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movements is to keep the image of the visual surroundings stable on the retina, even during eye movements or head and body movements. This is achieved by (1) conjugate eye movements (both eyeballs move in parallel)—gaze-holding, smooth pursuit, saccades, vestibulo-ocular nystagmus, and optokinetic nys- tagmus; and (2) disconjugate eye movements—convergence and divergence. All of these different eye movements are reflexive movements except saccades and convergence/divergence. Clinical examin- ation of eye movements should include tests of (1) eye position (latent or manifest strabismus, in particular vertical divergence/ skew deviation); (2) nystagmus (in particular peripheral ves- tibular spontaneous nystagmus or central fixation nystagmus); (3) gaze-holding function (gaze-evoked nystagmus, sustained or unsustained endpoint nystagmus); (4) smooth pursuit (saccadic or smooth); and (5) saccades (velocity, accuracy, and conjugacy). Many abnormalities of eye movements and nystagmus are dis- tinctive and often indicate the site and the side of a lesion (mid- brain, pons, medulla or cerebellum), for example, vertical and torsional eye movements are generated and controlled in the mes- encephalon, whereas horizontal eye movements are generated and controlled in the pons: gaze-evoked nystagmus in all direc- tions, saccadic smooth pursuit, downbeat or rebound nystagmus, as well as hypermetric saccades indicate a lesion of the cerebellum or cerebellar pathways. Dizziness and vertigo Vertigo, dizziness, and disequilibrium are common complaints of pa- tients of all ages, particularly older people, with a lifetime prevalence of about 30%. Although the anatomy and the physiology of the ves- tibular and ocular motor systems are complex, a correct diagnosis can be made in most patients on the basis of the patient history and the bedside examination. Vertigo syndromes are commonly characterized by a combin- ation of phenomena involving (1) vertigo itself—resulting from a dis- turbance of cortical spatial orientation; (2) nystagmus—caused by a direction-specific peripheral or central imbalance in the vestibulo- ocular nystagmus, which activates brainstem neuronal circuitry; (3) postural imbalance—caused by inappropriate or abnormal acti- vation of monosynaptic and polysynaptic vestibulospinal pathways; and (4) unpleasant autonomic responses of nausea, vomiting, and anxiety—ascending and descending vestibulo-autonomic pathways activate the medullary vomiting centre. Clinical approach—the history is of special importance, with the patient’s symptoms giving an idea of the likely underlying cause and differentiating the different forms of peripheral, central or functional vestibular vertigo/dizziness as well as nonvestibular causes. Patient history should focus on four aspects: (1) duration and onset of the symptoms (attacks lasting seconds, minutes, or hours; acute onset of symptoms lasting days; permanent symptoms (>3 months); (2) type of vertigo/dizziness (spinning ver- tigo, dizziness or postural imbalance); (3) factors that provoke, in- crease or alleviate the symptoms (e.g. change of head or body position, walking, changes of pressure, certain social situations); and (4) accompanying symptoms (in particular, brainstem or cerebellar symptoms, symptoms arising from the ear, or symptoms typical for migraine). Careful and systematic combined bedside examination of the vestibular and ocular motor systems often allows an exact topo- graphic determination of the lesion. Additional laboratory investiga- tions often do not contribute materially to the diagnosis, except the video-head-impulse test and caloric irrigation. Particular causes—more than 60% of all patients presenting with dizziness, vertigo or disequilibrium in a neurological dizziness unit will be suffering from one of the following: (1) benign paroxysmal

 positional vertigo; (2) functional dizziness; (3) central vestibular dis- orders; (4) vestibular migraine; (5) Menière’s disease; (6) acute unilat- eral peripheral vestibulopathy. Prognosis and treatment—many forms of vertigo have a be- nign cause

and are characterized by spontaneous recovery of vestibular function or central compensation of a vestibular tone imbalance. Most forms of vertigo can be relieved by (1) pharmaco- logical treatment—depending on the particular cause; for example,
vestibular suppressants for symptomatic treatment, probably anti migraineous drugs for vestibular migraine, probably high dosage of β-histine dihydrochloride for Menière's disease, corticoster- oids for acute unilateral vestibulopathy (one controlled trial), antiepileptic drugs for vestibular paroxysmia (one controlled trial), or aminopyridines for downbeat nystagmus and episodic ataxia type 2 (controlled trials); (2) physical therapy—liberatory man- oeuvres for benign paroxysmal positional vertigo (multiple con- trolled trials) or vestibular exercises and balance training—for uni- or bilateral vestibular failure (few controlled trials) or central forms of vertigo;
(3) psychotherapy—in particular for functional dizziness; or (very rarely); (4) surgery for vestibular schwannoma or superior canal dehiscence syndrome. Introduction The disorders underlying vertigo and dizziness are often combined with disturbances of eye movements; reciprocal effects occur be- cause of the anatomical and functional overlap of the vestibular and ocular motor systems. Therefore, both systems must always be tested in patients complaining of vertigo and dizziness. Using a systematic approach, it is possible to make a correct diagnosis in more than 90% of patients. The history is of special importance and one should already have an idea, from the symptoms reported by the patient, what the underlying cause of the vertigo is in order to differentiate the different forms of peripheral, central, and functional vestibular vertigo/dizziness and nonvestibular forms. A careful and systematic examination of the ocular motor and ves- tibular systems often allows an exact topographic determination of the lesion, in particular to differentiate between central and periph- eral lesions in patients with acute symptoms. Important additional laboratory examinations of the vestibular system are the video- head-impulse test and caloric irrigation to test the function of the vestibulo-ocular reflex (VOR) as well as in some cases vestibular evoked myogenic potentials to test the function of the otolith organs. Eye movements Different types of eye movements can be distinguished, each with particular functions, physiological properties, and specific anatom- ical substrates: smooth pursuit, saccades, optokinetic nystagmus, vestibulo-ocular nystagmus, and gaze-holding (all of these are con- jugate eye movements, i.e. both eyeballs move in parallel) as well as disconjugate eye movements (convergence and divergence). The major function of eye movements is to keep the image of the visual surroundings stable on the retina, even during eye or head and body movements. Normal vision relies on eye movements in two essential ways: on the one hand, eye movements make it possible to shift the gaze and to view objects of interest and, on the other, when the head or body moves during locomotion, the eyes move in a direction op- posite to that of the head and compensate for these head movements, thereby preventing involuntary shifts of the visual images projected on to the retina. The retinal images are kept steady. Optimal func- tioning of the eye movements is ensured by cooperation between the optokinetic reflex and the VOR as well as by visual fixation suppres- sion of the VOR when combined movements of the head and the visual target occur. For anatomical reasons many abnormalities of eye movements are distinctive and often indicate the site and the side of a lesion (e.g. vertical and torsional eye movements are generated and con- trolled in the mesencephalon), whereas horizontal eye movements are generated and controlled in the pons. The role of the cerebellum in eye movements and a precise diagnosis on the basis of disturbed cerebellar eye movements is often neglected. Frequent oculomotor signs such as saccadic smooth pursuit, gaze-holding deficit in all directions or dysmetric saccades are caused by an impairment of the flocculus/paraflocculus, nodulus, vermis, or fastigial nucleus. All in all, a systematic examination of the ocular motor system is very useful

for topographic diagnosis, a method that can still be superior to imaging techniques, in particular in the acute phase. It is therefore important that the doctor examines in detail all types of eye movements of patients with, for example, double or blurred vision, oscillopsia (apparent movement of the visual surroundings due to retinal slip), vertigo, dizziness, or postural imbalance be- cause they can, by this means, often differentiate between 'periph- eral' and 'central' ocular motor disorders and thereby also between peripheral and central vestibular disorders. In their excellent book Neurology of eye movements, Leigh and Zee correctly state that 'an understanding of the properties of each functional class of eye movements will guide the physical examination; a knowledge of the neural substrate will aid topological diagnosis'. Here the clinical examination techniques of the ocular motor system and common pathological findings, as well as the typical fea- tures of the different forms of nystagmus, are summarized. Eye position, range of eye movements, nystagmus, and gaze-holding function The following eye movements should be examined: fixation when looking straight ahead, gaze-holding function, smooth pursuit, saccades, convergence, optokinetic nystagmus, and vestibular nys- tagmus. Clinical examination should begin with examination of the eyes in nine different positions (i.e. looking straight ahead, to the right, left, up, and down, as well as diagonally right up, right down, left up, and left down) to determine ocular alignment (e.g. a possible misalignment of the eye axes), which may be accompanied by a head tilt as in trochlear palsy, fixation deficits, spontaneous nystagmus, impaired range of movement, and disorders of gaze-holding abil- ities. The examination can be performed with an object for fixation or a small rod-shaped flashlight. In primary position one should look for a misalignment of the eye position, in particular for a latent strabism ('phoria') or a mani- fest strabism ('tropia') by means of the cover-test (Fig. 24.6.2.1) and the alternating cover-test which allows the maximal angle of eye

 deviation to be determined. For the differentiation between acute central and peripheral vertigo it is important to look for a vertical divergence ('skew deviation') which indicates a central lesion as a component of the ocular tilt reaction. With their eyes in the primary position the patient should also be examined for periodic eye movements, in particular a spontan- eous nystagmus. The leading symptoms of patients with nystagmus are blurred vision, oscillopsia, and/or reduced visual acuity. In most forms of nystagmus, the pathological eye movement is the slow drift (slow phase), followed by rapid corrective saccadic eye movement (quick phase) which brings the eyes back to the 'central position'. The direction of a nystagmus, however, is given according to the quick phase. During this quick phase, cortical mechanisms suppress oscillopsia. The different forms of nystagmus can be differentiated by the direction and factors that provoke the nystagmus or modify its in- tensity. Clinically relevant examples are as follows: a horizontal– rotatory peripheral vestibular spontaneous nystagmus, which is typically suppressed by fixation as in acute unilateral vestibulopathy, or a central fixation nystagmus, which typically is not suppressed by visual fixation, such as downbeat or upbeat nystagmus. Downbeat nystagmus is most often caused by an im- paired function of the flocculus, upbeat nystagmus can be due to a lesion in the medullar or midbrain. Infantile nystagmus typically beats horizontally at various frequencies and amplitudes, and in- creases during fixation. Ocular flutter (intermittent rapid bursts of horizontal oscillations without an intersaccadic interval) or opsoclonus (combined horizontal, vertical, and torsional oscilla- tions) occurs in various disorders such as encephalitis, tumours of the brainstem or cerebellum, or paraneoplastic syndromes, or in intoxication (in a strict sense they are not a nystagmus). Square- wave jerks (small saccades—0.5–5°) that cause the eyes to oscillate around the primary position increasingly can

occur in progressive supranuclear palsy or certain cerebellar syndromes. The examination of the eyes with Frenzel's spectacles or M glasses (Fig. 24.6.2.2) which largely prevent visual fixation is a sensitive method for the differentiation of the two types of spon- taneous nystagmus: peripheral vestibular spontaneous nystagmus, which typically can be suppressed by visual fixation, versus central (a) ORTHOPHORIE ESOPHORIE (b) EXOPHORIE ORTHOPHORIE HYPOPHORIE HYPERPHORIE (c) Fig. 24.6.2.1 Cover-test to look for the eye position. With the cover-test in primary eye position (a) and in the eight other eye positions an ocular misalignment can be detected. The alternating cover-test shows the maximum angle of eye deviation. Typical eye deviations indicating a latent strabismus are an esophoria or an exophoria (b). In patients with acute vertigo one should look in particular for a vertical misalignment (i.e. vertical divergence/skew deviation) (c) because this indicates a central lesion. Skew deviation is one of the four possible components of the ocular tilt reaction. In contrast to trochlear palsy, which also leads to a vertical divergence, in skew deviation the angle of eye deviation does not depend very much on the eye position and patients typically do not complain of double vision because this is due to a central lesion of graviceptive pathways. (a) (b) Fig. 24.6.2.2 Clinical examination with Frenzel's spectacles (a) or M glasses (b): the magnifying lenses (+16 D) prevent visual fixation, which could suppress peripheral vestibular spontaneous nystagmus. These devices also enable the clinician to observe spontaneous eye movements better. Examination should include spontaneous, head-shaking nystagmus (instruct the patient to rotate the head about 20 times and observe eye movements after head-shaking), positioning nystagmus as in benign paroxysmal positional nystagmus (BPPV) or central positional nystagmus, as well as hyperventilation-induced nystagmus as in vestibular paroxysmia or vestibular schwannoma.

24.6.2 Eye movements and balance 5925 fixation nystagmus, which is often present although the patient is fixating a target. This is because in a central lesion the patient cannot use retinal slip as an error signal to suppress the nystagmus whereas in a pure peripheral lesion the patient is able to do so. However, pa- tients with acute brainstem lesions are sometimes able to suppress their nystagmus. First, in clinical practise simply the characteristics of the nystagmus and pathological eye movements should be de- scribed because in this way the various forms of nystagmus can be easily diagnosed even with no additional laboratory examination, since the classification is based on purely descriptive criteria. After checking for possible misalignment of the axes of the eyes and eye movements in the primary position, the examiner should then establish the range of eye movements monocularly and binocu- larly in the eight end-positions. Use of a small rod-shaped flashlight has the advantage that the corneal reflex images can be observed and thus ocular misalignments can be easily detected (note: it is important to observe the corneal reflex images from the direction of the illumination and to ensure that the patient attentively fixates the object of gaze). Deficits of the range of eye movements found can indicate: (a) extraocular muscle dysfunction (e.g. chronic pro- gressive external ophthalmoplegia often associated with bilateral palsy); (b) impaired neuromuscular transmission (as in myasthenia gravis typically affecting different eye muscles in both eyes with use-dependent weakness and ptosis), cranial nerve palsy (N. III, IV, VI); (c) central lesions with a supranuclear gaze palsy (as in pro- gressive supranuclear gaze palsy or Niemann-Pick type C disease) or an internuclear opthalmoplegia with the pathognomonic clinical sign of an adduction deficit on the side of the lesion of the medial longitudinal fascicle. A gaze-evoked nystagmus, indicating a gaze-holding deficit, is de- termined by examining eccentric gaze position. An isolated vertical gaze-evoked nystagmus is observed in midbrain lesions, indicating a lesion of the interstitial nucleus of Cajal, the neural integrator for vertical eye movements. An isolated horizontal gaze-evoked nys- tagmus most often indicates a

lesion in the lower brainstem affecting the nucleus prepositus hypoglossi and/or vestibular nuclei. A gaze- evoked nystagmus in all directions indicates an impaired function of the cerebellar flocculus (i.e. the neural eye velocity to position integrator). The latter can be caused by alcohol or medication (in particular anticonvulsants and benzodiazepines) or cerebellar dis- orders.
A dissociated horizontal gaze-evoked nystagmus (greater in the abducting than the adducting eye) in combination with an ad- duction deficit points to internuclear ophthalmoplegia due to a defect of the medial longitudinal fascicle, ipsilateral to the adduction deficit (which is the clinical hallmark of internuclear opthalmoplegia). Downbeat nystagmus usually increases in eccentric gaze position and when looking down because it is combined with a gaze-holding deficit. To examine for a so-called rebound nystagmus the patient should gaze for at least 30 s to one side and then return the eyes to the primary position; this can cause a transient nystagmus to ap- pear with slow phases in the direction of the previous eye position. Rebound nystagmus also indicates cerebellar dysfunction (floc- culus) or damage to the cerebellar pathways. Downbeat nystagmus, one of the most frequent acquired persisting forms of nystagmus, typically increases when looking down and especially to the side. A nystagmus beating diagonally and downward is found in the side- ward gaze. The cause of downbeat nystagmus is generally a bilat- erally impaired function of the flocculus/paraflocculus. Smooth pursuit The patient is asked to visually track an object moving slowly in horizontal and vertical directions (10–20°/s) while keeping the head stationary. The signal for smooth pursuit eye movements is ‘retinal slip’. During clinical examination corrective (catch-up or back-up) saccades are looked for; they indicate a smooth pursuit gain that is too low or (rarely) too high (ratio of eye movement velocity to object velocity). Many anatomical structures (visual cortex, motion-sensitive areas MT, V5, frontal eye fields, dorso- lateral pontine nuclei, cerebellum, and vestibular and oculomotor nuclei) are involved in smooth pursuit eye movements, which keep the image of a moving object stable on the fovea. These eye movements are also influenced by alertness, various drugs, and age. Even healthy individuals exhibit a slightly saccadic smooth pursuit during vertical downward gaze. For these reasons a sac- cadic smooth pursuit does not as a rule allow either an exact topo- graphical or an aetiological classification. Marked asymmetries of smooth pursuit, however, indicate a structural lesion; strongly impaired smooth pursuit is observed in intoxication (anticon- vulsants, benzodiazepines, or alcohol) as well as degenerative disorders involving the cerebellum, in particular the flocculus/ paraflocculus. A reversal of slow smooth pursuit eye movements during optokinetic stimulation is typical of infantile/congenital nystagmus (see earlier). Saccades First, it is necessary to observe spontaneous saccades triggered by visual or auditory stimuli. Then the patient is asked to glance back and forth between two horizontal or between two vertical targets. The velocity, accuracy, and the conjugacy of the saccades should be noted. Normal individuals can immediately reach the target with a fast single movement with or without one small corrective saccade. Slowing of saccades—often accompanied by hypometric saccades— occurs, for example, with intoxication (medication, especially anti- convulsants or benzodiazepines) or in neurodegenerative disorders. Isolated slowing of horizontal saccades is generally observed in pon- tine lesions, indicating a dysfunction of the ipsilateral paramedian pontine reticular formation. Slowing of vertical saccades only in- dicates a midbrain lesion in which the rostral interstitial nucleus of the medial longitudinal fascicle (riMLF) is involved, not only in ischaemic or inflammatory diseases, but also in neurodegenerative diseases, especially progressive supranuclear palsy. In Niemann- Pick type C there is typically first a slowing of vertical downward, then upward saccades and later also of horizontal saccades. Since the cerebellum is responsible for the accuracy and not the velocity of saccades a dysmetria typically indicates an impaired function of the cerebellum or cerebellar pathways. Hypermetric saccades, which can be identified by a

corrective saccade back to the object, indicate lesions of the cerebellum (especially the fastigial nucleus) or the cerebellar pathways. Patients with Wallenberg's syn- drome make hypermetric saccades towards the side of the lesion due to a dysfunction of the inferior cerebellar peduncle; conversely, de- fects of the superior cerebellar peduncle lead to contralateral hypo- metric saccades. Hypometric saccades in all directions indicate a dysfunction of the dorsal ocular motor vermis. A slowing of the adducting saccade ipsilateral to a defective medial longitudinal fascicle is pathognomonic of an internuclear

section 24 Neurological disorders 5926 opthalmoplegia. Delayed-onset saccades are mostly caused by supratentorial cortical disturbances (Balint's syndrome). Vergence test and convergence reaction A target is moved from a distance of about 50 cm towards the patient's eyes or the patient looks back and forth between a dis- tant and a near target. Looking at a near target causes vergence, ac- commodation and miosis (i.e. the convergence reaction). Neurons important for the convergence reaction are in the area of the mes- encephalic reticular formation and the oculomotor nucleus. This explains why the convergence reaction is disturbed in rostral mid- brain lesions and tumours of the pineal region and thalamus, and why abnormalities of vertical gaze are often associated with these defects. In certain neurodegenerative disorders such as progres- sive supranuclear palsy, convergence is also often impaired. Inborn defects of the convergence reaction also occur in some forms of strabismus. Convergence-retraction nystagmus can be induced by having the patient look upward, having him make saccades verti- cally upward, or look at a moving optokinetic drum with its stripes going downward. Instead of vertical saccades, rapid, convergent eye movements result that are associated with retractions of the eyeball. The site of damage is the posterior commissure or in rare cases a bilateral disorder of the riMLF. As a general rule, most often it is necessary to combine the patho- logical clinical findings of the different eye movement systems to differentiate between a central and a peripheral vestibular disorder, and to make an exact topographical diagnosis within the brainstem and cerebellum. Dizziness and vertigo Vertigo, dizziness, and disequilibrium are common complaints of patients of all ages, particularly older people. The lifetime preva- lence of vertigo and dizziness is about 30%. The clinical spectrum of vertigo is broad, extending from vestibular rotatory vertigo with nausea and vomiting to postural imbalance, gait disorders, and presyncope light-headedness, from drug intoxication to hypo- glycaemic dizziness, from visual vertigo to phobias and panic attacks, and from motion sickness to height vertigo. Appropriate preventions and treatments differ for the various types of dizziness and vertigo; they include drug therapy, physical therapy, psycho- therapy, and surgery. Vertigo usually implies a mismatch of the vestibular, visual, and somatosensory systems. These three sensory systems subserve both static and dynamic spatial orientation, locomotion, and control of posture by constantly providing reafferent cues. The sensory in- formation is partially redundant in that two or three senses may simultaneously provide similar information about the same action. Thanks to this overlap of their functional ranges, it is possible for one sense to substitute, at least in part, for deficiencies in the others. When information from two sensory sources conflicts, the inten- sity of the vertigo is a function of the degree of mismatch: it is in- creased if information from an intact sensory system is lost as, for example, in patients with pathological vestibular vertigo who close their eyes. The distressing sensorimotor consequences of the mis- match are frequently based on our earlier experiences with orienta- tion, balance, and locomotion (i.e. there is a mismatch between the expected and the actually perceived pattern of multisensory input). Vertigo may thus be induced by physiological stimulation of the intact sensorimotor systems (height vertigo, motion sickness) or by pathological dysfunction of any of the stabilizing sensory sys- tems, especially the

vestibular system. The symptoms of vertigo in- clude sensory qualities identified as arising from vestibular, visual, and somatosensory sources. As distinct from one’s perception of self-motion during natural locomotion, the experience of vertigo is linked to impaired perception of a stationary environment; this perception is mediated by central nervous system (CNS) processes known as ‘space constancy mechanisms’. Loss of the external sta- tionary reference system—required for orientation and postural regulation—contributes to the distressing mixture of self-motion and surround motion. Physiological and clinical vertigo syndromes are commonly char- acterized by a combination of phenomena involving perceptual, ocular motor, postural, and autonomic manifestations: vertigo, nys- tagmus, ataxia, and nausea. These four manifestations correlate with different aspects of vestibular function and emanate from different sites within the CNS: 1 The vertigo itself results from a disturbance of cortical spatial orientation. 2 Nystagmus (see earlier) is caused by a direction-specific imbal- ance in the VOR, which activates brainstem neuronal circuitry from the labyrinth to the eyes but also to the cerebellum and cortex. 3 Postural imbalance is caused by inappropriate or abnormal activation of monosynaptic and polysynaptic vestibulospinal pathways. 4 The unpleasant autonomic responses with nausea, vomiting, and anxiety travel along ascending and descending vestibuloautonomic pathways to activate the medullary vomiting centre. More than 50% of all patients presenting with dizziness, vertigo, or disequilibrium in a neurological dizziness unit will be suffering from one of the six following common syndromes (Table 24.6.2.1): Table 24.6.2.1 Frequency of different vertigo syndromes in 30682 patients seen in a outpatient dizziness unit Diagnosis Frequency n %

1. Functional dizziness 4556 14.8
2. BPPV 4532 14.8
3. Central vestibular vertigo 4101 13.4
4. Vestibular migraine 3650 11.9
5. Menière’s disease 3028 9.9
6. Unilateral vestibulopathy 2797 9.1
7. Bilateral vestibulopathy 2081 6.8
8. Vestibular paroxysmia 1000 3.3
9. Psychogenic vertigo 776 2.5
10. Perilymph fistula/SCDS unknown vertigo syndromes other disorders 159 1352 2650 0.5 4.4 8.6 BPPV, benign paroxysmal positional vertigo.

24.6.2 Eye movements and balance 5927 benign paroxysmal positional vertigo (BPPV), functional, central vertigo, vestibular migraine, Menière’s disease, or acute unilateral vestibulopathy. Clinicians unfamiliar with patients complaining of dizziness can most effectively deepen their knowledge by acquainting them- selves with these six most frequently met and challenging condi- tions of vertigo. Diagnosis and management of vertigo syndromes always require interdisciplinary thinking, and history taking is still much more important than recordings of eye movements or brain imaging techniques. Although most clinicians welcome the attempts to develop computer interview systems for use with neuro-otological patients, and expert systems as diagnostic aids in otoneurology, their application in a clinical setting is still quite limited. The sensation of spinning vertigo indicates a dysfunction of the labyrinth (specifically of the semicircular canals which sense ro- tary acceleration), the vestibular nerve, or the caudal brainstem, which contains the vestibular nuclei. Dizziness is more difficult to assess because of its subjective character and its variety of sensa- tions. The patient history is the key to the diagnosis. One should focus on four aspects, ‘the

triple T A's': 1 Time course of the symptoms A) attacks: sec–min: BPPV (<1 min), vestibular paroxysmia (<1 min), superior canal dehiscence syndrome; min–hrs: vestibular migraine (5 min–72 h), Menière's disease (20 min–12 h); B) acute onset, lasting days to weeks acute unilateral vestibulopathy ('vestibular neuritis'), brainstem or cere- bellar infarction; C) persisting symptoms (>6 months) bilateral vestibulopathy, functional dizziness, neurodegenerative disorders. 2 Type/form of vertigo, for example, spinning vertigo, dizziness, or postural imbalance. 3 Triggers, situations, and circumstances when the symptoms occur (e.g. changes of head or body position typical of BPPV, changes of pressure typical of superior canal dehiscence syn- drome), or improve (e.g. small amounts of alcohol or sports, typical of functional dizziness). 4 Accompanying symptoms (from the inner ear such hearing loss, pressure in the affected ear, or tinnitus typical of Menière's disease; from the brainstem such as double vision, perioral par- aesthesia, facial weakness, or hemiparesis indicating a central lesion; or migraineous symptoms typical of vestibular migraine). Healthy control (1) L (2) (3) R Time Amplitude Head rotation Eye movement Lesion of the RIGHT labyrinth Saccade (b) (a) (3) (2) (1) (1) (2) (3) L R Head rotation Eye movement Eye position Fig. 24.6.2.3 Clinical bedside testing of the horizontal vestibulo- ocular reflex (VOR) by the Halmagyi–Curthoys head-impulse test. Fast 20–30° rotations of the head towards the side of the lesion show the dynamic deficit of the horizontal VOR. In contrast to the healthy control (a), the patient is not able to generate a fast contraversive eye movement and has to perform a corrective (catch-up) saccade to refixate the target (b). This is the clinical sign of the deficit of the VOR. It is important to instruct the patient to look carefully at the examiner's nose and to apply brief, high-acceleration head thrusts to detect a unilateral peripheral vestibular deficit (e.g. due to acute unilateral vestibulopathy or a vestibular schwannoma). Table 24.6.2.2 Pharmacological therapies for vertigo Therapy Type of vertigo/dizziness Vestibular suppressants Symptomatic relief of nausea (in acute peripheral and central vestibular lesions), prevention of motion sickness; should not be given for more than a few days Antiepileptic drugs (carbamazepine/oxcarbazepine) (limited evidence) Vestibular paroxysmia, epileptic vestibular aura (very rare), paroxysmal dysarthria or ataxia in multiple sclerosis, other central vestibular paroxysms, superior oblique myokymia β-Receptor blockers, antiepileptic drugs (topiramate, valproic acid) (limited evidence) Vestibular migraine β-histine dihydrochloride, high dosage (≥96 mg three times daily) and long term (≥12 months) (limited evidence) Menière's disease Ototoxic antibiotics (gentamicin, transtympanically; several controlled trials) Menière's disease (Menière's drop attacks—'Tumarkin's otolithic crisis') Corticosteroids (limited evidence) Acute unilateral vestibulopathy, autoimmune inner ear disease, in particular Cogan's syndrome 4-Aminopyridine (5 to 10 mg three times daily; two controlled trials) or its sustained-release form (10 mg two times per day) Downbeat nystagmus 4-Aminopyridine (5 mg three times daily; one controlled trial) or its sustained-release form (10 mg two times per day) Episodic ataxia type 2 Selective serotonin reuptake inhibitors (limited evidence) Functional dizziness

section 24 Neurological disorders 5928 History taking also allows the early differentiation of vertigo and disequilibrium disorders into seven categories that serve as a prac- tical guide for differential diagnosis: 1 Dizziness and light-headedness (functional dizziness, presyncopal dizziness, or drug intoxication) 2 Spontaneous recurrent attacks of spinning vertigo (vestibular paroxysmia, Menière's disease, vestibular migraine) 3 Spinning vertigo for many days (acute unilateral vestibulopathy, Wallenberg's syndrome) 4 Positioning/positional vertigo (BPPV, central positional vertigo) 5 Postural imbalance and gait disorder (typical of bilateral vestibulopathy) 6 Oscillopsia (apparent motion of the visual scene), acute unilat- eral vestibulopathy or downbeat nystagmus; it also occurs in

bilateral vestibulopathy, but only when patients walk or turn their head 7 Vertigo associated with auditory dysfunction (Menière's disease, Cogan's syndrome) Every patient who has vertigo or dizziness has to be examined by six tests: first, look for a spontaneous nystagmus with and without Frenzel's spectacles or M glasses as described earlier. Second, apply the head-impulse test for the VOR. The VOR holds images of the seen world steady on the retina during brief head rotations and locomotion. This important clinical bedside test of the horizontal VOR is illustrated in Fig. 24.6.2.3. This test allows the doctor to find out whether there is a unilateral or bilateral peripheral vestibular deficit. Third, the diagnostic pos- itional manoeuvre looks for a positioning nystagmus (i.e. BPPV). Fourth, determination of the subjective visual vertical which is tilted in more than 90% of all patients with an acute unilateral central or peripheral vestibular disorders. Fifth, the Romberg test with the eyes open and closed. Sixth, the earlier detailed examination of eye movements is also important, to differen- tiate between peripheral and central forms of vertigo because the latter are almost always associated with central ocular motor dysfunction. To differentiate between an acute peripheral and a central lesion one should look for 'the big five': (1) skew deviation/vertical diver- gence; (2) peripheral vestibular spontaneous nystagmus versus cen- tral fixation nystagmus; (3) gaze-evoked nystagmus contralateral to the spontaneous nystagmus; (4) whether the head-impulse test is normal or pathological (if normal, this indicates a central lesion in acute vertigo) (5) patient not able to stand unaided. Management of the dizzy patient The prevailing good prognosis of vertigo should be emphasized be- cause of the following: • Many forms of vertigo have a benign cause and are characterized by spontaneous recovery of vestibular function or central com- pensation of a peripheral vestibular tone imbalance. • Most forms of vertigo can be effectively relieved by pharmaco- logical treatment (Table 24.6.2.2), physical therapy in the form of liberating manoeuvres for BPPV (Table 24.6.2.3) or vestibular exercises and balance training for uni- or bilateral vestibulo pathy or central forms of vertigo, psychotherapy, in particular for functional dizziness or—more and more rarely—surgery. There is, however, no common treatment, and vestibular suppressants provide only symptomatic relief of vertigo and nausea. A specific therapeutic approach thus requires recog- nition of the numerous particular pathomechanisms involved. Such therapy can include causative, symptomatic, or preventive approaches. H A P UT H H Cup P A UT RE LE 195° H H UT A P UT Cup A P RE LE 105° H P H UT A P H A UT Cup LE RE H P H UT A P H Cup A UT RE LE 1 2 3 4 90° Fig. 24.6.2.4 Schematic drawing of the Semont liberatory manoeuvre in a patient with typical benign paroxysmal positioning vertigo (BPPV) of the left ear. Boxes from left to right: position of body and head, position of labyrinth in space, position, and movement of the clot in the posterior canal and resulting cupula deflection, and direction of the rotatory nystagmus. The clot is depicted as an open circle within the canal; a black circle represents the final resting position of the clot. (1) In the sitting position, the head is turned horizontally 45° to the unaffected ear. The clot, which is heavier than endolymph, settles at the base of the left posterior semicircular canal. (2) The patient is tilted approximately 105° towards the left (affected) ear. The change in head position, relative to gravity, causes the clot to gravitate to the lowermost part of the canal and the cupula to deflect downwards, inducing BPPV with rotatory nystagmus beating towards the undermost ear. The patient maintains this position for 1 min. (3) The patient is turned approximately 195° with the nose down, causing the clot to move towards the exit of the canal. The endolymphatic flow again deflects the cupula so that the nystagmus beats towards the left ear, now uppermost. The patient remains in this position for 1 min. (4) The patient is slowly moved to the sitting position; this causes the clot to enter the utricular cavity. A, P, and H: anterior, posterior, and horizontal semicircular canals; Cup, cupula; UT, utricular cavity; RE, right eye; LE, left eye. Brandt T, Steddin S, Daroff RB (1994). Therapy for

benign paroxysmal positioning vertigo, revisited. Neurology, 44, 796–800. Copyright © 1994, American Academy
of Neurology.

24.6.2 Eye movements and balance 5929 The essential characteristics are given for benign paroxysmal pos- itional vertigo (Fig. 24.6.2.4, Box 24.6.2.1 and also see Table 24.6.2.3), Menière's disease (Box 24.6.2.2), acute unilateral vestibulopathy (Box 24.6.2.3), bilateral vestibulopathy (Box 24.6.2.4), and vestibular migraine (Box 24.6.2.5). Table 24.6.2.3 Physical therapies for vertigo Therapy Type of vertigo Liberatory or repositioning manoeuvres Benign paroxysmal positional vertigo (BPPV) Vestibular exercises and balance training Vestibular rehabilitation, central compensation of acute vestibular loss, habituation for prevention of motion sickness, improvement of balance skills in unilateral or bilateral peripheral vestibular deficits and central vestibular deficits Box 24.6.2.1 Benign paroxysmal positional vertigo (typical posterior semicircular canal type, p-BPPV) Clinical syndrome Brief recurrent attacks of rotational vertigo and concomitant vertical rotatory nystagmus precipitated by rapid head-trunk tilt towards the affected ear or by neck extension (when first lying down in bed, sitting up from a supine position, turning over in bed from one side to the other, extending the neck to look up): • Latency—vertigo and nystagmus begin 1 s or more after head tilt • Duration—attacks last less than 60 s • Nystagmus—vertical rotatory, with the fast phase beating upwards with a clockwise or anticlockwise rotatory component • Reversal—when the patient returns to the seated position, vertigo and nystagmus reoccur in the opposite direction • Fatigability—repetition of the manoeuvres results in ever-lessening symptoms Incidence/age/sex Most common cause of vestibular vertigo that manifests throughout life, particularly in older people. Lifetime prevalence: at least 3% with inci- dence peaking in the sixth and seventh decades. Pathomechanism 'Canalolithiasis' most often of the posterior semicircular canal; dislodged otoconia (degeneration, trauma) congeal to form a free-floating 'heavy' clot, which always gravitates to the most dependent part of the canal during changes in head position, thereby causing push or pull forces on the cupula. Aetiology • 'Idiopathic' forms over 95% • Symptomatic forms due to head trauma (relatively often bilateral BPPV), after acute unilateral vestibulopathy, known other inner ear disorders, vestibular migraine, or prolonged bed rest Course/prognosis Natural history is considered benign because it resolves spontaneously in 70% of the patients within weeks, persists in about 20–30% when un- treated, and recurs in 30–50% after variable periods of years. Management • Liberating/repositioning manoeuvres to free the canal of the 'heavy' clot (Fig. 24.6.2.4): Semont's manoeuvre or Epley's manoeuvre (both are equally effective) These are successful in less than 95% of patients within days or weeks. Differential diagnosis Central positional vertigo/nystagmus, BPPV of a horizontal canal, ves- tibular migraine with positioning or positional vertigo, vestibular paroxysmia, superior canal dehiscence syndrome. Based on Brandt T, Dieterich M, Strupp M (2012). Vertigo and dizziness— common complaints. 2nd edition Springer, London. Box 24.6.2.2 Menière's disease Clinical syndrome • Recurrent attacks of vertigo, lasting 20 min to 12 hours • Hearing impairment (<2000 Hz, at least 30 dB, related to the attacks of vertigo) • Fluctuating tinnitus in the affected ear • Subjective fullness of affected ear • Rarely, vestibular drop attacks (Tumarkin's otolith crisis) Monosymptomatic forms are possible at the beginning of the disease, with variable auditory and vestibular deficits in the intervals between attacks. Contrast-enhanced high-resolution MRI of the inner ear can show endolymphatic hydrops. Lifetime prevalence/age/sex • 0.5% • Affects mainly age group from 30 to 50 years • Incidence in males and females roughly equal • Rare in children Pathomechanism • Endolymphatic hydrops of the labyrinth due to insufficient endo- lymph reabsorption in the endolymphatic sac or blockage of

longitu- dinal endolymph flow • Attacks: periodic leakage or ruptures of the endolymph membrane with potassium-induced depolarization of the nerve • Intervals: persisting impaired vestibular and/or audiological deficits Aetiology • Idiopathic (aetiology not known in more than 95%) • Acquired, ‘delayed endolymphatic hydrops’ (i.e. inflammation or trauma, infectious, autoimmunological, traumatic), rarely hereditary Course/prognosis • Usually begins in one ear with increasing frequency of attacks and major auditory/vestibular deficit occurring during the first years • After 5 years both ears are affected in 15% of the patients if not treated Management • Medical: β-histine (e.g. β-histine dihydrochloride): at least 96 mg three times daily for at least 12 months as a prophylactic treatment (limited evidence) • If treatment with β-histine 96 mg three times per day does not pre- vent attacks, the dosage can be increased to up to 1440 mg per day. Very rarely steroids or ototoxic antibiotics are indicated: gentamicin transtympanically in low dosages of 10 mg with long intervals of at least 4 weeks because of the delayed ototoxicity—‘wait and see’. Differential diagnosis • Vertigo migraine • Superior canal dehiscence syndrome • Vestibular paroxysmia • Acute unilateral vestibulopathy • Transient ischaemic attacks • Cogan’s syndrome

section 24 Neurological disorders 5930 Box 24.6.2.3 Acute unilateral vestibulopathy (‘vestibular neuritis’) Clinical syndrome Acute onset of sustained: • Spinning vertigo • Postural imbalance with falls towards the affected ear • Horizontal–rotatory spontaneous nystagmus (towards the unaffected ear) • Nausea and vomiting • Pathological head-impulse test • Unilateral hypo- or unresponsiveness in caloric testing Incidence/age/sex Third most common cause of peripheral vestibular vertigo that mani- fests throughout life (affects mainly ages 30–60 years; rare in children) without preference of sex. Pathomechanism Acute partial unilateral loss of labyrinthine function (most often hori- zontal and anterior semicircular canal paresis only) with a vestibular tone imbalance in yaw and roll planes. Aetiology Most probably herpes simplex virus 1 infection of the superior division of the vestibular nerve trunk. Course/prognosis Spontaneous recovery within 1–6 weeks due to: • Peripheral restoration of labyrinthine function (incomplete in about 50%) • Central compensation of vestibular tone imbalance • (Contralateral) vestibular, somatosensory, and visual substitution of the vestibular deficit Management Medical treatment Corticosteroids (beginning, for instance, with 100 mg 6-methylprednisolone per day within 3 days after symptoms, then taper every fourth day by 20 mg) (so far only one randomized controlled trial) Antivertiginous drugs (for instance dimenhydrinate, but just for up to three days) Physical therapy (vestibular exercises) Differential diagnosis • Acute central brainstem lesions at the root entry zone of nerve VIII and the vestibular nucleus (multiple sclerosis plaques, small pontomedullary infarcts): ‘vestibular pseudoneuritis’ • Midline cerebellar infarction • Peripheral labyrinthine and vestibular nerve disorders, such as vas- cular anterior inferior cerebellar artery infarcts or Menière’s disease which may begin monosymptomatically • Vestibular migraine Box 24.6.2.4 Bilateral vestibulopathy Clinical syndrome Symptoms • Postural imbalance with unsteadiness of gait (particularly in the dark or on unlevel ground); no symptoms when sitting or lying down • Oscillopsia associated with head movements or when walking (40%) • There may be episodes of vertigo early in the development of bilateral vestibular failure but not in chronic state • Impaired spatial memory Signs • Bilateral pathological head-impulse test • Absent or markedly reduced vestibulo-ocular reflex with bithermal caloric testing and/or the video-head-impulse test • Increased postural sway with eyes closed and/or standing on foam rubber • Subtype associated with cerebellar ocular signs (in particular down- beat nystagmus) and polyneuropathy (so-called cerebellar ataxia, neuropathy, and vestibular areflexia syndrome—CANVAS) Incidence/age/sex • Often overlooked condition, in particular in older people; most fre- quent cause of postural imbalance in elderly subjects • Without

preference of sex Pathomechanism • Progressive loss of bilateral labyrinthine and/or vestibular nerve func- tion due to various aetiologies with concurrent somatosensory and visual ‘compensation’ (substitution) of vestibular function for spatial orientation, ocular stabilization, and postural control Aetiologies • Unclear in 75% (idiopathic, neurodegenerative), ototoxicity (oto- toxic antibiotics), bilateral Menière’s disease, meningitis, associated with cerebellar degeneration and downbeat nystagmus, so-called CANVAS, bilateral vestibular schwannomas in neurofibromatosis type 2, immune-mediated inner ear disease, bilateral sequential vestibular neuritis, congenital malformations, familial vestibulopathy Course/prognosis Bilateral vestibular failure may develop simultaneously or sequentially, take an abrupt or slowly progressive course, and be complete or incom- plete. Permanent loss of vestibular function is most frequent. Management • Explanation of the deficit to the patient often causes considerable relief • Prevention (very restrictive with the use ototoxic drugs, in particular gentamycin) • Causative treatment (Menière’s disease, autoimmune inner ear dis- eases, such as Cogan syndrome) • Vestibular rehabilitation/balance training Differential diagnosis • Of the various disorders causing bilateral vestibulopathy • Of disorders similar in symptomatology (unsteadiness and oscillopsia): — Cerebellar ataxia and cerebellar ocular motor disorders without bilateral vestibular failure (e.g. downbeat nystagmus), which, how- ever, is often associated with bilateral vestibulopathy — Functional dizziness — Intoxication — Vestibular paroxysmia — Superior canal dehiscence syndrome — Orthostatic hypotension — Visual disorders — Unilateral vestibular loss

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