed from videotape (in dogs in 1991 and in a human in 1993) and subsequently studied using eye-movement recordings.[32,176–181] In achiasma, all retinal fibers remain ipsilateral, passing to the ipsilateral lateral geniculates and visual cortexes. Thus, each visual cortex has a representation of the entire visual field, but stereopsis is impossible. There is no bitemporal hemianopia in achiasma. Figure 11–15 shows both the horizontal CN and the vertical component of the see-saw nystagmus in an achiasmatic canine (Fig. 11–15A) and an achiasmatic human (Fig. 11–15B). The hori-

TABLE 11–6. Saccadic Intrusions and Oscillations*

Bobbing/dipping	Saccadic lateropulsion
Inverse bobbing	Ipsipulsion
Reverse bobbing	Contrapulsion
Convergence-retraction "nystagmus"	Saccadic pulses/pulse trains
"Nystagmus" retractoris	Abduction "nystagmus"
Double saccadic pulses (single/multiple)	Ataxic "nystagmus"
Saccadic intrusions/oscillations	Saccadic intrusions/oscillations
Dynamic overshoot	Stepless saccades
"Quiver"	Square-wave jerks/oscillations
Dysmetria	Gegenrucke
Flutter	Hopping "nystagmus"
Flutter dysmetria	"Lightning eye movements"
Macrosaccadic oscillations	Myoclonus
Myoclonus	Saccadic intrusions/oscillations
Laryngeal "nystagmus"	Zickzakbewegungen
"Lightning eye movements"	Square-wave pulses (bursts/single)
Pharyngeal "nystagmus"	"Macro square-wave jerks"
Opsoclonus	Kippdeviationen/"Kippnystagmus"
"Dancing eyes"	"Pendular macro-oscillations"
"Lightning eye movements"	Saccadic "nystagmus"
Saccadomania	Saccadic oscillations/intrusions
Psychogenic flutter	Superior oblique myokymia
Hysterical flutter	
Hysterical "nystagmus"	
"Ocular fibrillation"	
"Ocular shuddering"	
Psychological "nystagmus"	
Voluntary flutter	
Voluntary "nystagmus"	

* Synonyms and other terms are indented under either the preferred or the more inclusive designation; quoted terms are erroneous or misleading.

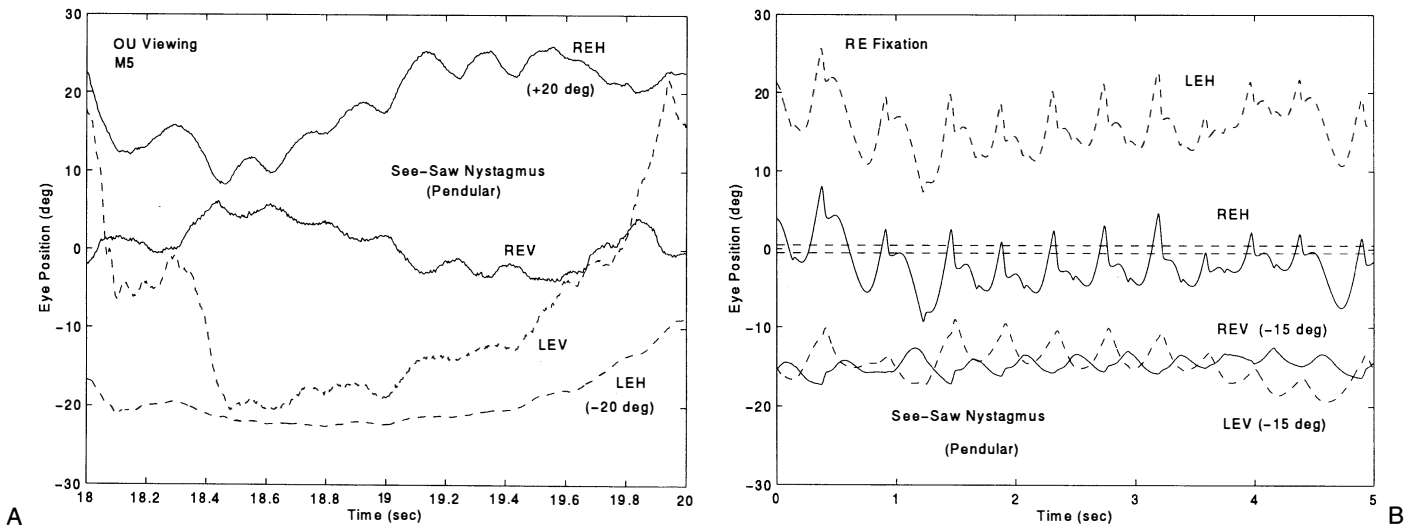

Fig. 11–15. The horizontal congenital nystagmus and vertical component of see-saw nystagmus in an achiasmatic Belgian sheepdog during binocular (*OU*) viewing **(A)** and an achiasmatic human during right-eye fixation **(B).** Note that the left eye in (B) was approximately 15° esotropic. When indicated, traces were shifted for clarity. *Dashed lines* in (B) define the foveal extent. *REH*, right eye horizontal; *LEH*, left eye horizontal; *REV*, right eye vertical; *LEV*, left eye vertical. Upward deflections indicate rightward or upward eye movements.

zontal and vertical waveforms of the canine's nystagmus and the human's vertical nystagmus were pendular, whereas the human's horizontal waveforms were pendular with foveating saccades (P_{FS}) or pseudopendular with foveating saccades (PP_{FS}). Since the achiasmatic human subject was not always able to achieve well-developed foveation, as shown by her inability to repeatedly foveate the target with her fixating right eye, the expanded NAF would be required to assess the best potential visual acuity in this segment. Unlike CN, which may or may not be associated with a particular sensory deficit, the see-saw nystagmus appears to be directly associated with achiasma in both species. In achiasma, there is no lesion, indeed no chiasm, and disruption of thalamic inputs to the nucleus of Cajal, postulated as the cause of acquired see-saw nystagmus, cannot be causal. In *hemichiasma*, abnormalities at the chiasm prevent decussation of the retinal fibers from one eye, the other decussating normally.[182] Whereas achiasma appears to be sufficient for SSN, hemichiasma is not. Because of the rarity of congenital see-saw nystagmus and its identification in both canines and humans with achiasma and in one of two canines with hemichiasma, we regard its presence in infants as a diagnostic sign of possible achiasma or hemichiasma.[183]

> The presence of SSN in an infant is a strong indication for imaging of the optic chiasm to rule out achiasma or structural abnormalities conducive to hemichiasma.

Tenotomy of the vertical and oblique muscles can damp SSN.[27]

Cerebellum

Some of the various eye signs seen with cerebellar system disease are discussed above and in Chapter 10. Descriptions of others will follow.

SACCADIC INTRUSIONS AND OSCILLATIONS

Non-nystagmic (*i.e.*, saccadic) ocular oscillations and intrusions represent specific and classifiable eye movement anomalies (Table 11–6). Many reflect cerebellar dysfunction. In Table 11–6, 16 types of saccadic intrusions and oscillations are identified, the most important of which are discussed below.

Square-Wave Jerks/Oscillations

Square-wave jerks (SWJs), so named because of their rectangular appearance on eye movement records (Fig. 11–16), are usually small-amplitude (0.5° to 5°), conjugate saccadic eye movements that spontaneously move the eyes away from, and back to, a fixational point. Between the two saccades that constitute this saccadic intrusion is a latent period of about 200 msec (the visual reaction time). SWJs have a maximum frequency of about 2 Hz and occur in normals on closure of eyelids. However, when they are prominent during fixation, they must be considered abnormal, although lacking diagnostic specificity, much like saccadic pursuit. SWJs are a subtle disturbance that is easily missed clinically. However, they are obvious with eye-movement recordings, which also allow other types of saccadic intrusions to be identified.[184] Clinically, they are often best identified during slit-lamp biomicroscopy or funduscopy, but they may be difficult to distinguish among other intrusions.

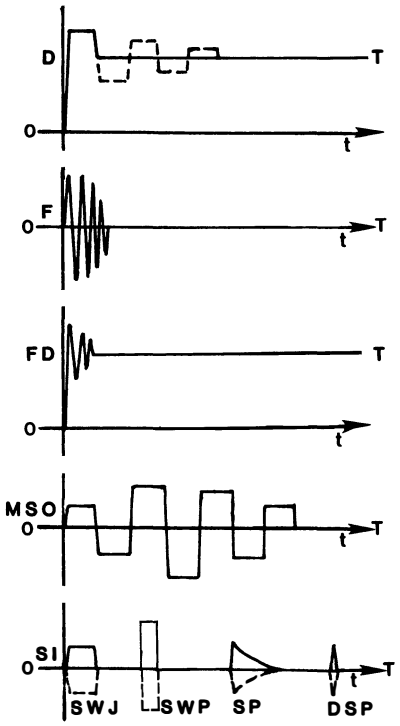

Fig. 11–16. Schematic illustrations of dysmetria (*D*), flutter (*F*), flutter dysmetria (*FD*), macro-saccadic oscillations (*MSO*), and the saccadic intrusions (*SI*): square-wave jerks (*SWJ*), square-wave pulses (*SWP*), saccadic pulses (*SP*), and double saccadic pulses (*DSP*). *T*, target; *O*, primary position; *t*, time.

The occurrence of SWJs is significantly greater in the elderly population than in young subjects. Their appearance at a rate greater than 9/minute in young patients is considered abnormal. SWJs also are found in 70% of patients with acute or chronic focal cerebral lesions and are the rule in progressive supranuclear palsy and Parkinson's disease. Schizophrenic patients and their parents[185] have been found to exhibit SWJs, which are also present during smooth pursuit and have been mistaken for a deficit in the pursuit system.

Square-wave oscillations (SWOs) are continuously occurring SWJs and have been recorded in patients with a variety of neurologic deficits. The characteristics are identical to those of SWJs (Table 11–7). In a patient with progressive supranuclear palsy, SWOs appeared to

TABLE 11–7. Characteristics of Saccadic Instabilities

	Square-wave jerks	Square-wave oscillations	Square-wave pulses*	Macro-saccadic oscillations
Amplitude	0.5°–5°† Constant	0.5°–5°† Constant	4°–30° Variable	1°–30° Increasing then decreasing
Time course	Sporadic/bursts	Bursts	Bursts/sporadic	Bursts
Latency	200 msec	200 msec	50–150 msec	200 msec
Foveation	Yes	Yes	Yes	No
Presence in darkness	Yes	Yes	Yes	No

* Previously designated macro–square-wave jerks.
† Occasionally up to 10°.

be part of a continuum with SWJs; at times, single or several SWJs occurred, and at other times there were long runs of SWJs that were identified as SWOs.[186]

Square-Wave Pulses

Square-wave pulses (SWPs), originally called "macro square-wave jerks," are usually larger in amplitude than SWJs, are related to fixation, and have a frequency of about 2 Hz.[187] They generally occur in bursts but may appear as a single saccadic intrusion. Both eyes suddenly and conjugately move off target with a saccade, and after a latent period of only about 80 msec, a nonvisually evoked reflex saccade brings them back on target (see Fig. 11–16). SWPs are not merely large SWJs; the characteristics of both are summarized in Table 11–7. SWPs usually occur in patients with marked extremity ataxia suggestive of cerebellar outflow disease, especially when the patient has demyelinating lesions.[187] A unique variety of SWP, present with binocular fixation at distance but stopping when either eye was closed, prompted the designation "inverse latent SWP."[188]

Macro-Saccadic Oscillations

Macro saccadic oscillations (MSOs) increase and then damp in amplitude, bypassing the fixation angle with each saccade (see Fig. 11–16).[189] Unlike SWJs, SWOs, and SWPs, MSOs are not present in darkness and have a longer latency for the return saccade than do SWPs. In a patient with suspected multiple sclerosis, MSOs were recorded as part of a constellation of saccadic intrusions and oscillations including SWJs, saccadic pulses (SPs), double saccadic pulses (DSPs), flutter, and flutter dysmetria (FD)[184] (see below for descriptions of these latter eye signs). A case has been reported in which SWP and MSO appeared to have a vertical component.[190] Administration of several sedative drugs caused these oscillations to disappear.

A comparison of the features of the four saccadic instabilities described above (SWJ, SWO, SWP, and MSO) appears in Table 11–7.

Saccadic Pulses/Pulse Trains

Saccadic pulses are intrusions on fixation caused by a spurious pulse of innervation, provided by the burst cells without the usual accompanying step; they were originally called "stepless saccades." The resultant eye movement is a saccade off-target followed immediately by a glissadic drift back to the target (see Fig. 11–16). The glissadic drift in SP represents failure of the neural integrator to produce a step of innervation from the burst producing the SP. This difference from SWJ suggests dysfunction in the pause cell/burst cell circuitry for SP and a more central dysfunction for SWJ.

Saccadic pulse trains (SPTs) are continuous runs of SPs that are often confused with nystagmus. Even on good eye-movement records, SPTs cannot be distinguished from jerk nystagmus with decreasing-velocity slow phases, unless both eye position and target position are known. The initiation of an SP is a saccade off-target, whereas jerk nystagmus is initiated by the slow phase off-target, with the saccadic fast phase bringing the eye back to the target. The so-called abduction nystagmus of internuclear ophthalmoplegia is SPT.[191] Recordings of several patients with congenital achromatopsia and thought to have CN have been recorded; however, their oscillations did not contain any of the known CN waveforms and were most consistent with SPT. The waveforms mimicked those of LMLN, but there were no evident effects of monocular fixation.

Double Saccadic Pulses

Double saccadic pulses (DSPs) are intrusions on fixation, consisting of two back-to-back saccades without latency between them (see Fig. 11–16).[184] Small DSPs are common in normals and also occur occasionally in some CN patients. Multiple DSPs (mDSPs) are runs of

DSPs.[184] There is a continuum between the saccadic intrusion DSP, mDSP, and the saccadic oscillation, flutter.[186]

Dysmetria

Strictly speaking, dysmetria refers to any inaccurate saccadic eye movement. With small saccades, normal subjects may undershoot or overshoot; with large saccades, small undershooting is the rule. Consistent overshooting during small refixations (10° or less), or more than occasional overshooting during refixations greater than 30°, is abnormal and indicative of cerebellar dysfunction (see Fig. 11–16).[192] The term *ocular dysmetria* is used to denote pathologic hypermetria. In experimental animals with cerebellar lesions, dysmetria may be unequal in the two eyes.[193] The components of the oscillation are usually flat at the peaks, indicating an intersaccadic latency,[192] but they may also be triangular or sinusoidal in appearance; the latter are probably cycles of flutter dysmetria (FD) (see below).

Quantitative studies can differentiate normal from pathologic saccadic dysmetria,[194] especially for saccades of 20° or more. Saccadic dysmetria with preserved smooth pursuit has been reported to be caused by midline lesions of cerebellar structures.[195] This occurs despite the known involvement of these areas with control of smooth pursuit. Dorsal cerebellar vermis angioma has produced dysmetria of all types of saccades (visually guided and visually, vestibularly, and cervically remembered)[196]; the observation that final eye position was normal in the memory-guided saccades suggests that this area is involved in the neural integration of the saccadic pulse for such saccades.

Flutter

Ocular flutter was originally defined clinically as any brief, intermittent, binocular, horizontal ocular oscillation occurring spontaneously during straight-ahead fixation. It differs from the oscillation of dysmetria, which always follows a saccadic refixation. In eye-movement recordings, flutter is triangular or sinusoidal in appearance, consisting of several back-to-back saccades (see Fig. 11–16).

Flutter represents a disturbance of the pause cells in the pontine paramedian reticular formation subserving horizontal eye movements.[197] Inappropriate inhibition of the pause cells leads to the burst cell activity that produces the flutter. Rarely, a blink will initiate a large-amplitude ocular flutter in patients with neurologic disease, and short bursts of low-amplitude flutter in normal subjects.[198] A microflutter ("microsaccadic" flutter) has been described in five patients with no identifiable neurologic disorders.[199] It was attributed to malfunction of the omnipause neurons. Flutter has also been reported with the AIDS-related complex[200] and in association with opsoclonus and myoclonus in patients with anti-Ri antibodies.[201]

Flutter and opsoclonus represent a continuum of ocular motor instability. Patients recovering from opsoclonus often develop a picture of flutter in which opsoclonus emerges, especially during upward gaze. As with opsoclonus, flutter may be a manifestation of a paraneoplastic syndrome,[202] and it may remit spontaneously even before the neoplasm is diagnosed.[203]

Flutter Dysmetria

Flutter dysmetria (FD) is the occurrence of flutter immediately after a saccade (see Fig. 11–16).[197] Although it superficially resembles dysmetria, eye-movement recordings reveal that FD is an oscillation about the intended fixation angle and consists of back-to-back saccades with no intersaccadic latencies. This contrasts with dysmetria in which the saccadic oscillation has normal intersaccadic latencies. FD is seen in a setting of cerebellar disease.

Opsoclonus

Opsoclonus is a bizarre ocular motor oscillation consisting of rapid, involuntary, chaotic, repetitive, unpredictable, conjugate saccadic eye movements in all directions and persisting during sleep. The movements are usually continuous except during patient recovery and in mild forms, during which brief paroxysms interrupt stable fixation. In this instance, the continuum between opsoclonus and ocular flutter, mentioned earlier, is readily apparent. Some paroxysms have characteristic oblique or half-circle vectors,[204] whereas others are entirely horizontal and indistinguishable from flutter.

Opsoclonus, usually associated with extremity myoclonus and ataxia, occurs in a number of clinical settings. In children, opsoclonus and generalized limb myoclonus may continue enigmatically for years, except when suppressed by adrenocorticotropic hormone (ACTH) therapy, which seems to be considerably more effective than corticosteroids. Opsoclonus and acute cerebellar ataxia may represent the sole manifestations of occult neuroblastoma, and the eye movements usually, but not always, remit after tumor removal. This variety of opsoclonus may also respond to ACTH. Opsoclonus only on eye closure was reported in two brothers with hereditary cerebellar ataxia.[205]

Rarely, opsoclonus is a self-limiting phenomenon that occurs in otherwise normal neonates. The so-called ocular tics seen in children usually occur with other types of tics, may be imitated on request, and may be associated with stress.[206] They appear to be bursts of opsoclonus when recorded.[207] In adults, opsoclonus can be secondary to a postinfectious syndrome (which has an

excellent prognosis for a complete recovery); brain stem encephalitis; toxicity due to amitriptyline, lithium, haloperidol, chlordecone, thallium, toluene, chlorophenothane, phenytoin, or diazepam; hyperosmolar nonketotic coma; and degenerative diseases.[208,209] It also occurs as a nonmetastatic, paraneoplastic complication of visceral carcinoma; some of these patients have anticerebellar antibodies in the serum and cerebrospinal fluid,[210,211] and their manifestations may improve with steroid[201,212] or immunoadsorption[213] therapy. Brain stem pause cell dysfunction is the presumed etiology, but these cells are normal pathologically in this syndrome.[214] Radiologic and pathologic correlation in a patient suggests involvement of both cerebellum and brain stem.[215] Electrophysiologic data suggest brain stem and cerebellar circuits are involved in idiopathic opsoclonus-myoclonus.[216] Extensive reviews of the literature are available.[217,218]

Myoclonus

Ocular myoclonus is a pendular oscillation that conforms to our definition of nystagmus and is indeed regarded as nystagmus by European writers. However, the eye movement is usually classified separately as myoclonus because of associated rhythmic movements of nonocular muscles in synchrony with the eyes. The soft palate is most commonly involved, but the tongue, facial muscles, pharynx, larynx, and diaphragm may also participate.

The term *myoclonus* is used, often confusingly, to describe several movement disorders. It may refer to spontaneous, episodic, single or multiple jerks of the extremities that constitute a form of seizure particularly prevalent in infants. The same movement provoked by a loud noise is termed *startle myoclonus* and occurs in adults with specific types of cerebral dysfunction, such as anoxic encephalopathy or Creutzfeldt-Jakob disease. Similar movements occur in normal subjects before falling asleep and represent a physiologic phenomenon, probably of spinal origin. Myoclonus also describes the arrhythmic, asymmetric, sudden, brief, involuntary jerks of one or more muscles of the extremities, often reflecting a metabolic derangement or degenerative central nervous system disease with cerebellar involvement.

Ocular myoclonus is a form of segmental myoclonus and is characterized by continuous, rhythmic, to-and-fro pendular oscillation, usually in the vertical plane, with a rate of 1.5 to 5 beats per second. Only the coexisting movements of other structures, such as the palate, distinguish ocular myoclonus from pendular nystagmus. Actually, isolated palatal myoclonus (symptomatic or essential)[219] is more common than the oculopalatal variety and may be a benign, self-limited process that variably responds to anticonvulsants. At times the eye movements have an oblique and rotary vector.[220]

Oculopalatal myoclonus has a rather specific pathologic correlate—hypertrophy of the inferior olivary nucleus in the medulla. The myoclonic triangle involves three structures: the red nucleus in the midbrain, the ipsilateral inferior olive in the medulla, and the contralateral dentate nucleus of the cerebellum. The connecting pathways are the central tegmental tract, the inferior cerebellar peduncle, and the superior cerebellar peduncle. Pathologic involvement of the central tegmental tract produces hypertrophy of the ipsilateral inferior olive after a latency of 2 to 49 months, with a mean at about 10.5 months.[221] Damage to a dentate nucleus results in contralateral olivary hypertrophy after a similar latency. Oculopalatal myoclonus develops as a consequence of the olivary hypertrophy and, therefore, is not a manifestation of acute lesions. The mechanism for the hypertrophy is believed to be denervation supersensitivity[221] related to transneuronal degeneration.[222] Once established, myoclonus ordinarily persists, even during sleep, as a chronic sign until the death of the patient.[223] Occasionally, isolated palatal myoclonus disappears during sleep.[224] A single case of ocular myoclonus responded dramatically to valproic acid[225] and another to chronic one-eye patching.[226] Trihexyphenidyl seems to be the most effective therapy.[227]

Superior Oblique Myokymia

Superior oblique myokymia is an intermittent, small-amplitude, monocular, torsional eye movement ("microtremor") evoking oscillopsia, which appears spontaneously in otherwise healthy adults and only rarely, perhaps even coincidentally, with other neurologic disease.[228] The oscillation is rapid in rate (12 to 15 per second) and reflects phasic contraction of the superior oblique muscle.[229] The movement is detected most readily during ophthalmoscopy or by use of the slit lamp. Eye movement recordings reveal either slow, sustained tonic intorsion and depression, or a phasic intorsion with superimposed high-frequency oscillations in both the vertical and torsional planes; each intorsion is followed by a decreasing-velocity return.[230,231] The spectrum of the oscillations includes low-amplitude components up to 50 Hz and high-amplitude components from 1 to 6 Hz.

Recognition of the entity and reassurance of the patient are essential. Rosenberg and Glaser[232] have presented an extensive longitudinal study of patients and emphasize that the disorder may have varying clinical manifestations and that spontaneous remissions and relapses occur. Treatment with carbamazepine provides short-term benefit to most patients.[232] There is disagreement as to the appropriateness of the term *myokymia,*[233] but the usual benignity of the condition can no longer remain unquestioned.[230] The source of the oscillation is

uncertain.[234,235] A review of the history and results of treatment is available.[236]

Bobbing/Dipping

Ocular bobbing is a distinctive spontaneous eye-movement disturbance, readily distinguished from downbeat nystagmus and ocular myoclonus. Bobbing refers to fast downward jerks of both eyes followed by a slow drift to midposition. The downward jerks may be disconjugate in the two eyes, and often the eyes remain deviated for several seconds before returning to midposition. Bobbing usually occurs in comatose patients with extensive destruction of the pons, but extrapontine compressions, obstructive hydrocephalus, metabolic encephalopathy, and encephalitis occasionally are causative.[237]

Bobbing can be divided into three types. Typical bobbing involves both eyes and appears in patients with paralysis of horizontal conjugate eye movements. A monocular type reflects co-existing contralateral third-nerve paresis. The third category, atypical bobbing, includes downward bobbing with convergence movements, asymmetric bobbing without an associated oculomotor palsy, and bobbing with intact spontaneous or reflex horizontal eye movements; the latter variety suggests diffuse encephalopathy, hydrocephalus, or organophosphate poisoning, rather than severe intrinsic pontine disease. The pathophysiology of all forms of ocular bobbing is uncertain, but imaginative hypotheses abound. In two cases, a pontine lesion plus an oculomotor lesion resulted in uniocular bobbing,[238] but in another, no explanation could be found.[239]

In addition to these three types of bobbing (typical, monocular, and atypical), we described a phenomenon designated "reverse bobbing," in which the eyes jerked upward with a fast movement and then slowly returned to the horizontal; the patients were deeply comatose as a result of metabolic encephalopathy. Reverse bobbing may co-exist with typical bobbing with lesions of the dorsal median portion of the pontine tegmentum.[240]

In 1981 there were two reports of comatose patients who demonstrated a slow downward eye movement, followed, after a variable delay, by a quick saccade up to midposition. This disorder was called "inverse bobbing" in one report[241] and "ocular dipping" in the other.[242] The latter term, *dipping,* seems to have achieved favor.[243,244] The upward jerking of the eyes is occasionally associated with contraction of the orbicularis oculi.[245] The phenomenon is regarded as mechanistically similar to the sustained down-gaze deviation seen occasionally in comatose patients. This sign occurred in a patient with a pinealoblastoma[246]; a depressed level of consciousness is not a prerequisite for its appearance. Some patients in coma may demonstrate all three types of spontaneous vertical movements: ocular bobbing, ocular dipping, and reverse bobbing.[247]

Voluntary "Nystagmus"

Voluntary "nystagmus" consists of bursts of an extremely rapid, conjugate, horizontal oscillation that appears pendular but actually consists of back-to-back saccades.[248] As shown in Table 11–6, it is equivalent to flutter.[197] It may be used as a party trick or as a conscious attempt to feign illness. The oscillation is readily identified by the extreme rapidity (approximately 20 Hz, with a range of 8 to 23 Hz) and brevity of each burst (maximum duration usually less than 30 seconds). Most subjects do not sustain the oscillation for more than 10 seconds, and manifest facial distortions with eyelid closure to "rest" their eyes in preparation for another outburst. The ability to perform this stunt may be hereditary, and is present in about 5% of the population.[249] Rarely, voluntary "nystagmus" is in the vertical plane[250] or is multidirectional, mimicking opsoclonus.[251]

REFERENCES

1. Wartenberg R: Diagnostic Tests in Neurology. A Selection for Office Use. Chicago, Yearbook, 1953
2. Doslak MJ, Dell'Osso LF, Daroff RB: Alexander's law: a model and resulting study. Ann Otol Rhinol Laryngol 91:316, 1982
3. Barton JJS, Sharpe JA: Oscillopsia and horizontal nystagmus with accelerating slow phases following lumbar puncture in the Arnold-Chiari malformation. Ann Neurol 33:418, 1993
4. Abel LA, Traccis S, Dell'Osso LF et al: Variable waveforms in downbeat nystagmus imply short-term gain changes. Ann Neurol 13:616, 1983
5. Gresty MA, Bronstein AM, Page NG et al: Congenital-type nystagmus emerging in later life. Neurology 41:653, 1991
6. Hertle RW, Dell'Osso LF: Clinical and ocular motor analysis of congenital nystagmus in infancy. J Am Pediatr Ophthalmol Strab 3:70, 1999
7. Dell'Osso LF, Daroff RB: Congenital nystagmus waveforms and foveation strategy. Doc Ophthalmol 39:155, 1975
8. Dell'Osso LF, Gauthier G, Liberman G et al: Eye movement recordings as a diagnostic tool in a case of congenital nystagmus. Am J Optom Arch Am Acad Optom 49:3, 1972
9. Dell'Osso LF, Weissman BM, Leigh RJ et al: Hereditary congenital nystagmus and gaze-holding failure: the role of the neural integrator. Neurology 43:1741, 1993
10. Optican LM, Zee DS: A hypothetical explanation of congenital nystagmus. Biol Cyber 50:119, 1984
11. Tusa RJ, Zee DS, Hain TC et al: Voluntary control of congenital nystagmus. Clin Vis Sci 7:195, 1992
12. Harris CM: Problems in modelling congenital nystagmus: towards a new model. In Findlay JM, Walker R, Kentridge RW (eds): Eye Movement Research: Mechanisms, Processes and Applications, p 239. Amsterdam, Elsevier, 1995
13. Goldstein HP: Extended slow phase analysis of foveation, waveform and null zone in infantile nystagmus. Invest Ophthalmol Vis Sci 36:S174, 1995
14. Dell'Osso LF, Flynn JT, Daroff RB: Hereditary congenital nystagmus: an intrafamilial study. Arch Ophthalmol 92:366, 1974
15. Tusa RJ, Smith CB, Herdman SJ: The development of nystagmus in infant monkeys following visual deprivation. Soc Neurosci Abstr 13:172, 1987
16. Demer JL, Poukens V, Micevych P: Nitroxidergic and catecholaminergic innervation of the smooth muscle of the medial rectus pulley in humans. Invest Ophthalmol Vis Sci 36:S959, 1995

17. Bedell HE, White JM: The torsional component of idiopathic congenital nystagmus. Invest Ophthalmol Vis Sci 36:S174, 1995
18. Abadi RV, Dickinson CM: Waveform characteristics in congenital nystagmus. Doc Ophthalmol 64:153, 1986
19. Stahl JS, Rottach KG, Averbuch-Heller L et al: A pilot study of gabapentin as treatment for acquired nystagmus. Neuro-ophthalmology 16:107, 1996
20. Dell'Osso LF: Congenital, latent and manifest latent nystagmus—similarities, differences and relation to strabismus. Jpn J Ophthalmol 29:351, 1985
21. Dell'Osso LF, Van der Steen J, Steinman RM et al: Foveation dynamics in congenital nystagmus I: fixation. Doc Ophthalmol 79:1, 1992
22. Zubcov AA, Stärk N, Weber A et al: Improvement of visual acuity after surgery for nystagmus. Ophthalmology 100:1488, 1993
23. Dell'Osso LF: Fixation characteristics in hereditary congenital nystagmus. Am J Optom Arch Am Acad Optom 50:85, 1973
24. Bedell HE, White JM, Abplanalp PL: Variability of foveations in congenital nystagmus. Clin Vision Sci 4:247, 1989
25. Abadi RV, Worfolk R: Retinal slip velocities in congenital nystagmus. Vision Res 29:195, 1989
26. Guo S, Reinecke RD, Goldstein HP: Visual acuity determinants in infantile nystagmus. Invest Ophthalmol Vis Sci 31:83, 1990
27. Dell'Osso LF, Hertle RW, Williams RW, Jacobs JB: A new surgery for congenital nystagmus: effects of tenotomy on an achiasmatic canine and the role of extraocular proprioception. J Am Acad Pediatr Ophthalmol Strab 3:166, 1999
28. Abadi RV, Pascal E, Whittle J et al: Retinal fixation behavior in human albinos. Optom Vis Sci 66:276, 1989
29. Dell'Osso LF, Van der Steen J, Steinman RM et al: Foveation dynamics in congenital nystagmus II: smooth pursuit. Doc Ophthalmol 79:25, 1992
30. Dell'Osso LF, Van der Steen J, Steinman RM et al: Foveation dynamics in congenital nystagmus III: vestibulo-ocular reflex. Doc Ophthalmol 79:51, 1992
31. Sheth NV, Dell'Osso LF, Leigh RJ et al: The effects of afferent stimulation on congenital nystagmus foveation periods. Vision Res 35:2371, 1995
32. Dell'Osso LF: See-saw nystagmus in dogs and humans: an international, across-discipline, serendipitous collaboration. Neurology 47:1372, 1996
33. Halmagyi GM, Gresty MA, Leech J: Reversed optokinetic nystagmus (OKN): mechanism and clinical significance. Ann Neurol 7:429, 1980
34. Gresty MA, Halmagyi GM, Leech J: The relationship between head and eye movement in congenital nystagmus with head shaking: objective recordings of a single case. Br J Ophthalmol 62:533, 1978
35. Dell'Osso LF, Leigh RJ: Oscillopsia suppression: efference copy or foveation periods? Invest Ophthalmol Vis Sci 36:S174, 1995
36. Dell'Osso LF, Leigh RJ: Foveation period stability and oscillopsia suppression in congenital nystagmus. An hypothesis. Neuro-ophthalmology 12:169, 1992
37. Dell'Osso LF, Leigh RJ: Ocular motor stability of foveation periods. Required conditions for suppression of oscillopsia. Neuro-ophthalmology 12:303, 1992
38. Dell'Osso LF: Evaluation of smooth pursuit in the presence of congenital nystagmus. Neuro-ophthalmology 6:383, 1986
39. Leigh RJ, Dell'Osso LF, Yaniglos SS et al: Oscillopsia, retinal image stabilization and congenital nystagmus. Invest Ophthalmol Vis Sci 29:279, 1988
40. Goldstein HP, Gottlob I, Fendick MG: Visual remapping in infantile nystagmus. Vision Res 32:1115, 1992
41. Bedell HE, Currie DC: Extraretinal signals for congenital nystagmus. Invest Ophthalmol Vis Sci 34:2325, 1993
42. Daroff RB, Dell'Osso LF: Periodic alternating nystagmus and the shifting null. Can J Otolaryngol 3:367, 1974
43. Kurzan R, Büttner U: Smooth pursuit mechanisms in congenital nystagmus. Neuro-ophthalmology 9:313, 1989
44. Dell'Osso LF, Leigh RJ, Daroff RB: Suppression of congenital nystagmus by cutaneous stimulation. Neuro-ophthalmology 11: 173, 1991
45. Abadi RV: Visual performance with contact lenses and congenital idiopathic nystagmus. Br J Physiol Optics 33:32, 1979
46. Allen ED, Davies PD: Role of contact lenses in the management of congenital nystagmus. Br J Ophthalmol 67:834, 1983
47. Dell'Osso LF, Traccis S, Abel LA et al: Contact lenses and congenital nystagmus. Clin Vision Sci 3:229, 1988
48. Matsubayashi K, Fukushima M, Tabuchi A: Application of soft contact lenses for children with congenital nystagmus. Neuro-ophthalmology 12:47, 1992
49. Shallo-Hoffmann J, Watermeier D, Petersen J et al: Fast-phase instabilities in normally sighted relatives of congenital nystagmus patients—autosomal dominant and x-chromosome recessive modes of inheritance. Neurosurg Rev 11:151, 1988
50. Gottlob I: Eye movement abnormalities in carriers of blue-one monochromatism. Invest Ophthalmol Vis Sci 35:3556, 1994
51. Dell'Osso LF, Schmidt D, Daroff RB: Latent, manifest latent and congenital nystagmus. Arch Ophthalmol 97:1877, 1979
52. Shallo-Hoffman J, Faldon ME, Acheson JF et al: Temporally directed deficits for the detection of visual motion in latent nystagmus: evidence for adaptive processing. Neuro-ophthalmology 16:343, 1996
53. Dickinson CM, Abadi RV: Pursuit and optokinetic responses in latent/manifest latent nystagmus. Invest Ophthalmol Vis Sci 31:1599, 1990
54. Fuchs AF, Mustari MJ: The optokinetic response in primates and its possible neuronal substrate. In Wallman J, Miles FA (eds): Reviews of Oculomotor Research, Vol 5, Visual Motion and its Role in Stabilization of the Gaze, p 343. Amsterdam, Elsevier, 1993
55. Steinbach MJ, Smith D, Crawford JS: Egocentric localization changes following unilateral strabismus surgery. J Pediatr Ophthalmol Strab 25:115, 1988
56. Dell'Osso LF, Leigh RJ, Sheth NV et al: Two types of foveation strategy in 'latent' nystagmus. Fixation, visual acuity and stability. Neuro-ophthalmology 15:167, 1995
57. Dell'Osso LF, Traccis S, Abel LA: Strabismus—a necessary condition for latent and manifest latent nystagmus. Neuro-ophthalmology 3:247, 1983
58. Schor CM, Wilson N, Fusaro R: Prediction of early onset esotropia from components of the infantile squint syndrome. Invest Ophthalmol Vis Sci 36:S645, 1995
59. Zubcov AA, Reinecke RD, Gottlob I et al: Treatment of manifest latent nystagmus. Am J Ophthalmol 110:160, 1990
60. Gresty MA, Metcalfe T, Timms C et al: Neurology of latent nystagmus. Brain 115:1303, 1992
61. Dell'Osso LF, Ellenberger C Jr, Abel LA et al: The nystagmus blockage syndrome: congenital nystagmus, manifest latent nystagmus or both? Invest Ophthalmol Vis Sci 24:1580, 1983
62. Yee RD, Baloh RW, Honrubia V: Eye movement abnormalities in rod monochromacy. Ophthalmology 88:1010, 1981
63. Leigh RJ, Zee DS: Eye movements of the blind. Invest Ophthalmol Vis Sci 19:328, 1980
64. Melvill Jones G, Mandl G, Cynader M et al: Eye oscillations in strobe reared cats. Brain Res 209:47, 1981
65. Hoyt CS, Aicardi E: Acquired monocular nystagmus in monozygous twins. J Pediatr Ophthalmol Strab 16:115, 1979
66. Lavery MA, O'Neill JF, Chu FC et al: Acquired nystagmus in early childhood: a presenting sign of intracranial tumor. Ophthalmology 91:425, 1984
67. Lambert SR, Newman NJ: Retinal disease masquerading as spasmus nutans. Neurology 43:1607, 1993
68. Allarakhia IN: Opsoclonus-myoclonus presenting with features of spasmus nutans. J Child Neurol 10:67, 1995
69. Gresty MA, Leech J, Sanders MD et al: A study of head and eye movement in spasmus nutans. Br J Ophthalmol 160:652, 1976
70. Weismann BM, Dell'Osso LF, Abel LA et al: Spasmus nutans: a quantitative prospective study. Arch Ophthalmol 105:525, 1987
71. Barton JJS, Cox TA: Acquired pendular nystagmus: its characteristics, localizing value and pathophysiology. J Neurol Neurosurg Psychiatry 56:262, 1993
72. Barton JJS: Is acquired pendular nystagmus always phase locked? J Neurol Neurosurg Psychiatry 57:1263, 1994

73. Kori AA, Robin NH, Jacobs JB et al: Pendular nystagmus in autosomal peroxisomal disorder. Arch Neurol 55:554, 1998
74. Averbuch-Heller L, Tusa RJ, Fuhry L et al: A double-blind controlled study of gabapentin and baclofen as treatment for acquired nystagmus. Ann Neurol 41:818, 1997
75. Barton JS, Huaman AG, Sharpe JA: Muscarinic antagonists in the treatment of acquired pendular and downbeat nystagmus: a double-blind, randomized trial of three intravenous drugs. Ann Neurol 35:319, 1994
76. Tomsak RL, Remler BF, Averbuch-Heller L et al: Unsatisfactory treatment of acquired nystagmus with retrobulbar injection of botulinum toxin. Am J Ophthalmol 119:489, 1995
77. Averbuch-Heller L, Remler B: Opsoclonus. Semin Neurol 16:21, 1996
78. Averbuch-Heller L, Zivotofsky AZ, Das VE et al: Investigations of the pathogenesis of acquired pendular nystagmus. Brain 118:369, 1995
79. Baloh RW, Winder A: Acetazolamide-responsive vestibulocerebellar syndrome: clinical and oculographic features. Neurology 41:429, 1991
80. Kramer PL, Yue Q, Gancher ST et al: A locus for the nystagmus-associated form of episodic ataxia maps to an 11 cM region on chromosome 19p. Am J Hum Genet 57:182, 1995
81. Lawden MC, Bronstein AM, Kennard C: Repetitive paroxysmal nystagmus and vertigo. Neurology 45:276, 1995
82. Brandt T, Daroff RB: The multisensory physiological and pathological vertigo syndromes. Ann Neurol 7:195, 1980
83. Holtmann S, Clarke A, Scherer H: Cervical receptors and the direction of body sway. Arch Otorhinolaryngol 246:61, 1989
84. Zee DS, Preziosi TJ, Proctor LR: Bechterew's phenomenon in a human patient. Ann Neurol 12:495, 1982
85. Dayal VS, Farkashidy J, Mai M et al: Vestibular compensation and nystagmus. Acta Otolaryngol Suppl (Stockh) 406:105, 1984
86. Reker U: Peripheral-vestibular spontaneous nystagmus. Analysis of reproducibility and methodologies. Arch Otorhinolaryngol 226:225, 1980
87. Abel LA, Parker L, Daroff RB et al: Endpoint nystagmus. Invest Ophthalmol Vis Sci 17:539, 1978
88. Shallo-Hoffmann J, Schwarze H, Simonsz HJ et al: A reexamination of end-point and rebound nystagmus in normals. Invest Ophthalmol Vis Sci 31:388, 1990
89. Eizenman M, Cheng P, Sharpe JA et al: End-point nystagmus and ocular drift: an experimental and theoretical study. Vision Res 30:863, 1990
90. Lopez L, Bronstein AM, Gresty MA et al: Torsional nystagmus. A neuro-otological and MRI study of thirty-five cases. Brain 115:1107, 1992
91. Halmagyi GM, Aw ST, Dehaene I et al: Jerk-waveform seesaw nystagmus due to unilateral mesodiencephalic lesion. Brain 117:789, 1994
92. Barton JJS: Blink- and saccade-induced seesaw nystagmus. Neurology 45:831, 1995
93. Frisén L, Wikkelsø C: Posttraumatic seesaw nystagmus abolished by ethanol ingestion. Neurology 36:841, 1986
94. Zimmerman CF, Roach ES, Troost BT: See-saw nystagmus associated with Chiari malformation. Arch Neurol 43:299, 1986
95. Samkoff LM, Smith CR: See-saw nystagmus in a patient with clinically definite MS. Eur Neurol 34:228, 1994
96. May EF, Truxal AR: Loss of vision may result in seesaw nystagmus. J Neuro-ophthalmol 17:84, 1997
97. Nakada T, Kwee IL: Seesaw nystagmus. Role of visuovestibular interaction in its pathogenesis. J Clin Neuro-ophthalmol 8:171, 1988
98. Bergin DJ, Halpern J: Congenital see-saw nystagmus associated with retinitis pigmentosa. Ann Ophthalmol 18:346, 1986
99. Daroff RB, Hoyt WF, Sanders MD et al: Gaze-evoked eyelid and ocular nystagmus inhibited lby the near reflex: unusual ocular motor phenomena in a lateral medullary syndrome. J Neurol Neurosurg Psychiatry 31:362, 1968
100. Safran AB, Berney J, Safran E: Convergence-evoked eyelid nystagmus. Am J Ophthalmol 93:48, 1982
101. Lavin PJM, Traccis S, Dell'Osso LF et al: Downbeat nystagmus with a pseudocycloid waveform: improvement with base-out prisms. Ann Neurol 13:621, 1983
102. Cox TA, Corbett JJ, Thompson HS et al: Upbeat nystagmus changing to downbeat nystagmus with convergence. Neurology 31:891, 1981
103. Noda S, Ide K, Umezaki H et al: Repetitive divergence. Ann Neurol 21:109, 1987
104. Oohira A, Goto K, Ozawa T: Convergence nystagmus. Neuro-ophthalmology 6:313, 1986
105. Nelson KR, Brenner RP, Carlow TJ: Divergent-convergent eye movements and transient eyelid opening associated with an EEG burst-suppression pattern. Neuro-ophthalmology 6:43, 1986
106. Averbuch-Heller L, Zivotofsky AZ, Remler BF et al: Convergent-divergent pendular nystagmus: possible role of the vergence system. Neurology 45:509, 1995
107. Sharpe JA, Hoyt WF, Rosenberg MA: Convergence-evoked nystagmus: congenital and acquired forms. Arch Neurol 32:191, 1975
108. Hara T, Kawazawa S, Abe Y et al: Conjugate pendular nystagmus evoked by accommodative vergence. Eur Neurol 25:369, 1986
109. Guyer DR, Lessell S: Periodic alternating nystagmus associated with albinism. J Clin Neuro-ophthalmol 6:82, 1986
110. Abadi RV, Pascal E: Periodic alternating nystagmus in humans with albinism. Invest Ophthalmol Vis Sci 35:4080, 1994
111. Leigh RJ, Robinson DA, Zee DS: A hypothetical explanation for periodic alternating nystagmus: instability in the optokinetic-vestibular system. Ann NY Acad Sci 374:619, 1981
112. Furman JMR, Wall C III, Pang D: Vestibular function in periodic alternating nystagmus. Brain 113:1425, 1990
113. Waespe W, Cohen B, Raphan T: Dynamic modification of the vestibulo-ocular reflex by the nodulus and uvula. Science 228: 199, 1985
114. Campbell WW Jr: Periodic alternating nystagmus in phenytoin intoxication. Arch Neurol 37:178, 1980
115. Halmagyi GM, Rudge P, Gresty MA et al: Treatment of periodic alternating nystagmus. Ann Neurol 8:609, 1980
116. Nuti D, Ciacci G, Giannini F et al: Aperiodic alternating nystagmus: report of two cases and treatment by baclofen. Ital J Neurol Sci 7:453, 1986
117. Lewis JM, Kline LB: Periodic alternating nystagmus associated with periodic alternating skew deviation. J Clin Neuro-ophthalmol 3:115, 1983
118. Kennard C, Barger G, Hoyt WF: The association of periodic alternating nystagmus with periodic alternating gaze. J Clin Neuro-ophthalmol 1:191, 1981
119. Vighetto A, Froment JC, Trillet M et al: Magnetic resonance imaging in familial paroxysmal ataxia. Arch Neurol 45:547, 1988
120. Baloh RW, Spooner JW: Downbeat nystagmus: a type of central vestibular nystagmus. Neurology 31:304, 1981
121. Halmagyi GM, Rudge P, Gresty MA et al: Downbeating nystagmus. A review of 62 cases. Arch Neurol 40:777, 1983
122. Rosengart A, Hedges TR III, Teal PA et al: Intermittent downbeat nystagmus due to vertebral artery compression. Neurology 43:216, 1993
123. Schmidt D: Downbeat nystagmus. A clinical review. Neuro-ophthalmology 11:247, 1991
124. Egan DJ: Optical treatment of downbeat nystagmus induced oscillopsia. Invest Ophthalmol Vis Sci 36:S351, 1995
125. Gresty MA, Barratt H, Rudge P et al: Analysis of downbeat nystagmus. Arch Neurol 43:52, 1986
126. Baloh RW, Yee RD: Spontaneous vertical nystagmus. Rev Neurol 145:527, 1989
127. Rousseaux M, Dupard T, Lesoin F et al: Upbeat and downbeat nystagmus occurring successively in a patient with posterior medullary hemorrhage. J Neurol Neurosurg Psychiatry 54:367, 1991
128. Tokumasu K, Fujino A, Yoshio S et al: Upbeat nystagmus in primary eye position. Acta Otolaryngol (Stockh) 481:366, 1991
129. Ranalli PJ, Sharpe JA: Upbeat nystagmus and the ventral tegmental pathway of the upward vestibuloocular reflex. Neurology 38:1329, 1988
130. Fisher A, Gresty MA, Chambers B et al: Primary position upbeating nystagmus: a variety of central positional nystagmus. Brain 106:949, 1983
131. Keane JR, Itabashi HH: Upbeat nystagmus: clinicopathologic study of two patients. Neurology 37:491, 1987
132. Büttner U, Helmchen Ch, Büttner-ennever JA: The localizing

value of nystagmus in brainstem disorders. Neuro-ophthalmology 15:283, 1995
133. Albera R, Luda E, Machetta G et al: Cyclosporine A as a possible cause of upbeating nystagmus. Neuro-ophthalmology 17:163, 1997
134. Kattah JC, Dagi TF: Compensatory head tilt in upbeating nystagmus. J Clin Neuro-ophthalmol 10:27, 1990
135. Sibony PA, Evinger C, Manning KA: Tobacco-induced primary-position upbeat nystagmus. Ann Neurol 21:53, 1987
136. Bondar RL, Sharpe JA, Lewis AJ: Rebound nystagmus in olivocerebellar atrophy: a clinicopathological correlation. Ann Neurol 15:474, 1984
137. Helmchen Ch, Büttner U: Centripetal nystagmus in a case of Creutzfeldt-Jakob disease. Neuro-ophthalmology 15:187, 1995
138. Traccis S, Rosati G, Monaco MF et al: Successful treatment of acquired pendular elliptical nystagmus in multiple sclerosis with isoniazid and base-out prisms. Neurology 40:492, 1990
139. De Jong JMBV, Bless W, Bovenkerk G: Nystagmus, gaze shift, and self-motion perception during sinusoidal head and neck rotation. Ann NY Acad Sci 374:590, 1981
140. Hamann KF: Kritische Anmerkungen zum sogenannten zervikogenen Schwindel. Laryngol Rhinol Otol 64:156, 1985
141. Norre ME, Stevens A: Diagnostic and semiological problem with special emphasis upon "cervical nystagmus." Acta Otorhinolaryngol Belg 41:436, 1987
142. Schmidt D, Dell'Osso LF, Abel LA et al: Myasthenia gravis: dynamic changes in saccadic waveform, gain and velocity. Exp Neurol 68:365, 1980
143. Howard RS: A case of convergence evoked eyelid nystagmus. J Clin Neuro-ophthalmol 6:169, 1986
144. Brodsky MC, Boop FA: Lid nystagmus as a sign of intrinsic midbrain disease. J Neuro-ophthalmol 15:236, 1995
145. Lavin PJM: Pupillary oscillations synchronous with ictal nystagmus. Neuro-ophthalmology 6:113, 1986
146. Kaplan PW, Lesser RP: Vertical and horizontal epileptic gaze deviation and nystagmus. Neurology 39:1391, 1989
147. Tusa RJ, Kaplan PW, Hain TC et al: Ipsiversive eye deviation and epileptic nystagmus. Neurology 40:662, 1989
148. Thurston SE, Leigh RJ, Osorio I: Epileptic gaze deviation and nystagmus. Neurology 35:1518, 1985
149. Kaplan PW, Tusa RJ: Neurophysiologic and clinical correlations of epileptic nystagmus. Neurology 43:2508, 1993
150. Von Baumgarten R, Benson A, Brand U et al: Effects of rectilinear acceleration and optokinetic and caloric stimulations in space. Science 225:208, 1984
151. Paige GD: Caloric responses after horizontal canal inactivation. Acta Otolaryngol (Stockh) 100:321, 1985
152. Buettner UW, Zee DS: Vestibular testing in comatose patients. Arch Neurol 46:561, 1989
153. Baloh RW, Honrubia V, Jacobson K: Benign positional vertigo: clinical and oculographic features in 240 cases. Neurology 37: 371, 1987
154. Lin J, Elidan J, Baloh RW et al: direction-changing positional nystagmus. Am J Otolaryngol 7:306, 1986
155. Brandt T, Steddin S, Daroff RB: Therapy for benign paroxysmal positioning vertigo, revisited. Neurology 44:796, 1994
156. Kattah JC, Kolsky MP, Luessenhop AJ: Positional vertigo and the cerebellar vermis. Neurology 34:527, 1984
157. Baloh RW, Jacobson K, Honrubia V: Horizontal semicircular canal variant of benign positional vertigo. Neurology 43:2542, 1993
158. Lempert T: Horizontal benign positional vertigo. Neurology 44: 2213, 1994
159. Esser J, Brandt T: Pharmakologisch verursachte Augenbewegungsstörungen—Differentialdiagnose und Wirkungsmechanismen. Fortschr Neurol Psychiatr 51:41, 1983
160. Coppeto JR, Monteiro MLR, Lessel S et al: Downbeat nystagmus. Arch Neurol 40:754, 1983
161. Corbett JJ, Jacobson DM, Thompson HS et al: Downbeating nystagmus and other ocular motor defects caused by lithium toxicity. Neurology 39:481, 1989
162. Rosenberg ML: Reversible downbeat nystagmus secondary to excessive alcohol intake. J Clin Neuro-ophthalmol 7:23, 1987
163. Kattah JC, Schilling R, Liu S-J et al: Oculomotor manifestations of acute alcohol intoxication. In Smith JL, Katz RS (eds): Neuro-Ophthalmology Enters the Nineties, p 233. Miami, Dutton Press, 1988
164. Maas EF, Ashe J, Spiegel BA et al: Acquired pendular nystagmus in toluene addiction. Neurology 41:282, 1991
165. Yokota J-I, Imai H, Okuda O et al: Inverted Bruns' nystagmus in arachnoid cysts of the cerebellopontine angle. Eur Neurol 33:62, 1993
166. Waespe W, Wichmann W: Oculomotor disturbances during visual-vestibular interaction in Wallenberg's lateral medullary syndrome. Brain 113:821, 1990
167. Waespe W, Baumgartner R: Enduring dysmetria and impaired gain adaptivity of saccadic eye movements in Wallenberg's lateral medullary syndrome. Brain 115:1125, 1992
168. Dieterich M, Brandt T: Wallenberg's syndrome: lateropulsion, cyclorotation, and subjective visual vertical in thirty-six patients. Ann Neurol 31:399, 1992
169. Morrow MJ, Sharpe JA: Torsional nystagmus in the lateral medullary syndrome. Ann Neurol 24:390, 1988
170. Brazis PW: Ocular motor abnormalities in Wallenberg's lateral medullary syndrome. Mayo Clin Proc 67:365, 1992
171. Ranailli PJ, Sharpe JA: Contrapulsion of saccades and ipsilateral ataxia: a unilateral disorder of the rostral cerebellum. Ann Neurol 20:311, 1986
172. Solomon D, Galetta SL, Grant TL: Possible mechanisms for horizontal gaze deviation and lateropulsion in the lateral medullary syndrome. J Neuro-ophthalmol 15:26, 1995
173. Collewijn H, Apkarian P, Spekreijse H: The oculomotor behaviour of human albinos. Brain 108:1, 1985
174. Apkarian P, Shallo-Hoffmann J: VEP projections in congenital nystagmus; VEP asymmetry in albinism: a comparison study. Invest Ophthalmol Vis Sci 32:2653, 1991
175. Cheong PYY, King RA, Bateman JB: Oculocutaneous albinism: variable expressivity of nystagmus in a sibship. J Pediatr Ophthalmol Strabismus 29:185, 1992
176. McCarty JW, Demer JL, Hovis LA et al: Ocular motility anomalies in developmental misdirection of the optic chiasm. Am J Ophthalmol 113:86, 1992
177. Williams RW, Hogan D, Garraghty PE: Target recognition and visual maps in the thalamus of achiasmatic mutant dogs. Nature 367:637, 1994
178. Apkarian P, Dell'Osso LF, Ferraresi A, Van derSteen J: Ocular motor abnormalities in human achiasmatic syndrome. Invest Ophthalmol Vis Sci 35:1410, 1994
179. Dell'Osso LF: Evidence suggesting individual ocular motor control of each eye (muscle). J Vestib Res 4:335, 1994
180. Dell'Osso LF, Williams RW: Ocular motor abnormalities in achiasmatic mutant Belgian sheepdogs: unyoked eye movements in a mammal. Vision Res 35:109, 1995
181. Dell'Osso LF, Williams RW, Jacobs JB et al: The congenital and see-saw nystagmus in the prototypical achiasma of canines: comparison to the human achiasmatic prototype. Vision Res 38:1629, 1998
182. Dell'Osso LF, Williams RW, Hogan D: Eye movements in canine hemichiasma. Invest Ophthalmol Vis Sci 38:S1144, 1997
183. Dell'Osso LF, Daroff RB: Two additional scenarios for see-saw nystagmus: achiasma and hemichiasma. J Neuro-ophthalmol 18:112, 1998
184. Doslak MJ, Dell'Osso LF, Daroff RB: Multiple double saccadic pulses occurring with other saccadic intrusions and oscillations. Neuro-ophthalmology 3:109, 1983
185. Whicker L, Abel LA, Dell'Osso LF: Smooth pursuit and fixation in the parents of schizophrenics. Soc Neurosci Abstr 9:70, 1983
186. Abel LA, Traccis S, Dell'Osso LF et al: Square wave oscillation. The relationship of saccadic intrusions and oscillations. Neuro-ophthalmology 4:21, 1984
187. Dell'Osso LF, Troost BT, Daroff RB: Macro square wave jerks. Neurology 25:975, 1975
188. Dell'Osso LF, Abel LA, Daroff RB: "Inverse latent" macro square wave jerks and macro saccadic oscillations. Ann Neurol 2:57, 1977
189. Selhorst JB, Stark L, Ochs AL et al: Disorders in cerebellar ocular motor control. II. Macro saccadic oscillation: an oculo-

graphic, control system and clinico-anatomical analysis. Brain 99:509, 1976
190. Fukazawa T, Tashiro K, Hamada T et al: Multisystem degeneration: drugs and square wave jerks. Neurology 36:1230, 1986
191. Herishanu YO, Sharpe JA: Saccadic intrusions in internuclear ophthalmoplegia. Ann Neurol 14:67, 1983
192. Selhorst JB, Stark L, Ochs AL et al: Disorders in cerebellar ocular motor control. I. Saccadic overshoot dysmetria: an oculographic, control system and clinico-anatomical analysis. Brain 99:497, 1976
193. Vilis T, Snow R, Hore J: Cerebellar saccadic dysmetria is not equal in the two eyes. Exp Brain Res 51:343, 1983
194. Bötzel K, Rottach K, Büttner U: Normal and pathological saccadic dysmetria. Brain 116:337, 1993
195. Büttner U, Straube A, Spuler A: Saccadic dysmetria and "intact" smooth pursuit eye movements after bilateral deep cerebellar nuclei lesions. J Neurol Neurosurg Psychiatry 57:832, 1994
196. Kanayama R, Bronstein AM, Shallo-Hoffmann J et al: Visually and memory guided saccades in a case of cerebellar saccadic dysmetria. J Neurol Neurosurg Psychiatry 57:1081, 1994
197. Zee DS, Robinson DA: a hypothetical explanation of saccadic oscillations. Ann Neurol 5:405, 1979
198. Hain TC, Zee DS, Mordes M: Blink induced saccadic oscillations. Ann Neurol 19:299, 1986
199. Ashe J, Hain TC, Zee DS et al: Microsaccadic flutter. Brain 114:461, 1991
200. Kaminski HJ, Zee DS, Leigh RJ et al: Ocular flutter and ataxia associated with AIDS-related complex. Neuro-ophthalmology 11:163, 1991
201. Dropcho EJ, Kline LB, Riser J: Antineuronal (anti-Ri) antibodies in a patient with steroid-responsive opsoclonus-myoclonus. Neurology 43:207, 1993
202. Prier S, Larmande P, Dairou R et al: Oscillations macro-saccadiques au cours d'un cas d'encéphalopathie myoclonique paranéoplasique. Rev Neurol 135:339, 1979
203. Furman JMR, Eidelman BH, Fromm GH: Spontaneous remission of paraneoplastic ocular flutter and saccadic intrusions. Neurology 38:499, 1988
204. Gresty MA, Findley LJ, Wade P: Mechanism of rotatory eye movements in opsoclonus. Br J Ophthalmol 64:923, 1980
205. Hattori T, Takaya Y, Tsuboi Y et al: Opsoclonus showing only during eye closure in hereditary cerebellar ataxia. J Neurol Neurosurg Psychiatry 56:1036, 1993
206. Binyon S, Prendergast M: Eye-movement tics in children. Dev Med Child Neurol 33:343, 1991
207. Shawket F, Harris CM, Jacobs M et al: Eye movement tics. Br J Ophthalmol 76:697, 1992
208. Hunter S, Kooistra C: Neuropathologic findings in idiopathic opsoclonus and myoclonus. Their similarity to those in paraneoplastic cerebellar cortical degeneration. J Clin Neuro-ophthalmol 6:236, 1986
209. Dehaene I, Van Vleymen B: Opsoclonus induced by phenytoin and diazepam. Ann Neurol 21:216, 1987
210. Greenlee JE, Lipton HL: Anticerebellar antibodies in serum and cerebrospinal fluid of a patient with oat cell carcinoma of the lung and paraneoplastic cerebellar degeneration. Ann Neurol 19: 82, 1986
211. Anderson NE, Corinna CB, Budde-Steffen C: Opsoclonus, myoclonus, ataxia, and encephalopathy in adults with cancer: a distinct paraneoplastic syndrome. Medicine 67:100, 1988
212. Herishanu Y, Apte R, Kuperman O: Immunological abnormalities in opsoclonus cerebellopathy. Neuro-ophthalmology 5:271, 1985
213. Nitschke M, Hochberg F, Dropcho E: Improvement in paraneoplastic opsoclonus-myoclonus after protein A column therapy. N Engl J Med 332:192, 1995
214. Ridley A, Kennard C, Scholtz CL et al: Omnipause neurons in two cases of opsoclonus associated with oat cell carcinoma of the lung. Brain 110:1699, 1987
215. Tuchman RF, Alvarez LA, Kantrowitz AB et al: Opsoclonus-myoclonus syndrome: correlation of radiographic and pathological observations. Neuroradiology 31:250, 1989
216. Gwinn KA, Caviness JN: Electrophysiological observations in idiopathic opsoclonus-myoclonus syndrome. Mov Disord 12: 438, 1997
217. Borodic GE, Miller DC, Bienfang DC: Opsoclonus: three cases and literature review. In Smith JL, Katz RS (eds): Neuro-Ophthalmology Enters the Nineties, p 213. Miami, Dutton Press, 1988
218. Caviness JN, Forsyth PA, Layton DD et al: The movement disorder of adult opsoclonus. Mov Disord 10:22, 1995
219. Deuschl G, Mischke G, Schenck E, et al: Symptomatic and essential rhythmic palatal myoclonus. Brain 113:1645, 1990
220. Nakada T, Kwee IL: Oculopalatal myoclonus. Brain 109:431, 1986
221. Matsuo F, Ajax ET: Palatal myoclonus and denervation supersensitivity in the central nervous system. Ann Neurol 5:72, 1979
222. Koeppen AH, Barron KD, Dentinger MP: Olivary hypertrophy: histochemical demonstration of hydrolytic enzymes. Neurology 30:471, 1980
223. Keane JR: Acute vertical ocular myoclonus. Neurology 36:86, 1986
224. Jacobs L, Newman RP, Bozian D: Disappearing palatal myoclonus. Neurology 31:748, 1981
225. Carlow TJ: Medical treatment of nystagmus and ocular motor disorders. In Beck RW, Smith CH (eds): Neuroophthalmology, p 251. Boston, Little, Brown, 1986
226. Herishanu YO, Zigoulinski R: The effect of chronic one-eye patching on ocular myoclonus. J Clin Neuro-ophthalmol 11: 166, 1991
227. Jabbari B, Rosenberg M, Scherokman B et al: Effectiveness of trihexyphenidyl against pendular nystagmus and palatal myoclonus: evidence of cholinergic dysfunction. Mov Disord 2:93, 1987
228. Neetens A, Martin JJ: Superior oblique myokymia in a case of adrenoleukodystrophy and in a case of lead intoxication. Neuro-ophthalmology 3:103, 1983
229. Kommerell G, Schaubele G: Superior oblique myokymia. An electromyographical analysis. Trans Ophthalmol Soc UK 100: 504, 1980
230. Morrow MJ, Sharpe JA, Ranalli PJ: Superior oblique myokymia associated with a posterior fossa tumor: oculographic correlation with an idiopathic case. Neurology 40:367, 1990
231. Leigh RJ, Tomsak RL, Seidman SH et al: Superior oblique myokymia: quantitative characteristics of the eye movements in three patients. Arch Ophthalmol 109:1710, 1991
232. Rosenberg ML, Glaser JS: Superior oblique myokymia. Ann Neurol 13:667, 1983
233. Breen LA, Gutmann L, Riggs JE: Superior oblique myokymia. A misnomer. J Clin Neuro-ophthalmol 3:131, 1983
234. Thurston SE, Saul RF: Superior oblique myokymia: quantitative description of the eye movement. Neurology 41:1679, 1991
235. Komai K, Mimura O, Uyama J et al: Neuro-ophthalmological evaluation of superior oblique myokymia. Neuro-ophthalmology 12:135, 1992
236. Brazis PW, Miller NR, Henderer JD et al: The natural history and results of treatment of superior oblique myokymia. Arch Ophthalmol 112:1063, 1994
237. Rudick R, Satran R, Eskin T: Ocular bobbing in encephalitis. J Neurol Neurosurg Psychiatry 44:441, 1981
238. Dehaene I, Lammens M, Marchau M: Paretic ocular bobbing. Neuro-ophthalmology 13:143, 1993
239. Gaymard B: Disconjugate ocular bobbing. Neurology 43:2151, 1993
240. Brusa A, Firpo MP, Massa S et al: Typical and reverse bobbing: a case with localizing value. Eur Neurol 23:151, 1984
241. Knobler RL, Somasundaram M, Schutta HS: Inverse ocular bobbing. Ann Neurol 9:194, 1981
242. Ropper AH: Ocular dipping in anoxic coma. Arch Neurol 38: 297, 1981
243. Van Weerden TW, Van Woerkom TCAM: Ocular dipping. Clin Neurol Neurosurg 84:221, 1982

244. Stark SR, Masucci EF, Kurtzke JF: Ocular dipping. Neurology 34:391, 1984
245. Safran AB, Berney J: Synchronism of inverse ocular bobbing and blinking. Am J Ophthalmol 95:401, 1983
246. Toshniwal P, Yadava R, Goldbarg H: Presentation of pineal-oblastoma with ocular dipping and deafness. J Clin Neuro-ophthalmol 6:128, 1986
247. Rosenberg ML: Spontaneous vertical eye movements in coma. Ann Neurol 20:635, 1986
248. Shults WT, Stark L, Hoyt WF et al: Normal saccadic structure and voluntary nystagmus. Arch Ophthalmol 95:1399, 1977
249. Nagle M, Bridgeman B, Stark L: Voluntary nystagmus, saccadic suppression, and stabilization of the visual world. Vision Res 20:717, 1980
250. Krohel G, Griffin JF: Voluntary vertical nystagmus. Neurology 29:1153, 1979
251. Yee RD, Spiegel PH, Yamada T et al: Voluntary saccadic oscillations, resembling ocular flutter and opsoclonus. J Neuro-ophthalmol 14:95, 1994

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Third Edition

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