11. Nystagmus and other ocular motor oscillations

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INTRODUCTION

In this chapter, I have endeavored to define and list at least one relevant reference for each type of nystagmus and other ocular motor oscillations. For those specific types in which noteworthy contributions have been made in the past 18 months, additional discussion has been presented. This format will result in an inter-edition variation in the amount of coverage of each specific type of oscillation; it will depend on the quantity of work published for the preceding 18 months. However, every edition will contain a definition and at least one good reference for each type.

NYSTAGMUS

The word 'nystagmus' is derived from the Greek word, $\nu\upsilon\sigma\tau\alpha\gamma\mu\acute{o}\varsigma$, meaning drowsiness, which in turn is derived from $\nu\upsilon\sigma\tau\acute{\alpha}\zeta\epsilon\iota\nu$, meaning to nod in one's sleep. It should be noted that this nodding oscillation is generated and sustained by the slow downward drifting of the head; the upward head jerks are corrective in that they serve to restore upright head posture.

In keeping with this original definition, nystagmus is defined as follows: a biphasic ocular oscillation containing slow eye movements which are responsible for its genesis and continuation. Fast eye movements (saccades), if they are present, serve a corrective function and do not represent the basic instability. The two phases of ocular nystagmus are approximately equal in amplitude. In preparing this chapter, I have identified 41 distinct varieties of nystagmus which have been characterized in the literature by 83 different terms. In addition, 8 terms using the word 'nystagmus' have been applied to ocular motor oscillations which do not fall into the category of nystagmus, as herein defined; they are discussed in the following section.

Abduction nystagmus

Abduction nystagmus is the dissociated nystagmus of the abducting eye seen in patients with internuclear ophthalmoplegia (1). The clinical picture presented by the patient with a total internuclear ophthalmoplegia is that of an acquired jerk nystagmus of the abducting eye (with abducting fast phases) while the fellow eye

remains motionless in primary position. If the internuclear ophthalmoplegia is bilateral, abduction nystagmus will be present in both extremes of gaze, always in the abducting eye only. Abduction nystagmus has also been called 'ataxic' nystagmus of Harris. Careful recordings, using high bandwidth methods and simultaneous velocity tracings, have shown that the nystagmus slow phases are decreasing-velocity exponentials and the fast phases of the abducting eye are always accompanied by hypometric saccades in the adducting eye. In fact, if the gaze angle is such that the adducting eye eventually reaches the target, the abduction nystagmus will cease as soon as the adducting eye reaches the target and the hypometric saccades cease. It is only in the full-blown internuclear ophthalmoplegia, where the adducting eye does not adduct beyond midline, that abduction nystagmus persists. If these saccadic pulses are truly the cause of this oscillation, then abduction 'nystagmus' should be classified as a non-nystagmic oscillation.

A recent study of the abduction nystagmus of internuclear ophthalmoplegia (2) has shown that although the slow phases of abduction nystagmus are decreasing-velocity exponentials, the slow phases of the vertical nystagmus exhibited by these patients have linear slow phases (i.e. constant velocity). The slow phases of the horizontal abduction nystagmus present in the patients studied consisted of two distinct components: the first is a rapid exponential drift towards the center, and the second is a slower, more linear drift, again towards the center. The authors offer an interesting explanation for the generation of abduction nystagmus in internuclear ophthalmoplegia. It consists of a pulse step mismatch in neural innervation, which is brought about by an increase in saccadic pulse gain, in addition to an impaired position-maintenance signal. They postulate that the position-maintenance signal is impaired both horizontally and vertically.

Acquired nystagmus

Nystagmus acquired in infancy secondary to progressive bilateral visual loss presents a diagnostic problem. It should not be classified as congenital if it is documented that nystagmus was absent at, and shortly after, birth. On rare occasions nystagmus may be acquired following uniocular visual loss in a child (3). Nystagmus may also be acquired in infants with CNS disease. It is quite variable when compared to that acquired in adults.

Nystagmus acquired by adults may be either pendular or jerk. If it is pendular, it may reflect brainstem and/or cerebellar dysfunction or it may occur in patients with vascular or demyelinating disease. It is multivectorial and is usually associated with a head tremor. There may be marked dissociation between the two eyes which does not correlate with visual acuity differences. On rare occasions, an adult with sight in one eye may develop nystagmus in that eye secondary to the diminished visual acuity; it may be vertical. Acquired jerk nystagmus may reflect vestibular dysfunction or, if it is not present in primary position, it may be of the gaze-evoked type and reflect brainstem or cerebellar dysfunction. Drugs may also cause bidirectional gaze-evoked nystagmus. Fixation is said to cause some types of acquired nystagmus where the nystagmus changes with eye closure; this is not strong enough evidence to establish causality, as has been shown in congenital nystagmus. The various types of acquired nystagmus will be discussed further under their proper headings.

Arthrokinetic nystagmus

Arthrokinetic nystagmus is a horizontal jerk nystagmus induced in darkness by passively rotating the horizontally extended arm of a stationary subject about a vertical axis in the shoulder joint. The induced nystagmus will have a fast phase beating in the direction opposite to the arm movement. The slow phase velocity will vary directly with the actual arm velocity up to about 15° per second. The mean position of the eyes will deviate towards the fast phase. The nystagmus persists after cessation of stimulation (arthrokinetic after-nystagmus) (4).

Audiokinetic nystagmus

Rotating acoustic stimuli (white noise or a series of clicks) can produce, in a person seated in darkness, a sensation of being rotated (circularvection). In addition, audiokinetic nystagmus is induced. This jerk nystagmus consists of slow phases in the direction of the moving sound and oppositely directed fast phases (5, 6). The rotating sound field can be produced by physically rotating a sound source or by rotating the subject at a constant velocity in the presence of a fixed sound source. Audiokinetic nystagmus is similar to optokinetic nystagmus.

Bruns nystagmus

Bruns nystagmus is a horizontal jerk nystagmus whose direction is dependent upon gaze and whether or not fixation is suppressed. It is characteristic of cerebellar-pontine angle tumors. With gaze directed toward the side of the lesion, a large-amplitude, gaze-evoked nystagmus is seen. The fast phases are in the direction of gaze and the slow phases are decreasing-velocity exponentials. With gaze directed to the side opposite the lesion, a small-amplitude, linear slow phase nystagmus is elicited with the fast phases in the direction of gaze. When the eyes are closed, a nystagmus beating in the direction opposite the side of the lesion predominates. Bruns nystagmus is due to a combination of gaze-evoked nystagmus, caused by brainstem compression on one side, and vestibular nystagmus in the opposite direction, caused by vestibular paralysis on the same side of the brainstem as the compression (7).

Centripetal nystagmus

Centripetal nystagmus is a jerk nystagmus not present in primary position in which the slow phase is a decreasing-velocity exponential directed centrifugally; the fast phases are directed centripetally. Centripetal nystagmus has been documented in cases of cerebellar disease (8). The occurrence of centripetal nystagmus is quite variable; it may be unilateral or bilateral and occur under conditions of darkness, eyelid closure, fixation, or any combination of these. Since centripetally beating nystagmus is commonly encountered in patients with loss of labyrinthine function (vestibular disease) when gaze is directed towards the side of the lesion, confusion can result. It is possible to differentiate the two, however. A peripheral nystagmus is unidirectional for all positions of gaze and the slow phase of the vestibular nystagmus is linear, whereas that found in patients with cerebellar disease is a

decreasing-velocity exponential. A possible mechanism for the generation of centripetal nystagmus in cerebellar disease was presented by Leech et al. (8). They hypothesized a net summing of pathological and compensatory drifts which result in an offsetting or wandering of the neutral point of the eyes.

Cervical nystagmus

Cervical (neck-torsion, vertebral-basilar artery insufficiency) nystagmus is a jerk nystagmus allegedly caused by: cervical spondylosis (with secondary occlusion of vertebral basilar artery inducing brainstem and cerebellar ischemia); whiplash (with either vertebral artery trauma or stem injury); cervical muscle impairment (interfering with proprioceptive input); and cervical cord disease. Since, in the first two cases, it is most likely that brainstem ischemia or stem injury is the true cause of the nystagmus, and since cervical muscle impairment or cervical cord disease has not been established in humans, cervical nystagmus is not a very well-defined entity. At present, the exact contribution of each of these possible mechanisms is unknown and indeed some are highly suspect (9).

A prerequisite to making a significant contribution to the understanding of cervical nystagmus is careful control and elimination of all possible influences on the nystagmus except the one being studied. When dealing with patients, this also encompasses ruling out drug effects and positional vestibular influences. A surprising finding of a recent study of the trunk-ocular reflex in man was that the gain of this reflex appeared to be 0.5 (10). Comparison of this with the vestibulo-ocular gain of 0.4 to 0.7 and the neck-ocular gain of less than 0.1 raises the possibility that interference with the signals responsible for the trunk-ocular reflex by cervical manipulation may play a part in the generation of cervical nystagmus.

Circular/elliptic/oblique nystagmus

Circular and elliptic (circumduction) nystagmus are forms of pendular nystagmus in which the globe oscillates in a circular path. They should not be confused with torsional (rotary) nystagmus in which the globe itself rotates about an anterior-posterior axis. Rather, it represents the sum of simultaneous horizontal and vertical pendular oscillations which are 90° out of phase. If the amplitudes of the two components are equal, circular nystagmus results; if they are unequal, elliptic nystagmus results. Often the nystagmus varies between elliptic and circular and may be dissociated or uniocular. Oblique (diagonal, radiary) nystagmus may be pendular or jerk. If the components are pendular, they are either in phase or 180° out of phase. If the nystagmus is a jerk nystagmus, the vertical and horizontal components are in phase. These nystagmus types may be congenital or acquired. If acquired, circular/elliptic nystagmus occurs in multiple sclerosis, where it is often dissociated in the two eyes, and almost always coexists with truncal or extremity ataxia (11). Oblique nystagmus is more commonly acquired than congenital. A curious case of diagonal jerk nystagmus, in which the vector of the nystagmus rotated slowly as the blades of a windmill (first clockwise and then counterclockwise), was described and named 'alternating windmill nystagmus' (12). It occurred in a patient who was blind from ophthalmic disease.

Congenital nystagmus

Congenital nystagmus (CN) is present at birth or shortly thereafter. It may accompany afferent visual defects but is not caused by defects in the visual system. Indeed, the oft-quoted association of pendular CN with a sensory defect and jerk CN with a primary motor defect is erroneous. The fact that in many cases one cannot distinguish by clinical observation alone the difference between the several pendular waveforms of CN and the more numerous jerk waveforms further complicates such claims (which were made without eye movement recordings). Systematic ocular motility investigations have found no consistent association between waveform and the presence or absence of visual impairment, and both pendular and jerk waveforms have been documented in a single family with hereditary CN (13). Although the visual deficit is not causal, it can contribute to the intensity of CN. CN is a high gain instability in the slow eye movement subsystem and fixation attempt (the effort to see) is its primary driving force; thus, CN is not a fixation nystagmus. Obviously, poor vision will increase fixation attempt thereby causing nystagmus intensity to increase. CN can be diagnosed definitely by accurate eye movement recordings. The slow phases of jerk CN are increasing-velocity exponentials. Three pendular (pendular, asymmetric pendular, and pendular with foveating saccades), 8 jerk (jerk, jerk with extended foveation, pseudo-cycloid, pseudo-jerk, pseudo-pendular, pseudo-pendular with foveating saccades, triangular, and bidirectional jerk), and one combination of pendular and jerk (dual jerk) waveforms have been identified as CN waveforms (14). CN usually damps with convergence and, in many cases, a gaze angle can be found at which the intensity is minimal. Therapeutically, the nulling with convergence may be exploited by the use of base out prisms and the null angle may be exploited either by prisms or, if the null angle is far removed from primary, by corrective surgery.

A recent paper on congenital horizontal gaze palsy and scoliosis (15), in addition to discussing this syndrome, mentions the presence of nystagmus in 3 of the 5 cases; other references for nystagmus in this syndrome are also presented. In the one case where eye movement recordings are shown, the nystagmus can clearly be identified as CN. Despite the figure legends of Figure 3 in the paper, the nystagmus shown consists of pseudo-cycloid and jerk with extended foveation; both are CN waveforms. Careful ocular motor studies of patients with congenital horizontal gaze palsy and scoliosis may reveal that CN is an additional characteristic of this syndrome. Another recent paper on CN (16) deals with suppression of CN. Unfortunately, the methodology employed in this study is poor (bitemporal EOG electrodes with AC-coupled amplification). The point of this study was to investigate the effects of blocking of fixation on suppression of CN despite the fact that it has been clearly shown that neither retinal illumination nor eyelid position is responsible for the genesis or modulation of CN (17). There are several misstatements of fact in this paper (including the first sentence for which I am incorrectly referenced) and it is, therefore, not recommended reading for the uninitiated for whom a recent, concise review of CN waveforms and foveation would be a good introduction to the subject (18).

A significant paper on the relationship between head movement and CN has recently been published (19). The major conclusion of this paper is that head-

nodding in CN is pathological in origin and not a compensatory mechanism as has been previously suggested. Head oscillation appears during periods of increased fixation attempt, but the oscillation of the head is compensated for by the patient's normal vestibulo-ocular reflex so that the flat portions of the CN waveform (i.e., when there is no eye motion and the target is on the fovea) are maintained. Thus, although the recording of eye in head does not appear to have motionless periods, if one adds the head motion to the eye recording to obtain the eye position in space, the motionless foveation periods of the eye become apparent. Thus, the patient's acuity is not affected by this additional oscillation.

A recent survey has been published of 40 individuals who were registered with the Canadian National Institute for the Blind as 'blind' from congenital nystagmus (20). It was found that 15 of these cases were due to autosomal recessive conditions and another 15 to X-linked disorders; 3 additional cases were consistent with either of these possible genetic factors. Of the remaining 7 cases, one was regarded as environmental and no specific factors were detected for the other 6. If one excludes from consideration the 8 patients whose vision was better than 20/100 in at least one eye (these could hardly be called blind patients), of the remaining 32, only 8 had normal foveas. Thus, the thesis that these patients were 'blind from congenital nystagmus' is difficult to defend. It seems much more likely that their very poor acuity was due to their associated visual abnormalities and not to their nystagmus.

Although surgical treatment for CN has been practiced for over 25 years, until recently there has never been a quantitative evaluation of the effects of such surgery on the variation of CN with gaze angle. The recent publication of such a study has provided us with interesting insights into some unknown facets of this surgery as well as the ground work for accurately determining the amount of surgery required and predicting whether or not a visual acuity increase will result (21). The effects of CN surgery, as measured by quantitative oculography, were: shifting of the nystagmus nulls; broadening of the null region of nystagmus; and an overall reduction in the nystagmus intensity at all gaze angles. Surgical rotation also produced improved visual acuity in all cases. Postoperative acuity at primary position was better than preoperative acuity both at primary and at the patient's preferred gaze angle. This was true even for the patient whose preoperative acuity did not substantially improve with her preferred head turn. The rationale for the methodology employed in making the measurements presented in this study as well as a thorough discussion of the individual results are carefully presented in this paper. In addition, a curve was derived which could be used to determine preoperatively the amount of surgical rotation necessary based on data gathered in the ocular motility laboratory. Several points should be made with regard to this study. First, the cases discussed were documented CN cases based on identification of CN waveforms. No such documentation exists in any previous study of CN surgery. This is extremely important in light of the fact that many patients who are diagnosed as having CN actually have manifest latent nystagmus (this is discussed in the section on latent/manifest latent nystagmus). CN and manifest latent nystagmus are two entirely different types of oscillation requiring separate consideration with regard to surgical therapy. Although another recent paper (22) attempts to deal with the obvious differences seen in patients who are diagnosed as having CN, the distinguishing characteristic of binocularity or lack of binocularity is not sufficient

to clearly delineate the two types of nystagmus which may be present. While it is true that binocularity would suggest CN whereas its absence would suggest manifest latent nystagmus, we have numerous examples of patients with both strabismus and CN. Another important result of the quantitative measurements of null angle both pre- and post-operatively is in the absolute documentation of the initial and long-term effects of this type of surgery. The 'success' of the surgery is not left to clinical impression. It has become clear that if the initial null shift was adequate, the postoperative null position will be at primary position immediately postoperatively and will not change as time goes on. Anecdotal observations of 'development in time of a lesser head turn than was present preoperatively' reflect inadequate surgery followed by the natural establishment of a head turn to utilize the surgically imposed null angle, and not the emergence of a mysterious new null angle somewhere between the original null angle and primary position. A final note on therapy associated with CN involves the use of biofeedback. A recent short paper has claimed that its use has resulted in a reduction of nystagmus intensity and increase in visual acuity (23). While the eye movement recording shown in the paper does not show a dramatic decrease in intensity, some decrease is evident and further work in this promising area is certainly warranted.

Convergence nystagmus

Convergence nystagmus is a rare form of acquired, pendular, horizontal nystagmus which is, by nature, dissociated. Convergence nystagmus may be present when fixating at distance or may be convergence-evoked; this latter form is discussed in the next section. We have recorded a patient with convergence nystagmus who had progressive supranuclear palsy (unreported case).

Convergence-evoked nystagmus

Convergence-evoked nystagmus is unusual and may be congenital, acquired, conjugate or dissociated (24). The nystagmus is pendular and is only present during near binocular fixation or tracking. Neuropathological examination of a congenital case, whose movements were conjugate, revealed no morphological explanation; in the acquired form, the patient had demyelinating disease with a spastic paraparesis and no cranial nerve abnormality other than the ocular motor findings. Since the movements of the acquired case were totally dissociated (i.e. dysjunctive), this was convergence-evoked convergence nystagmus.

Dissociated nystagmus

Significant asymmetry (of either amplitude or direction) of the nystagmus (pendular or jerk) in the two eyes is designated 'dissociated (dysjunctive) nystagmus'. The most commonly observed dissociated nystagmus is that of the abducting eye (abduction nystagmus) in internuclear ophthalmoplegia discussed above. Patients with multiple sclerosis may have dissociated pendular nystagmus (11). A variety of nystagmus dissociations with diverse posterior fossa lesions has also been described (25).

Downbeat nystagmus

Downbeat is a vertical jerk nystagmus present in primary position with linear upward slow phases and fast phases beating in the downward direction. It is highly suggestive of a disorder of the cranial-cervical junction such as Arnold-Chiari malformations. Contrary to Alexander's Law, it is not maximum in the extreme of downward gaze but usually of maximal intensity when the eyes are deviated laterally and slightly below the horizontal. It has also been described in patients with presumed parenchymal cerebellar disease (26). A defect in downward pursuit has been suggested as the cause of this form of pursuit-defect nystagmus (27).

Drug-induced nystagmus

A horizontal or horizontal-rotary jerk nystagmus which is gaze-evoked may be induced by the administration of barbiturate (barbiturate nystagmus), tranquilizer, phenothiazine, and anticonvulsant drugs. Vertical nystagmus is often present on upward gaze but only rarely on downward gaze. The nystagmus may be quite dissociated in the two eyes despite the lack of structural disease. Severe intoxication may result in a horizontal-pendular nystagmus at primary position. Careful history-taking and drug-screening blood studies are essential in evaluating patients with nystagmus.

In a recent paper, Alpert (28) described two cases of downbeat nystagmus due to anticonvulsant toxicity. Isolated downbeat nystagmus has not been previously reported as a result of drug administration. Both patients showed no nystagmus with eyes closed and absent downward tracking; the latter was presented as supporting evidence for the hypothesis that downbeat nystagmus is a pursuit-defect nystagmus. Riker et al. (29) have found that there is no predictable relationship between blood level of phenytoin and nystagmus. Unfortunately, they used bitemporal EOG electrodes and their tracings were quite noisy so it is impossible to tell whether the slow phases of the nystagmus shown are linear or decreasing-velocity exponentials. Since approximately 50% of the normal population has end-point nystagmus (which has a linear slow phase) and since anticonvulsant drugs are known to be related to the occurrence of nystagmus, it is quite possible that these drugs cause physiological end-point nystagmus to appear at a lateral gaze angle closer to primary than normal.

Epileptic nystagmus

Epileptic nystagmus was first described by Féré in 1890. Two, more recent, papers describe 'horizontal jerk and pendular nystagmus' (30) and 'counter-clockwise right-downward rotary nystagmus' (31). Although the nystagmus undoubtedly exists, one cannot be sure of its direction(s), type(s) or slow phase waveform(s) until it is properly studied with DC recording methods.

Flash-induced nystagmus

Flash(flicker)-induced nystagmus is a jerk nystagmus induced by intermittent photic

stimulation of one eye. The direction of flash-induced nystagmus is always towards the stimulated eye; for this reason it has been suggested that flash-induced nystagmus is related to latent nystagmus (32). Flash-induced nystagmus differs from optokinetic nystagmus in that it is abolished after bilateral labyrinthectomy and is affected by head and body position (33).

Gaze-evoked nystagmus

Gaze-evoked nystagmus (GEN) is the most common form of nystagmus encountered in clinical practice. It is a jerk nystagmus elicited by attempted maintenance of eccentric eye position; no nystagmus is present in primary position. GEN may have a linear slow phase or a decreasing-velocity exponential slow phase (gaze-paretic nystagmus). In the absence of drugs, horizontal GEN indicates brainstem and/or cerebellar dysfunction; more exact localization is not possible at this time without analysis of associated neurological signs and symptoms. Multiple sclerosis sometimes causes nystagmus in extreme lateral gaze (deviational nystagmus). When horizontal GEN is bilateral, upward-beating vertical GEN is often present; it is rarely present without bilateral horizontal GEN. Downward-beating GEN is usually absent. The most common cause of bilateral GEN is sedative or anticonvulsant drugs as was discussed in the section on drug-induced nystagmus.

Abel et al. (34), using a relatively simple model of the saccadic system which they developed and simulated on an analog computer, were able to generate GEN in either of two ways. The model showed that GEN could result from either a proportional deficit in the neuronal pool responsible for integration of the pulse of high-frequency firing which initiates each saccade or a saturation of these neurons when their firing reached a certain level. When these proposed deficits were simulated in the model using a leaky integrator or a saturation circuit for the respective deficits, subtle differences were noted in the saccadic behavior as well as the GEN. These differences occurred both in the nystagmus-free range of gaze angles and after the nystagmus appeared. Thus, the model not only demonstrated that each of the hypothesized deficits would produce GEN but suggested subtle ocular motor signs which would be present in patients with GEN. The type of GEN simulated in this model is gaze-paretic nystagmus (i.e., the slow phase is a decreasing-velocity exponential). Recently, Meienberg et al. (35) have described a dissociated gaze-paretic nystagmus in a patient with left inferior rectus paresis. He had strong horizontal GEN to both sides but when looking down, a dissociated gaze-paretic nystagmus occurred. Their analysis suggested that the lesion responsible for this disturbance interrupted fibers ascending from the left vestibular nucleus to the nuclei that innervate the left inferior rectus and right superior oblique muscles. Schmidt (36) reported on two brothers with ataxia telangiectasia (Louis-Bar syndrome). In addition to several other ocular motor abnormalities, these patients with cerebellar disease showed GEN.

Horizontal nystagmus

Horizontal nystagmus of either the jerk or pendular variety is nystagmus in which the trajectory of the eyes is to the left and right with respect to the head; this is

irrespective of the tilt of the head. The slow phase waveforms of jerk nystagmus (i.e., linear, decreasing-velocity or increasing-velocity exponentials) are of diagnostic importance. Specific types of horizontal nystagmus are discussed in their respective sections.

Induced nystagmus

There are many forms of nystagmus which may be induced in the normal subject or in the patient with neurological disease. The stimuli used can be non-invasive (auditory, light flashes, limb or body position, and rotation) or invasive (drugs, electrical or pneumatic stimulation and caloric irrigation). The various types are discussed further in their specific sections.

Intermittent vertical nystagmus

The occurrence of intermittent attacks of vertical jerk (downbeat or upbeat) nystagmus is associated with the rare disorder, familial periodic ataxia (37). The episodic symptoms also include vertigo and ataxia. Intermittent vertical nystagmus has been linked to cerebellar or vestibular dysfunction, brainstem disorders caused by multiple sclerosis, and Arnold-Chiari malformation. The occurrence of rotary, vertical, or dissociated nystagmus has been documented in families affected with this disorder. Conversion from primary position vertical nystagmus to gaze-evoked horizontal jerk nystagmus has also been noted. In many cases a mild nystagmus and ataxia persisted between the acute attacks.

Jerk nystagmus

Jerk nystagmus consists of a slow phase in one direction followed by saccadic fast phase in the opposite direction. The direction of the nystagmus is the direction of the fast phases despite the fact that it is the slow phases which are responsible for generating the nystagmus. The slow phases may be linear, increasing-velocity exponentials, or decreasing-velocity exponentials. The specific types of jerk nystagmus are discussed in their respective sections.

Latent/manifest latent nystagmus

Latent nystagmus (LN) and manifest latent nystagmus (MLN) are nystagmus types elicited by monocular fixation (38). The nystagmus is jerk with the fast phase toward the viewing eye. Although LN/MLN is usually congenital, the slow phase is a decreasing-velocity exponential as opposed to true congenital jerk nystagmus which has an increasing-velocity exponential slow phase. MLN occurs in patients with amblyopia or strabismus who, although viewing with both eyes, are fixing monocularly. The direction of MLN in patients with alternating fixation is always in the direction of the fixing eye. Such patients are usually diagnosed as having

congenital nystagmus, since the nystagmus is present with both eyes open. Accurate eye movement recordings are the only way to document the nystagmus and diagnose it properly.

Although MLN does not have a null angle (this is shown in Figure 9 of Reference 38), the variation of MLN with gaze angle in accordance with Alexander's Law may result in a head turn. Usually the head turn is such that the viewing eye is in adduction. If the patient is an alternate fixer, he may adopt one head turn when viewing with the right eye and an opposite head turn when viewing with the left eye so that in each condition the viewing eye is in adduction. It becomes very important, therefore, to distinguish MLN from congenital nystagmus before any consideration of surgical intervention is made. Surgery for congenital nystagmus will depend on the location of a true null, whereas surgery for MLN should be performed only if the patient consistently fixes with one eye and accompanies this fixation with a head turn. Alternate fixers who adopt alternate head turns cannot be helped by surgical rotation. As pointed out in this paper, the situation is complicated by the fact that some patients do not have either a pure congenital nystagmus or a pure MLN; various combinations of the two exist and the only way to accurately diagnose the condition is by means of ocular motility recording and waveform analysis.

A classic example of a patient with MLN whose nystagmus amplitude followed Alexander's Law was reported on recently by Metz and Smith (39). Their eye movement recordings and graphical representation of the nystagmus variation with gaze angle document this condition. Unfortunately, they called this 'abduction nystagmus'; this can only create confusion with the abduction nystagmus of internuclear ophthalmoplegia. Although the fixing eye may be in abduction when the nystagmus is maximal, the other eye, which is also oscillating maximally, is in adduction. Since this patient with MLN always fixed with his right eye and had a right head turn, the possibility of surgical correction was a reasonable approach. Indeed, upon performing this surgery the nystagmus with the right eye fixing in primary position was reduced by approximately 5° (preoperatively, it was 8°). A curious and unexplained finding was a sudden reversal of nystagmus direction in far adduction.

An explanation for the occurrence of LN, based on the differences between monocular and binocular ego-direction, is presented in the paper by Dell'Osso et al. (38). This postulation of a basic central abnormality as the underlying mechanism for LN and MLN is consistent with the observations made in our laboratory and the data presented by others. Alternate hypotheses have been presented by Kommerell (40) and Ishikawa (41). Kommerell's hypothesis involves the interaction between pathological convergence innervation, inability to hold lateral gaze, and defect of smooth pursuit from nasal to temporal. According to this theory, the first element results in an esotropia and the addition of the second and third elements generates the exponential slow phase jerk nystagmus. The question of causality between esotropia and nystagmus has not been adequately answered. Ishikawa advanced the thesis that LN was secondary to a proprioceptive rather than a visual disturbance. Support for this explanation is the high incidence of strabismus in LN. A discussion of Ishikawa's observations, the implication of his hypothesis, and independent observations of eye drifting in LN patients upon cover and uncover testing can be found in Dell'Osso et al. (38).

Lateral medullary nystagmus

Lateral medullary nystagmus is a horizontal, rotary jerk nystagmus which beats away from the side of a medullary lesion when the eyes are open. If the eyes are closed, the nystagmus beats towards the side of the lesion. Occasionally, a horizontal gaze-evoked and uniocular downbeat nystagmus is elicited (42). Another rare manifestation is gaze-evoked lid and ocular nystagmus which is inhibited by the near reflex (43).

Lid nystagmus

Lid nystagmus is a rhythmic, upward jerking of the upper eyelids which usually represents coordinated movements of the lids and eyes during vertical ocular nystagmus. There are three types of pathological lid nystagmus (44). The first type coexists synchronously with vertical ocular nystagmus, but the amplitude of the lid movements exceeds that of the eyes; the second type is evoked by lateral gaze and is characterized by rapid twitches of the lids in synchrony with the fast phases of the horizontal ocular movements; the third variety is provoked by ocular convergence. Type one has no localizing value. Type two may be a sign of lateral medullary syndrome and the third type has been associated with a large area demyelination in the rostral medulla extending laterally across the medial lemnisci, immediately dorsal to the upper border of the inferior olives.

Miners' nystagmus

Miners' (occupational) nystagmus is a rare condition presumably limited to the mineworkers of Europe, especially in the United Kingdom. It is alleged to be a small amplitude, horizontal and vertical nystagmus which is more pronounced in upward gaze. The pathogenesis of this condition (if it indeed exists) is uncertain, but functional contamination with voluntary 'nystagmus' and undetected congenital nystagmus is suspected; a secondary gain setting is always present in these cases. Indeed, the only eye movement recording purported to be of a patient with miners' nystagmus that this author has ever seen in the literature can clearly be identified by the waveform as congenital nystagmus. Reports of other occupational nystagmus cases are undocumented by eye movement recordings.

Muscle-paretic nystagmus

Muscle-paretic (myasthenic) nystagmus is a jerk nystagmus, due to a paretic muscle which mimics gaze-evoked (gaze-paretic) nystagmus in any direction with dissociation between the two eyes. The slow phases are decreasing-velocity exponentials. Many times nystagmus of the abducting eye, coexisting with a paresis of adduction, mimics the abduction nystagmus of internuclear ophthalmoplegia. If administration of anticholinesterase medication abolishes the nystagmus, the diagnosis of myasthenic nystagmus is established (45).

Optokinetic nystagmus

Optokinetic nystagmus (OKN) is a form of induced jerk nystagmus which is extremely valuable diagnostically. The nystagmus is induced by presenting to the subject a visual pattern which moves with constant velocity in a given direction. The induced eye movements consist of constant-velocity (linear), conjugate eye movements in the direction of the moving stimulus interspaced with fast phases in the opposite direction. OKN testing can be used to document the existence of vision in infants or patients with functional visual loss, to localize cerebral hemispheric lesions, to induce convergence-retraction 'nystagmus', to demonstrate the adduction insufficiency in internuclear ophthalmoparesis, to diagnose ocular motor nerve misdirection, to diagnose ocular myasthenia gravis (by injecting anticholinesterase during the OKN test and noting the velocity of the fast phases) and to diagnose congenital nystagmus (by getting inversion).

Despite the clinical importance of OKN testing, the literature on the subject is as confusing as it is voluminous. There is disagreement among those currently doing OKN research about both the nature of an adequate OKN stimulus and the characteristics of a true OKN response. According to one school of thought, OKN is divided into two types, Stier and Schau nystagmus. This is based on the work of Ter Braak (46) and the Stier (field) OKN was equated with subcortical mechanisms while the Schau (object) OKN was related to cortical mechanisms. In humans this is equivalent to full-field versus central-field (foveal) OKN. Clinically, it is the foveal OKN which is stimulated by the familiar OKN tape. The work of Dichgans (47) seems to support the thesis that one can simulate a full-field stimulus with a 90° horizontal strip. At the other end of the spectrum, Robinson (48) is of the opinion that true OKN must induce circularvection and be followed by optokinetic after-nystagmus (OKAN). Any stimulus which does not produce OKAN and circularvection is, therefore, inducing a 'pseudo'-OKN which is probably mediated by the pursuit mechanism in humans. Because one cannot dissociate the function of pursuit in the full-field stimulus condition, Robinson proposed that the OKN mechanism can only be isolated by studying OKAN. The picture is further complicated by the interrelation between the vestibular system and the OKN system (49). A recent paper on pursuit after-nystagmus (50) has now raised serious questions about Robinson's definition of OKN. It was found that simple pursuit induced an after-nystagmus. Thus, we are now faced with the fact that both full-field stimulation and a simple foveal target, which is being pursued, can induce an after-nystagmus and it may be impossible to separate true OKN from pursuit OKN if, indeed, they result from different mechanisms. While it has been presumed that pursuit is a foveal reflex, evidence has been presented (51) that pursuit need not be foveal. It is within the context of these conflicting views on the nature of an adequate stimulus for OKN that one must read the literature on this subject. It is quite possible that, when all the evidence is in, we may find that despite differing functions and philogenetic origins, both the optokinetic and the pursuit response are mediated by the same neurophysiological efferent mechanisms and differ only in afferent magnitudes. That is, the magnitude of the following response will be related to the amount of retinal area stimulated and the percentage of that area that is in the direction of motion. Similarly, the ever-present interaction with the

vestibular system would be proportional to the following response elicited by the particular stimulus presented. Thus, a small stimulus in the periphery would elicit a weaker response than a stimulus whose image was a visual strip across the retina including the fovea where the long direction of the strip corresponds to image motion. As the stimulus becomes more compelling and the resultant following response harder to suppress, one would move from the 'pursuit domain' to the 'optokinetic domain' without necessarily changing the mechanism responsible for the respective responses. Of course, the retinal sensitivity map will vary from species to species depending upon the morphology of the individual retinas.

A recent paper by Dubois and Collewijn (52) found that the area of maximal optokinetic sensitivity in the rabbit was coextensive with the visual streak. OKN slow phase velocity was maximal for stimulation in the anterior direction and minimal for posterior movements. Moving up the philogenetic scale, Evinger and Fuchs (53) have shown that although the cat can pursue accurately only up to 0.6° per second, when a striped background moved with the target, they achieved velocities of up to 8.5° per second. Thus, their ability to generate slow eye movements was augmented by increasing the stimulus to the retina. Although no horizontal directional difference was found in the OKN responses in man, a significant difference was found between horizontal and vertical OKN responses (54). In addition, upward optokinetic responses were better, on average, than downward responses.

Recently, a study has been published of the nystagmus induced by viewing stationary visual patterns illuminated by intermittent flashes (55). The authors studied the effect on the induced OKN (σ-OKN) of varying flash intensity, flash frequency, and the jitter of the flash intervals. They concluded that the σ-movement perception and the σ-OKN are elicited by feedback of different motor signals controlling slow pursuit eye movements. In a subsequent paper (56), it was found that a long-lasting σ-OKAN is produced in monkeys but not in man; this is yet another stimulus which can induce an after-nystagmus. The observation that OKN can be induced by stereoscopic contours (57) is important clinically. Since stereopsis is a prerequisite for the perception of stereoscopic contours, their ability to induce OKN provides an objective basis for testing stereopsis.

Because of the intimate interrelationship between optokinetic and vestibular eye movements, their interaction has been a fruitful area for study. Such studies prompted Wallace et al. (58) to conclude that all smooth eye movements are mediated by the same efferent system and that any differences would have to be sought in the afferent sensory systems. They concluded that, as all conjugate fast eye movements are equivalent, so are all conjugate slow eye movements. Optokinetic and vestibular interaction, known to be present in secondary vestibular neurons, has been recently shown to be absent in primary vestibular afferents of the alert cat (59). The study of patients with acute labyrinthine lesions uncovered a directional preponderance of the slow phase velocities of OKN which corresponded to the spontaneous nystagmus present in these patients (60). The slow phase velocities were enhanced to the side of the lesion and depressed in the opposite direction. The authors concluded that both facilitation of OKN to the side opposite the lesion and inhibition of OKN to the same side were taking place; the basically normal performance of the OKN system was biased both ways by the vestibular

imbalance. They further concluded that the interaction was not just purely additive or subtractive, but consisted of a feed forward optokinetic gain control of the vestibular component (i.e. multiplication) which took place before the two signals were combined. They hypothesized that the gain control was performed by the vestibulo-cerebellar flocculus. Since the directional preponderance does not always exceed the range of preponderance observed in normals, it is difficult to separate this condition from a brainstem lesion. If, however, an unusually high slow phase velocity and high frequency of OKN toward the side of spontaneous nystagmus are seen, the suggestion of a vestibular imbalance and not a brainstem lesion is strong. Yee et al. (61) found a relatively unimpaired OKN in two patients with downbeat nystagmus. The OKN was characterized by a slow build-up of the slow phase velocity similar to that found in afoveate animals. However, the OKAN was preserved in these patients. They concluded that the lesion at the level of the cranial-cervical junction can selectively remove the contribution of normal smooth pursuit to the OKN response. Since this is not a common finding in patients with downbeat nystagmus, they concluded that the cerebellar flocculi are significantly involved in the pursuit response and only slightly involved in the optokinetic response. A defect in the optokinetic response in patients with ataxia-telangiectasia has also been recently demonstrated (62). They found that, although the velocity-amplitude characteristics of the saccadic fast phases of OKN and vestibular nystagmus were normal, a defect in their initiation resulted in a deviation of the eyes in the direction of the slow component rather than the fast component as in normal subjects.

Optokinetic after-nystagmus

Optokinetic after-nystagmus (OKAN) is a continuation of optokinetic nystagmus (OKN) induced after the cessation of visual stimulation in complete darkness; this is known as OKAN I or post-OKN. After variable periods of time, it is followed by OKAN II; this is a secondary optokinetic after-nystagmus or reverse post-OKN. OKAN I has the same direction as the preceding OKN, whereas OKAN II is in the opposite direction. The duration of OKAN I is variable.

In an effort to identify the mechanisms of OKAN I and OKAN II, Waespe et al. (63) have studied the effects on OKAN II of brief periods of visual fixation during OKAN I. They found that OKAN I and OKAN II were influenced in a reciprocal way (i.e., OKAN I is reduced when OKAN II is increased). In those human subjects who exhibited no OKAN II in the controlled experiments, the suppression of OKAN I resulted in an OKAN II. They concluded that OKAN II depended upon the parameters of the preceding OKN stimulation and not the occurrence of OKAN I. Attempts to inhibit OKAN II by brief fixation periods resulted in a return of the OKAN II and a second maximum in its intensity; OKAN I showed little recovery. They concluded that OKAN II was a sign of central activity or counter-regulation which played a decisive role during all phases of OKAN. Megighian et al. (64) investigated the influence of the cortex and superior culliculi on OKAN I and OKAN II in rabbits. In reading their paper, one should separate the results they obtained in rabbits from the speculations they make regarding the differences between rabbits (and other lower animals) and higher mammalians, since they state that higher animals do not exhibit OKAN II; as discussed above, OKAN II can be

induced in both man and monkey. Igarashi et al. (65) have shown that both enhancement and inhibition of post-stimulatory nystagmus occur when a combination of optokinetic and vestibular stimuli is used. They demonstrated that the amount of interaction depended upon the particular stimulus parameters used and their relation to the ability of the subjects (in this case, the squirrel monkey) to pursue.

Pendular nystagmus

Pendular nystagmus is a sinusoidal oscillation which contains no saccades (no fast phases). It may be acquired or congenital and may be dissociated. It is indicative of an instability in a closed loop control system. Pendular nystagmus may be purely horizontal, vertical, oblique, or may manifest itself as circular or elliptic nystagmus. Specific types of pendular nystagmus are discussed in their respective sections.

Periodic/aperiodic alternating nystagmus

Periodic alternating nystagmus (PAN) (nystagmus alternans) is an extraordinary phenomenon in which a persisting horizontal jerk nystagmus periodically changes direction. There may be a fixed sequence consisting of approximately 90 sec of nystagmus beating in one direction, 10 sec of a neutral phase in which the eyes stop, beat downward irregularly, or oscillate pendularly, followed by 90 sec of beating in the opposite direction. In many patients the timing is very asymmetric, but since the reversals continue to occur, it may be considered aperiodic alternating nystagmus (APAN). The waveforms of the slow phases will depend on the etiology in each case. PAN can be conceptualized as resulting from periodic shifts of the null zone of a manifest horizontal jerk nystagmus (66). PAN/APAN have been associated with congenital nystagmus, head trauma, encephalitis, syphilis, multiple sclerosis, spinocerebellar degenerations, and posterior fossa tumors and infarction.

Physiological nystagmus

Physiological nystagmus (microtremor) is a high frequency (50–100 Hz), low amplitude (5–30 sec of arc), dissociated, pendular oscillation. It occurs during fixation along with microdrifts and microsaccades (67).

Physiological end-point nystagmus is observed in normal individuals when the eyes are held in extremes of lateral gaze. It often has a latency of several seconds before onset and is jerk in type, small in amplitude, irregular, variably sustained, may be dissociated, and occurs in darkness (68).

In their study of end-point nystagmus, Abel et al. (69) divided physiological end-point nystagmus into 3 types: (1) fatigue nystagmus, (2) unsustained end-point nystagmus, and (3) sustained end-point nystagmus. They found that, regardless of the particular type of end-point nystagmus developed by their subjects, the slow phases were linear rather than exponential in form. This enables differentiation from pathological gaze-paretic nystagmus. End-point nystagmus was found to begin with only 20° lateral deviation in some subjects. The latency for the development of fatigue nystagmus was variable between subjects. In addition, the

high bandwidth recording technique they employed allowed detection of dynamic overshoots in the fast phases of this nystagmus. Their discovery of the existence of physiological end-point nystagmus at gaze angles considerably less than maximal makes the term 'end-point' nystagmus a misnomer.

Pursuit after-nystagmus

Pursuit after-nystagmus is a jerk nystagmus which has recently been induced in the dark following unidirectional pursuit of a small target (50). The after-nystagmus of pursuit (predominantly a foveal reflex) and that of optokinetic stimuli (predominantly a peripheral retinal reflex) are compared in this paper along with the possible functional significance of pursuit after-nystagmus.

Pursuit-defect nystagmus

Pursuit-defect nystagmus may be a vertical or horizontal jerk nystagmus and is supposedly caused by a unilateral defect in pursuit. Thus, a defect in downward pursuit would result in a drifting of the eye upward and give rise to downbeat nystagmus. Similarly, a defect in upward pursuit would cause upbeat nystagmus and a defect in pursuit to the left or right would cause a left beating or right beating horizontal pursuit-defect nystagmus (70). The slow phases of pursuit-defect nystagmus are linear.

Sharpe et al. (71) identified pursuit-defect nystagmus in 5 patients who were studied 8–12 years after cerebral hemidecortication. His patients had decreased smooth pursuit gain ipsilateral to the side of cortical ablation and increased contralateral pursuit gain. Thus, the defect need not be absolute to produce a nystagmus inducing imbalance. Also, we have recently recorded a young woman with a posterior fossa tumor who had a distinct horizontal pursuit asymmetry but no nystagmus. Apparently, there are also factors which prevent the manifestation of nystagmus in some patients with a pursuit imbalance.

In a recent letter (72), we have questioned the whole concept of 'pursuit-defect' nystagmus. To document the absence of pursuit in the presence of an ongoing nystagmus, we feel it is insufficient to show that the ongoing slow phase direction is not reversed by pursuit in the other direction. For pursuit to be regarded as totally absent, no change in the slope of the slow phase should result when pursuit is attempted in the other direction. Further study is necessary in this area.

Rebound nystagmus

Rebound nystagmus is a gaze-evoked horizontal jerk nystagmus which fatigues and changes direction with sustained lateral gaze and/or horizontal gaze-evoked nystagmus which, upon refixation to primary position, transiently beats in the opposite direction (73). The slow phases are decreasing-velocity exponentials. Rebound nystagmus is often present in patients with parenchymal cerebellar disease, but 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 be mistaken for periodic alternating nystagmus with asymmetric cycles (APAN).

Rebound nystagmus has recently been described in a patient with Dandy-Walker syndrome and agenesis of the corpus callosum (74). The importance of recognizing rebound nystagmus in diagnosing cerebellar dysfunction is emphasized in the paper by Morales-Garcia et al. (75). Sixteen of the 17 patients they found with rebound nystagmus had cerebellar signs on neurological examination and in one subject the rebound nystagmus was the first sign suggesting cerebellar involvement; several months later other cerebellar signs were present. The one additional patient with rebound nystagmus in this study had Parkinson's disease.

See-saw nystagmus

See-saw nystagmus is a conjugate, pendular, torsional oscillation with a superimposed disjunctive vertical vector. The intorting eye rises while the opposite, extorting eye, falls. Torsional movements predominate in all fields of gaze, but the see-saw vertical feature may be restricted to the primary position or to downward gaze. Acquired see-saw nystagmus is associated with bitemporal hemianopias consequent to parasella tumors expanding within the third ventrical. Other common etiologies are upper brainstem vascular disease and severe head trauma. It is felt that see-saw nystagmus reflects diencephalic (thalamic) dysfunction possibly of a pathway from the zona inserta to the interstitial nucleus of Cajal. See-saw nystagmus may be stopped by stereotactic destruction of the interstitial nucleus. Congenital see-saw nystagmus may manifest either in constant vertical disconjugacies without a significant torsional component or in conjugate torsional nystagmus where the vertical component of the intorting eye falls while the extorting eye elevates (opposite to the acquired variety) (76).

Spontaneous nystagmus

Spontaneous nystagmus is any nystagmus present in primary position. It may be acquired or congenital, pendular or jerk, and have any of the vectors described in this chapter. Specific forms of spontaneous nystagmus are discussed in their respective sections.

Torsional nystagmus

Torsional (rotary) nystagmus consists of torsional movements of the globes about their antero-posterior axis. The nystagmus produced by vestibular end-organ dysfunction usually has a rotational component mixed with a major horizontal or vertical component. Pure rotary nystagmus never occurs with vestibular end-organ disease. Small amplitude torsional nystagmus may reflect medullary lesions, whereas larger amplitude torsional nystagmus may be congenital. Acquired torsional nystagmus implicates diencephalic (thalamic) involvement; it is the underlying pattern in see-saw nystagmus.

Uniocular nystagmus

Uniocular nystagmus is a form of dissociated nystagmus present in one eye while the

other eye is still. It may be acquired or congenital, horizontal or vertical and pendular or jerk. Specific types of uniocular nystagmus are discussed in their respective sections.

A recent report documented acquired uniocular nystagmus in a case of spasmus nutans of monozygous twins (77). The nystagmus was primarily horizontal, but a slight vertical component was evident. In another recent case, acquired uniocular nystagmus in the vertical direction was an initial sign of chiasmal glioma (78). In this case the correct diagnosis was delayed because of the initial diagnosis of spasmus nutans; this case re-emphasizes the necessity of careful clinical and radiological assessment before assuming acquired monocular nystagmus to be benign.

Upbeat nystagmus

Upbeat nystagmus is a vertical jerk nystagmus present in primary position with downward linear slow phases and fast phases in the upward direction. Usually, the nystagmus is acquired and indicates structural disease; it may reflect drug intoxication. There are two types of upbeat nystagmus (79). The first type is a large amplitude nystagmus which increases in intensity during upward gaze in accordance with Alexander's Law; the second type is of small amplitude and decreases in intensity during upward gaze contrary to Alexander's Law. Type 1 supposedly suggests a lesion in the anterior vermis of the cerebellum and type 2, intrinsic medullary disease. An intermediate form behaves like type 2 except that the nystagmus initially exceeds 5° in amplitude in primary position. This intermediate form is most commonly a manifestation of Wernicke's encephalopathy prior to the administration of thiamine. Since patients with intrinsic medullary disease have been demonstrated to have both type 1 and type 2 nystagmus, the localizing ability of this categorization is doubtful. Patients with upbeat nystagmus are said to have a defect in upward pursuit but intact vestibulo-ocular movements in the upward direction. Thus, upbeat nystagmus has been called a pursuit-defect nystagmus. Congenital upbeat nystagmus has been described but never recorded.

Vertical nystagmus

Vertical nystagmus of either the jerk or pendular variety is nystagmus in which the trajectory of the eyes is up and down with respect to the head; this is irrespective of the tilt of the head. The slow phase waveforms of jerk nystagmus (i.e. linear, decreasing-velocity or increasing-velocity exponentials) are of diagnostic importance. Specific types of vertical nystagmus are discussed in their respective sections.

Vestibular nystagmus

Vestibular (labyrinthine) nystagmus is a jerk nystagmus which may be acquired due to central vestibular dysfunction, a peripheral (end-organ) vestibular disease or vestibular system plasticity reacting to dysfunction and producing compensatory nystagmus. It also may be induced (alternating current, caloric, caloric after, electrical, faradic, galvanic, perverted, pneumatic/compressive, positional/alcohol,

postrotational, pseudo-caloric, or rotational/per rotary). Pathological vestibular nystagmus may be spontaneous or may be induced by having the patient adopt certain positions (positional) or shaking his head (head shaking); in some patients the act of changing positions induces the nystagmus rather than the position finally achieved (positioning). The slow phase of primary position vestibular nystagmus is linear and the nystagmus increases with gaze toward the fast phase in accordance with Alexander's Law. Vertigo usually coexists with the nystagmus. Acute lesions of the cerebellar flocculus (the vestibular cerebellum) can produce a similar nystagmus. In normal subjects , some degree of vestibular nystagmus may be induced when the labyrinth is stimulated with warm or cold water applied to the tympanic membrane. Direction of this nystagmus is such that the fast phase beats opposite the side in which cold water is applied or in the same direction as the side in which warm water is applied. Caloric nystagmus and caloric after-nystagmus (also called secondary phase nystagmus) also coexist with vertigo and past pointing. The direction of the vertiginous environmental movement (circularvection) is in the direction of the fast phase of the nystagmus. Pseudo-caloric nystagmus is an appropriate cold caloric and an inappropriate warm caloric response from an ear with abolished vestibular function. Vestibular nystagmus is associated with Menière's disease and many disease processes of vestibular end-organ or nerve. Spontaneous vestibular nystagmus is directed to the side opposite the lesion.

Recent papers on caloric nystagmus include one by Wolfe (80) in which he showed that cold water stimulation produced more intense activation of the ipsilateral eye; warm water did not produce such asymmetry. He concluded that the use of only one stimulus (warm or cold) would not differentiate unilateral weakness from directional preponderance. Becker et al. (81) stated the following characteristics of pseudo-caloric nystagmus: (1) mild intensity with eyes closed and no nystagmus with eyes open; (2) it always beats away from the diseased ear regardless of the temperature of the irrigating water; and (3) the induced nystagmus will not reverse direction after inverting the ampulla. The clinical importance of establishing appropriately beating nystagmus to both ampullofugal and ampullopedal flow of endolymph is discussed. Liebman and Toglia (82) established that ablation of the occipital visual cortex or the super colliculi in cats did not affect visual inhibition of vestibular nystagmus. They concluded that the visual inhibition of vestibular nystagmus is a brainstem reflex to light mediated via the cerebellum. Greven et al. (83) found, in a comparison between water and air caloric stimulation, that the use of water was significantly stronger than the use of air. They concluded that water is the method of choice for caloric tests unless contraindicated. Bock and Zangemeister (84) presented a mathematical model of both air and water caloric nystagmus in an attempt to describe the time course of air caloric nystagmus and thereby shed more light on the different effects of the two types of irrigation. Their model is complete in that it includes the dynamics of air irrigation as well as the steady-state solution. In another study by the same authors (85), the influence of pneumatization of mastoid bone on caloric nystagmus response was studied and a mathematical model presented. They found significant differences in the caloric responses of patients with extensively or poorly pneumatized mastoid bones. They concluded that in ears with very strong caloric responses or striking side differences, a careful examination of the pneumatization of the mastoid bone is in order. Mulch

and Petermann (86) established the influence of age on the outcome of caloric testing. They found the intensity of the nystagmus increases with advancing age and also that the extent of the side difference excitability is age-dependent. Thus, standard values of a true quantitative evaluation of caloric testing must be age-matched.

In a recent study of positional nystagmus, Thomsen et al. (87) found that, although rare (1% of 10,730 patients), persistent positional nystagmus was always of central origin. Central positional nystagmus was found to have no latency, low and irregular frequency, was non-fatigable, and had no accompanying dizziness. Longridge and Barber (88) studied 114 patients with paroxysmal positional vertigo. Of these patients, 17 (15%) had bilateral positioning nystagmus and, of the remaining 97, half had positioning nystagmus in one head-hanging lateral position. The clinical implications of these findings are discussed in this paper.

Doslak et al. (89) have recently presented a model of the variation of vestibular nystagmus amplitude with intended gaze angle in accordance with Alexander's Law. The model utilized a gaze modulation of the vestibular signals going to the push-pull integrators responsible for maintaining eye position. The model successfully demonstrated first, second, and third degree vestibular nystagmus and their variations with gaze angle in accordance with certain assumptions implicit in Alexander's observations. The modulation of slow phase velocity was accomplished by the interaction of intended gaze angle signals with those from the vestibular nuclei. As stated in the paper, the assumptions employed in the modelling have yet to be verified by studies of the variation of vestibular nystagmus with gaze angle in human subjects. Chun and Robinson (90) presented a model of the quick phase generation of vestibular nystagmus. They postulated that the quick phases were generated by a local feedback loop in the pons which drove the eyes back to points in the orbits specified by a vestibular signal. They suggested that two internal signals specified the eye positions at which quick phases start and end. Basically, the model uses a desired eye position which is derived from the vestibular head velocity signal, a measurement of the error between the desired eye position and some internal state variable that behaves as eye position and, when the error reaches a threshold, the eye is rapidly reset to the desired eye position. In their study of the variables utilized in the production of the fast phase of nystagmus, Lau et al. (91) found that the threshold was dependent upon both eye position and eye velocity. Sills et al. (92) studied the applicability of the adaptation model of slow phase velocity variation of vestibular nystagmus and after-nystagmus. Although the model fits the experimental data in some cases, it was concluded that the model had limited overall applicability in clinical situations. In still another model, Raphan et al. (93) investigated 'velocity storage' in the vestibular system. It postulated a common storage mechanism for producing vestibular nystagmus, OKN, and OKAN. They noted that the stored activity is lost in a similar way when viewing stationary surrounds during either OKAN or vestibular nystagmus. They found that the activity stored is that which produces a slow phase eye velocity and their model shows how the visual and vestibular systems might utilize such velocity storage to produce the slow phases of nystagmus.

There have been several recent studies on the influence of vision on vestibular nystagmus (visual-vestibular interaction). Koenig et al. (94) found that the

combination of vestibular and optokinetic stimuli resulted in better correspondence of the slow phase velocity of the eye and the stimulus velocity at higher accelerations and velocities. They also found that depressing vestibular stimuli caused greater slow phase velocity modulation than enhancing of the stimuli. The paper concludes with a discussion of the three possible mechanisms which might be involved in visual-vestibular interaction: a switching mechanism; a weighted summation; and an algebraic summation. Waespe and Henn (95) found in their studies with Rhesus monkeys that, in the presence of conflicting visual-vestibular stimulation, the neuronal activity of the vestibular nuclei reflected higher thresholds of neuronal modulation than when the stimulation was purely vestibular. They could always dissociate the nystagmus slow phase velocity from the neuronal activity; the nystagmus was often totally suppressed, whereas the neuronal activity was only attenuated. They suggested that further information processing between vestibular and ocular motor nuclei was taking place in the generation of nystagmus.

Yee et al. (96) found that the use of interactive visual-vestibular tests could not differentiate patients with unilateral semicircular canal paralysis from normals but could separate patients with bilateral paralysis from normals. In a study of cerebellar and non-cerebellar patients, Dichgans et al. (97) found that deficits in fixation suppression of vestibular nystagmus were only found if optokinetic and smooth pursuit responses were impaired. Fixation suppression of vestibular nystagmus was diminished in the ipsilateral direction for patients with hemisphere and cerebellar lesions and in the contralateral direction in patients with brainstem damage. Patients with cerebellar atrophy, although having a normal vestibulo-ocular reflex gain and normal vestibular and optokinetic responses when tested independently, had abnormal visual-vestibular interaction (98). Dichgans and Brandt (99) have written an excellent chapter on visual-vestibular interaction which is recommended reading for all those interested in this area.

The utility of the intersaccadic interval analysis method of evaluating vestibular nystagmus in a clinical setting was recently discussed in a paper by Zangemeister and Bock (100). They concluded that, compared with the common nystagmus parameters normally measured, intersaccadic interval analysis was not a good diagnostic method. There has been an increasing use by large laboratories of microprocessor-based computers for the analysis of vestibular nystagmus. A comparative analysis of the various programs and types of computers in use is beyond the scope of this chapter. Such systems tend to be tailored to the particular needs of specific laboratories. Several recent papers on the subject are recommended reading for those interested in computer analysis of vestibular nystagmus (101–104).

OTHER OCULAR MOTOR OSCILLATIONS

Non-nystagmic ocular motor oscillations represent solely saccadic or saccadically initiated instabilities. I have identified 16 distinct varieties of such oscillations which have been characterized in the literature by 32 different terms, including 8 which erroneously contain the term 'nystagmus'.

Ocular bobbing

Ocular bobbing is a distinctive spontaneous ocular motor disturbance easily distinguished from downbeat nystagmus or ocular myoclonus. It is generated by fast downward jerks of both eyes (sometimes dissociated) followed by slow drifts to mid-position (105). It usually occurs in comatose patients to have extensive destruction of the pons; extrapontine compressions, obstructive hydrocephalus, and metabolic encephalopathy are occasionally causative. Bobbing has been divided into 3 types (106). Typical bobbing involved both eyes and appeared in patients with paralysis of horizontal conjugate gaze. A uniocular type reflected coexisting unilateral III nerve paresis. The third category, atypical bobbing, included downward bobbing with convergence movements, asymmetric bobbing without associated ocular motor palsies, or bobbing with intact spontaneous or reflex horizontal eye movements. The pathophysiology of all forms of ocular bobbing is uncertain. Occasionally, reverse bobbing (the eyes jerk upward) has been seen in patients who are deeply comatose from metabolic encephalopathy.

Convergence-retraction 'nystagmus'

Convergence-retraction 'nystagmus' ('nystagmus' retractorius) is a saccadic co-contraction of all the ocular muscles and is not nystagmus at all. Both globes simultaneously retract with a fast (saccadic) movement and then drift outward back to their normal position. Convergence-retraction nystagmus is a component of the dorsal midbrain (Parinaud's, pretectal, posterior commisural, sylvian aqueduct, Koerber-Salus-Elschnig) syndrome. Downgoing optokinetic targets are an effective way of eliciting convergence-retraction 'nystagmus' (107).

Recently, Ochs et al. (108) have published an excellent ocular motor study of the opposed adducting saccades in convergence-retraction 'nystagmus'. They have shown conclusively that, in agreement with published electromyograms, the adducting saccades are asynchronous by approximately 8 msec. Also, by using high-speed movies from a lateral view, they found that the globes of the patient they studied did not retract. As expected, the opposed adductions followed the normal velocity amplitude relationship of saccades. They postulated that the opposed adducting saccades arise out of the normal dynamic overshoot mechanism.

Dynamic overshoot

A dynamic overshoot consists of a no-latency return saccade which truncates a refixation saccade and returns the eye to some intermediate point between the initial gaze angle and that produced by the refixation saccade (109). Dynamic overshoots are uniocular and occur in normals. The clinical term 'quiver' has been used to describe the large dynamic overshoots seen in patients with myasthenia gravis; these movements resemble flutter dysmetria with only one cycle.

Ocular dysmetria

Ocular dysmetria is provided by refixation saccades and consists of undershooting

or overshooting followed by brief small-amplitude saccadic oscillations before the eyes come to a new fixation point; or conjugate overshooting followed by a single corrective saccade to bring the eye back to the target. There is an intersaccadic latency between the various corrective saccades. Dysmetria is a common sign of cerebellar system disease (110).

Ocular flutter

Flutter consists of spontaneous back-to-back horizontal saccades which interrupt fixation. Flutter usually occurs in brief intermittent bursts and the eye movements are conjugate. Since the saccades are back-to-back, there are no intersaccadic intervals. Patients with flutter usually also exhibit dysmetria. Flutter and opsoclonus represent a continuum of ocular motor instability; patients often pass through phases of flutter when recovering from opsoclonus (the opsoclonus may re-emerge with upward gaze).

Zee and Robinson (111) recently studied a patient with ocular flutter. Utilizing information derived from studies in monkeys, which have identified 3 types of premotor neurons associated with saccadic eye movements, they constructed a model using burst, tonic and pause cells. They demonstrated how their model would simulate ocular flutter when a short delay was introduced into one of the feedback loops. Since the pulse generator in their model has a high gain, it is inherently unstable and would oscillate when such a delay is introduced. They postulated 3 mechanisms which might induce this instability: a prolonged trigger signal, an inadequate bias, or unresponsive pause cells.

Flutter dysmetria

Flutter dysmetria consists of bursts of flutter which immediately follow saccadic refixations. Flutter dysmetria differs from classical dysmetria in that the oscillation about the intended fixation angle consists of back-to-back saccades without intersaccadic intervals. As with flutter and ocular dysmetria, flutter dysmetria is seen in patients with cerebellar disease.

Macro-saccadic oscillations

Macro-saccadic oscillations (MSO) are bursts of to-and-fro saccades with normal intersaccadic latencies whose amplitudes gradually increase and then decrease. MSO straddle fixation and are believed to result from a high loop gain in the saccadic system (112). MSO are associated with cerebellar disease.

Macro-square-wave jerks

Macro-square-wave jerks (MSWJ) (Kippdeviationen/'Kippnystagmus') are spontaneous saccades which move the eyes from the object of fixation to some point in space lateral to that object. After a short latency (50–100 msec) a non-visually mediated corrective saccade returns the eyes to target (113). MSWJ may occur singly or in bursts during fixation or following voluntary refixation. MSWJ have been

found in patients with cerebellar signs related to multiple sclerosis and are mechanically different from square-wave jerks (114). The contradictory term 'saccadic nystagmus' has been applied to MSWJ as has 'pendular macrooscillations'.

Myoclonus

The term 'myoclonus' has been loosely applied to a variety of ocular conditions ranging from oscillations which are clearly nystagmus to simple square-wave jerks; it has even been equated to 'lightning eye movements'. Since ocular myoclonus is usually associated with myoclonic jerks of other structures of the body, I have chosen to list myoclonus under the heading of 'Other Ocular Motor Oscillations' despite the fact that the actual movement of the eyes may be a combination of a pendular nystagmus and a jerk nystagmus where the saccades of the jerk nystagmus are synchronous with the myoclonic jerks of the involved body structures. Commonly involved with ocular myoclonus are the soft palate, tongue, facial muscles, pharynx, larynx and diaphragm. Palatal and oculopalatal myoclonus have a specific pathological correlate; it is pseudohypertrophy of the inferior olivary nucleus in the medulla. The myoclonic triangle involves the 3 structures: the red nucleus in the midbrain, the ipsilateral inferior olive in the medulla, and the contralateral dentate nucleus of the cerebellum. They are connected by the central tegmental tract, the inferior cerebellar peduncle, and the superior cerebellar peduncle. It is pseudohypertrophy of the inferior olives secondary to involvement of these tracts which causes the oculopalatal myoclonus.

Opsoclonus

Opsoclonus (saccodomania) consists of rapid, involuntary, chaotic, repetitive, unpredictable, conjugate saccadic eye movements in all directions which prevent fixation and persist during sleep. The terms 'dancing eyes' and 'lightning eye movements' have been used to describe the eye movements of patients with opsoclonus.

Opsoclonus has recently been studied in 2 cases of benign encephalitis (115). It was found that opsoclonus was triggered by both saccadic and non-saccadic eye movements. The strongest trigger for opsoclonic eye movements was eye closure, but decrease of luminance and loss of fixation also released these movements. During the initial stages of the disease, uniocular and dissociated eye movements were also seen. Although mostly horizontal, these patients also showed oblique and vertical opsoclonic eye movements.

Saccadic double pulses

Saccadic double pulses are small back-to-back saccades which interrupt fixation, taking the eyes off target and immediately returning them to the target. This type of saccadic intrusion is common in normals (where the saccadic double pulse may only be minutes of an arc in amplitude) and it has also been noted by this author as occurring in certain cases of congenital nystagmus.

Saccadic lateropulsion

Saccadic lateropulsion is a dramatic eye movement abnormality associated with lateral veering of body and limb movements. It has been reported in a patient with a left lateral medullary infarction (116). All saccades made to the left by this patient were very large (hypermetric) while those to the right were very small (hypometric). Even vertical saccades veered to the left along an oblique rather than the vertical path.

Frisén (117) found, in his study of saccadic lateropulsion, that the direction of lateropulsion was the direction in which the eyes veered during up and down saccades. This always coincided with the direction of horizontal hypermetria and with the direction of eye deviation under closed lids. In all cases he studied, the lateropulsion was toward the side of the lesion. Although several of his patients had Wallenberg's syndrome, other patients had disorders which showed that lateropulsion can occur with pontine lesions and large tumors of the cerebellar-pontine angle.

Saccadic pulses

Saccadic pulses are saccadic intrusions which consist of a saccadic movement of the eyes off fixation followed by an exponential drift back to the target (a stepless saccade). Saccadic pulses occur in normals along with saccadic double pulses.

Square-wave jerks

Square-wave jerks (SWJ) (Gegenrucke, hopping 'nystagmus', 'lightning eye movements', and Zickzackbewegungen) consist of a pair of saccades which initially take the eyes off fixation by a few degrees and after a suitable latency (about 200 msec) return the eyes to the target. SWJ intrusions may occur in normals (especially upon closure of the eyelids) or may represent pathology suggestive of cerebellar disease.

Two recent papers by Ciuffreda et al. (118, 119) discussed the occurrence of SWJ in patients with strabismus. Although referred to by the general term 'saccadic intrusions', the movements are clearly SWJ and not other forms of saccadic intrusions. Patients studied had either intermittent strabismus, amblyopia without strabismus, or constant strabismus amblyopia. SWJ were found frequently in patients with strabismus during monocular fixation with the amblyopic eye in the light. The frequency of SWJ could be reduced by instructing the patient to 'hold the eye steady' in the presence of a visible target in the light and when instructed to 'fixate' in complete darkness; in this latter case, the SWJ were replaced by jerk nystagmus. They concluded that the presence of saccadic intrusions was related to strabismus and not to amblyopia. Two possible mechanisms for producing SWJ are also discussed. In another paper by Dale et al. (120), SWJ were found to be present in 2 patients with Friedreich's ataxia.

Superior oblique myokymia

Superior oblique myokymia is a small-amplitude, uniocular, intermittent, torsional eye movement which evokes oscillopsia and appears spontaneously in otherwise healthy adults. It reflects phasic contraction of the superior oblique muscle and may be detected during ophthalmoscopy or by the use of the slit lamp. The repetition rate for this oscillation is usually 12–15 Hz. Superior oblique myokymia sometimes responds to the administration of the anticonvulsant drug, carbamazepine.

Voluntary 'nystagmus'

Voluntary (hysterical, psychological) 'nystagmus' is not nystagmus at all but a series of back-to-back saccades, interrupting fixation, whose timing is such that the waveform traced out appears to be pendular (i.e. a voluntary flutter) (121). The frequency of this oscillation, also called 'ocular fibrillation' and 'ocular shuddering', is typically 8–23 Hz. The oscillation is horizontal, conjugate, and each burst usually has a duration of less than 30 sec.

In a report on the coincidence of voluntary 'nystagmus', Zahn (122) found that 8% of a college-age population can produce this oscillation. Significantly, 79% of this sample had relatives who could also produce it. As a result of a literature survey, it was found that the mean frequency was 16 Hz, mean amplitude 5.2%, and mean duration 22.4 sec; there were wide variations in each of these parameters. A unique case of voluntary 'nystagmus' masquerading as Tullio's phenomenon was recently described by Coats et al. (123). Since the eye oscillations were induced when the patient hummed at a constant pitch (approximately middle C), it was initially thought to be an abnormal vestibular response to acoustical stimulation. Since examination of the auditory and vestibular systems proved negative, it was concluded that this was a case of hysterical 'nystagmus'. This was verified by accurate eye movement recordings which quantified the antecedent convergence movement, the fatigability and conjugacy of the movements, and the inability to elicit the nystagmus behind closed eyelids.

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