Vertigo and Dizziness: Common Complaints
Acute Unilateral Vestibulopathy/Vestibular Neuritis

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Term

- The neutral term “acute unilateral vestibulopathy” (AUVP) as well as “vestibular neuritis” are used in the International Classification of Vestibular Disorders (ICVD).

- Because the etiology of this disease has not yet been proven but is assumed to be viral in most cases.

Box 8.1 Diagnostic criteria for Acute Unilateral Vestibulopathy/Vestibular Neuritis

Each of the following criteria have to be fulfilled:

A. Acute or subacute onset of sustained spinning or non-spinning vertigo (i.e., an acute vestibular syndrome) of moderate to severe intensity with symptoms lasting for at least 24 hours.

B. Spontaneous peripheral vestibular nystagmus with a trajectory appropriate to the semicircular canal afferents involved, generally horizontal-torsional, direction-fixed, and enhanced by removal of visual fixation.

C. Unambiguous evidence of reduced VOR function on the side opposite the direction of the fast phase of the spontaneous nystagmus.

D. No evidence for acute central neurological, ontological or audiological symptoms.

E. No acute central neurological signs, namely no central ocular motor or central vestibular signs, in particular no pronounced skew deviation, no gaze-evoked nystagmus, and no acute audiologic or otological signs.

F. Not better accounted for by another disease or disorder.

Box 8.2 Diagnostic criteria for "Probable Acute Unilateral Vestibulopathy"

Each of the following criteria have to be fulfilled:

A. Acute or subacute onset of sustained spinning or non-spinning vertigo (i.e., an acute vestibular syndrome) of moderate to severe intensity with symptoms lasting for at least 24 hours.

B. Spontaneous peripheral vestibular nystagmus with a trajectory appropriate to the semicircular canal afferents involved, generally horizontal-torsional, direction-fixed, and enhanced by removal of visual fixation.

C. No clear evidence of reduced VOR function by bedside examination on the side opposite the direction of the fast phase of the spontaneous nystagmus.

D. No evidence for acute central neurological, ontological or audiological symptoms.

E. No acute central neurological signs, namely no central ocular motor or central vestibular signs, in particular no pronounced skew deviation, no gaze-evoked nystagmus, and no acute audiologic or otological signs.

F. Not better accounted for by another disease or disorder.

Epidemiology

- Annual incidence: 3.5–15.5/100,000
- Two studies found no evidence for seasonal differences
- Large cohort (n > 39,000): AUVP was the sixth most common cause of vertigo/ dizziness and the third most common cause of peripheral vestibular disorders (BPPV ranks first, Menière's disease second).
- Usual age: 30 – 60 (plateau: 40 – 50)
- No significant gender difference
- Recurrence rate: 1.9% - 10.7%

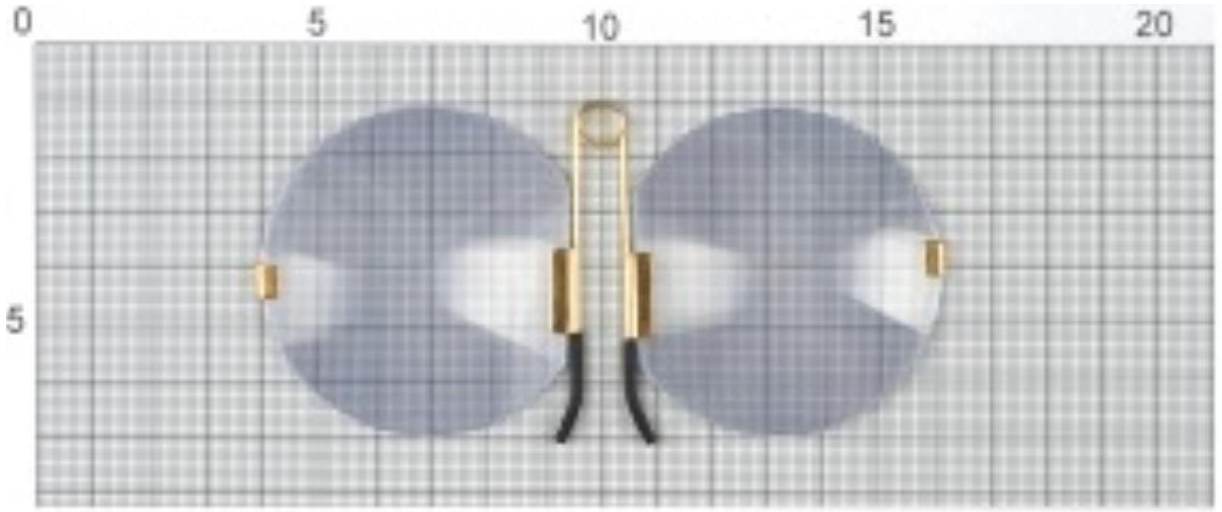
Patient History

- Acute or rarely subacute onset of sustained spinning or non-spinning vertigo, with symptoms untreated lasting at least 24 h
  - Occasional spells of vertigo a few days before
  - Vertigo worsens during head and body movements.
  - Apparent movement of the visual surroundings
- Postural imbalance with a tendency to fall in the direction of the slow phase of nystagmus
- Nausea and often vomiting
- No acute hearing loss, tinnitus, ear pain, or neurological symptoms

Bedside Examination (1)

- ***Horizontal-torsional nystagmus*** with the fast phase beating toward the suspected non-affected ear, and small upward component
- A peripheral vestibular spontaneous nystagmus is typically reduced in amplitude by fixation due to fixation suppression of the VOR.
  - **In the very acute phase patients are often not able to significantly suppress the nystagmus**
- The intensity of spontaneous nystagmus is enhanced with Frenzel's goggles or M-glasses as well as by eye closure (seen through closed eyelids)

Frenzel’s goggles



M-glasses

Bedside Examination (2)

- *Head impulse test:* Pathological with a refixation saccade when the head is turned toward affected side
- *Measurement of subjective visual vertical:* deviation toward the affected ear
- *Romberg Test:* falling toward slow phase of nystagmus, i.e., the affected ear
- *Examination for central ocular motor disorders:* There should be no central signs
- *Examination of hearing*: There should be no evidence of acute hearing loss.

Laboratory Tests

- *Video head impulse test* (video-HIT): examine whether there is a VOR deficit in the high-frequency range
  - Deficit: VOR gain < 0.7 and side difference > 0.3
  - Video-HIT is strongly recommended because of its high value for the diagnosis of AUVP
  - Video-HIT can be also used in the emergency department
- *Caloric test*: a hypo- or unresponsiveness of the affected horizontal canal (VOR in the low-frequency range of about 0.003 Hz)
  - Jongkees' formula = (((R30° + R44°) – (L30° + L44°))/ (R30° + R44° + L30° + L44°)) × 100
  - Vestibular paresis: > 25% asymmetry, or Sum SPV <6°/s

Complementary Tests (1)

- *Cervical/Ocular VEMP:* help to differentiate between superior AUVP, which is the most frequent form, very rare inferior AUVP, and even rarer complete AUVP
- *CT:* to rule out hemorrhage
- *CTA:* for vertebral and basilar artery stenosis
- MRI: to rule out stroke (even diffusion-weighted MRI in small brainstem or cerebellar lesions **<10 mm is normal** within the first 48 h after symptom onset in 50% of patients)
- This strongly further supports the importance of a systematic patient history and the clinical bedside examinations.

Complementary Tests (2)

- Positive findings in MRI:
- There might be a contrast enhancement of the vestibular nerve, in particular the superior vestibular nerve, 1–4 h after gadolinium injection
- High-resolution MRI examinations ≥6 months after symptom onset in patients with a persisting peripheral deficit might demonstrate an atrophy of the vestibular nerve

Complementary Tests (3)

- *Audiogram:* If there is evidence from the patient history and/or the clinical examination of an impairment of hearing

- *Otoscopy:* If a patient complains of ear pain, otoscopy is indicated, namely to look for herpes zoster or otitis media.

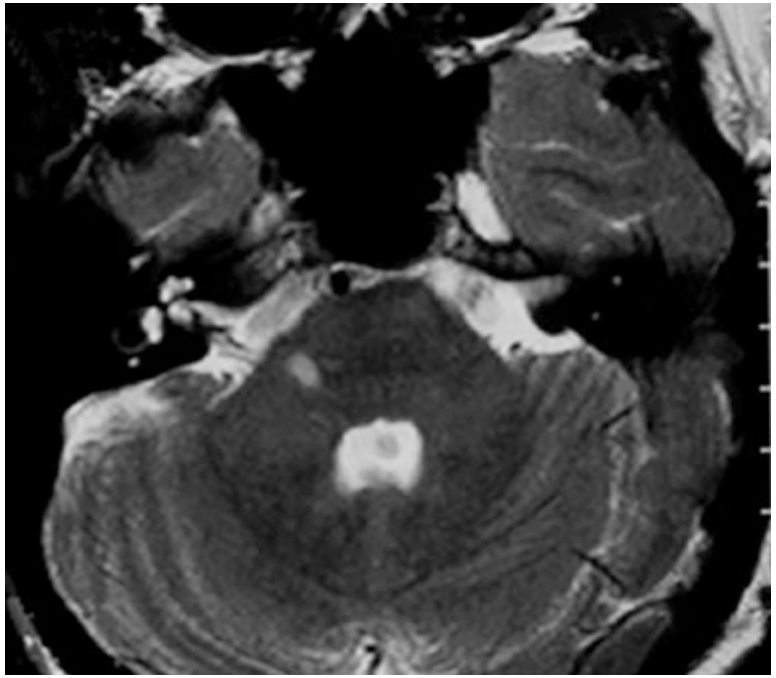
Differential Diagnosis

- Acute central vestibular syndrome: e.g., brainstem or cerebellar infarction
- Combined acute central and peripheral lesions: e.g., AICA infarction
- Other central vestibular syndromes: e.g., vestibular migraine
- Other inner ear diseases: e.g., first attack of Menière's disease

Acute Central Vestibular Syndrome (1)

Mimicking AUVP (vestibular pseudo-neuritis)

- Root entry zone of the vestibular nerve in the lateral medulla
- Vestibular nuclei
- Dorsolateral pons affecting the cerebellar peduncle (Chang and Wu 2010)
- A small cerebellar infarction, e.g., of the flocculus which can even lead to a pathological HIT



Acute Central Vestibular Syndrome (2)

Patient History (ABCD2)

- Cardiovascular risk factors
- Age > 60
- First attack
- Spontaneous occurrence
- Central additional symptoms

Acute Central Vestibular Syndrome (3)

Bedside Examination (HINTS and HINTS plus)

- Prominent vertical deviation/skew deviation (> 3°): low sensitivity (30%)
- Type of spontaneous nystagmus
- Not reduced by visual fixation
  - **It is important to note that that there are also central types of spontaneous nystagmus, e.g., in brainstem infarction, which can be reduced by fixation**
- Pure vertical or torsional nystagmus
- Pure horizontal nystagmus (except for horizontal BPPV)

Acute Central Vestibular Syndrome (4)

Bedside Examination (HINTS and HINTS plus) (cont.)

- A horizontal gaze-evoked nystagmus in the opposite direction to the fast phase of the spontaneous nystagmus i.e. a so- called **Bruns' nystagmus**
- A **normal head impulse test** in **acute vestibular syndrome** with **nystagmus** is not compatible with a peripheral lesion.
- The head impulse test can also be pathological in central lesions, in particular in a **fascicular** or **nuclear** lesion or in **floccular** lesions
- **Head-shaking nystagmus**: If horizontal head-shaking leads to a **change in the direction** of the nystagmus or to a **vertical nystagmus** (cross-coupling), this is compatible with a central lesion, but it is not very specific.

HINTS

- The combination of these clinical signs has a sensitivity and specificity of 80–95%.
- Neurologists who used HINTS had a sensitivity of 96.7% and a specificity of 94.8%.
- Physicians, including neurologists, working in an ENT department had a sensitivity of 83% and a specificity of only 44%.

vHIT

Central signs

- Bilaterally normal VOR gain
- Bilaterally reduced VOR gain
- Bilateral increased VOR gain
- Crossed vertical refixation saccades

Cerebellar Infarction

- **PICA infarction: vestibular pseudo-neuritis**
- **AICA infarction: pseudo-labyrinthitis:** strong lateropulsion, hearing impairment
- Incomplete ocular tilt reaction (OTR)
  - Dentate nucleus
  - Flocculus
  - Nodulus
  - Tonsil
  - Uvula
  - Middle cerebellar peduncle

Vestibular Migraine

- Sometimes like AUVP: VM can last for up to 72 h and which can also be associated with peripheral vestibular spontaneous nystagmus

- D/D: recurrent vertigo, a history of migraine, typical migrainous symptoms with the attack of vertigo, and a normal HIT
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Table 8.1 Peripheral vestibular syndromes as differential diagnoses for AUVP

Diagnosis	Clinical characteristics
Cogan's syndrome	Double triad: Vertigo, bilateral hearing loss/tinnitus, eye pain/"red eyes" Bilateral, often asymmetric peripheral vestibular deficits, bilateral hypoacusis, interstitial keratitis Symptoms or deficits often rapidly progress Mostly in young women; relatively rare, but requires immediate immunosuppressive therapy
Herpes zoster oticus (Ramsay-Hunt syndrome)	Initially burning ear pain and blisters, vertigo, hearing disorders, and facial paresis Can lead to complete AUVP, including a vertical deviation/skew deviation (Arbusow et al. 1998) Often contrast enhancement of the affected cranial nerves on MRI
Cupulolithiasis and canalithiasis of a horizontal canal	Clinical examination reveals horizontal spontaneous nystagmus which changes direction during the lean-and-bow test (Choi et al. 2018b) and during the diagnostic positioning maneuvers, which is helpful for the differential diagnosis. See also ► Chap. 9 and the current diagnostic criteria (von Brevern et al. 2015).
Serous or purulent labyrinthitis	Associated with ear pain, reduced hearing, and/or tinnitus. The course of the disease can be acute, subacute, or slowly progressive. Otoscopy is necessary.
Menière's disease	Can begin mono- or oligosymptomatically. Then, the differential diagnosis is difficult and can only be made during the course of the disease. See also ► Chap. 10 and the current diagnostic criteria (Lopez-Escamez et al. 2015).
Vestibular paroxysmia	In single cases, the oligosymptomatic attacks may last for hours and be associated with peripheral vestibular spontaneous nystagmus. Therefore, the diagnosis can only be made during the course of the disease. See also ► Chap. 11 and the current diagnostic criteria (Strupp et al. 2016).
Vestibular schwannoma	Often a slowly progressive course of the disease and associated with impairment of hearing and/or tinnitus. Nowadays, often diagnosed in patients who have impairment of hearing by means of contrast-enhanced MRI. Symptoms often occur only in the later stage of the disease. In rare cases, it may also be associated with attacks of vertigo.

Pathophysiology (1)

Static deficits

- Pathological processes affecting an end organ or vestibular nerve alter its firing frequency, thereby creating a vestibular tone imbalance
- **Perceptual: spinning vertigo**
- **Oculomotor: spontaneous nystagmus, ipsilateral ocular torsion**
- **Postural: ipsilateral gait deviation or falling**
- **Vegetative: nausea**
- The static deficits are compensated over weeks

Pathophysiology (2)

Dynamic deficits

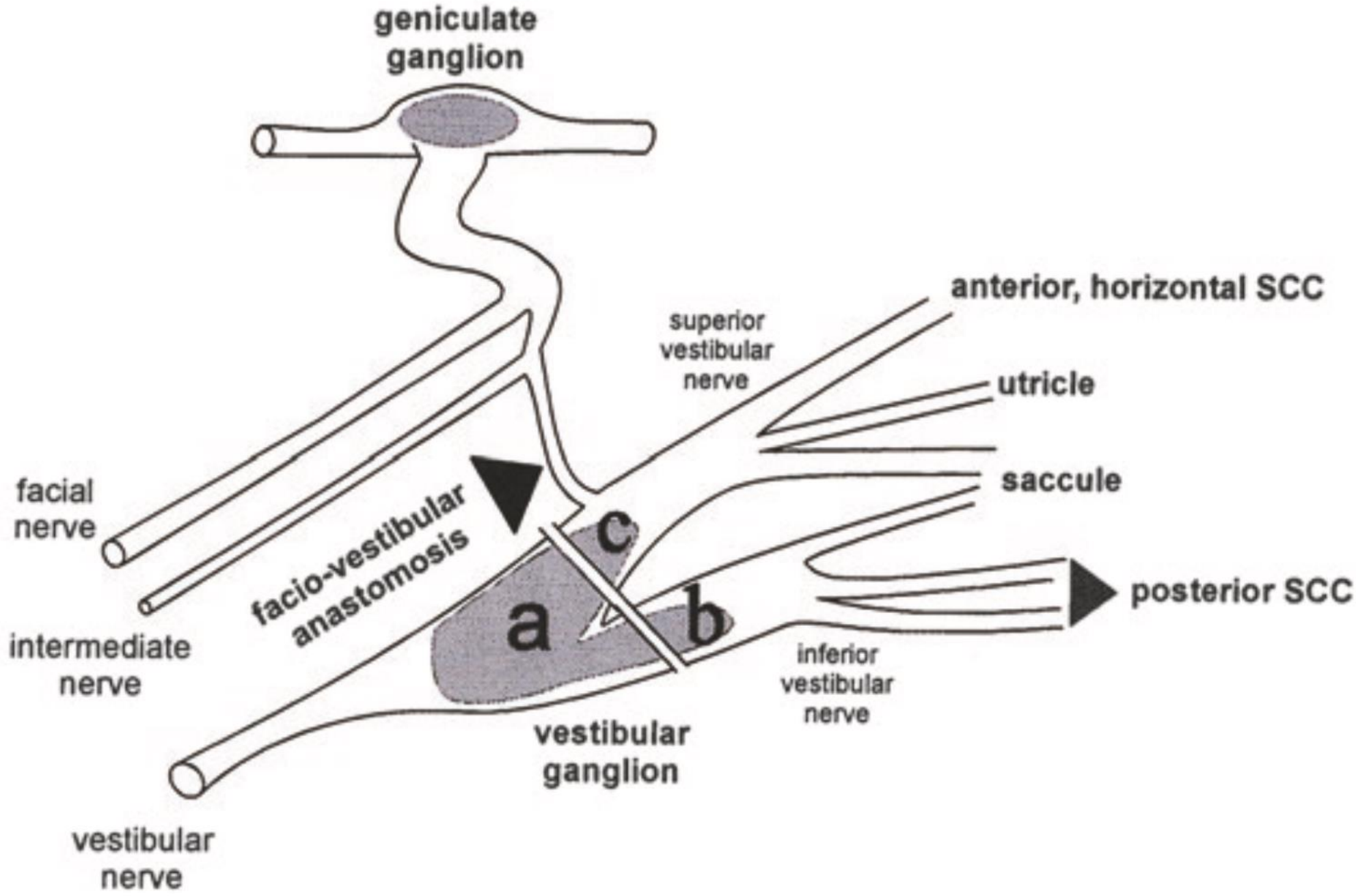
- Dynamic deficits of the VOR can be demonstrated by **HIT, video- HIT, caloric irrigation, and rotational testing.**
- If the peripheral vestibular deficit persists, the dynamic deficits do not recover because they cannot be compensated.

Pathological Anatomy (1)

- **AUVP most often affects the superior division of the vestibular nerve only – superior vestibular neuritis.**

Reasons

- The superior vestibular nerve runs through the longer and smaller bony canal.
- Double redundant innervation of the posterior canal with two nerves: the posterior ampullary and the accessory posterior ampullary nerve
- Anastomoses between the facial nerve and the superior vestibular nerve through which reactivated herpes virus may spread


geniculate ganglion
anterior, horizontal SCC
superior vestibular nerve
utricle
saccule
facial nerve
facio-vestibular anastomosis
c
a
b
posterior SCC
intermediate nerve
inferior vestibular nerve
vestibular ganglion
vestibular nerve

Pathological Anatomy (2)

The rare “inferior vestibular neuritis”

- Spontaneous nystagmus: contraversively torsional with downbeat component
- Often misdiagnosed as “central”

Total vestibular neuritis (superior plus inferior)

- Horizontal nystagmus with torsional nystagmus without vertical component
- This also occurs in zoster oticus which can even lead to a complete OTR including a prominent skew deviation.

Etiology

- A viral etiology of AUVP is—in analogy to Bell's palsy and some types of acute hearing loss—likely but so far not proven.
- **Evidence from autopsy**
  - **Inflammatory degenerations of the vestibular nerve**
  - **HSV-1 in vestibular ganglia**
  - **Activated CD8+ T cells**
- HSV-1 replicates and induces an inflammation and edema and, thereby, secondary cell damage of the vestibular ganglion cells and axons in the bony canals, which may also explain the therapeutic effect of steroids.

Recovery (1)

Recovery is the result of a combination of the following:

- Central compensation of the peripheral vestibular tone imbalance
- Substitution of the functional loss by the contralateral unaffected vestibular system as well as by somatosensory and visual input
- Restoration of peripheral vestibular function (generally incomplete)

Recovery (2)

- In the course of the illness, the peripheral vestibular function does not spontaneously recover in most patients.
- After 1 month 90% and after 6 months 80% of the patients still had a relevant deficit of peripheral vestibular function. In only 42% did a normalization occur in the further course.
- Even if the caloric test normalizes in these patients, the head impulse test on the affected side is pathological in 30%

Recovery (3)

The factors affecting prognosis

- A low VOR gain and many refixation saccades correlate with a poorer prognosis
- **Poor prognosis: Total AUVP > Superior AUVP > Inferior AUVP**
- Visuo-vestibular psychological and personality traits are important for the long-term prognosis after AUVP

Long-term recurrence rate: 2 – 11%

Therapy

- Causative pharmacotherapy
- Symptomatic pharmacotherapy
- Vestibular exercise

Causative Treatment (1)

In a randomized placebo-controlled four-arm trial

- Monotherapy with corticosteroids (methylprednisolone 100 mg per day, tapered every fourth day by 20 mg) significantly improved the recovery of peripheral vestibular function in AUVP after 12 months
- Valacyclovir led to neither a benefit nor an additional benefit.

Causative Treatment (2)

- In a single-blinded trial, corticosteroid therapy seems to enhance earlier complete AUVP resolution during the first 6 months, with, however, no added benefit in the long-term prognosis after 12 months.
- A Cochrane review and a meta-analysis made no general treatment recommendation for corticosteroids.
- **Another study:** All 9 patients treated within 24 h after symptom onset had a normal caloric response after 3 months, while only 58% of those 14 patients treated between 25 and 72 h did.
- Further randomized placebo-controlled trials are necessary to evaluate the effects of corticosteroids

Symptomatic Therapy

- H1R antagonist: dimenhydrinate, promethazine
- 5HT3R antagonist: ondansetron, granisetron
- $GABA_A$ agonist: BZD
- H1R agonist and H3R inverse agonist: betahistine
- D2R antagonist: metoclopramide, domperidone
- H4R antagonist
- Anticholinergics: scopolamine
- Since most of these drugs (except betahistine) are sedatives, they most likely delay vestibular compensation. They should not be given for longer than 3 days

Vestibular Exercise to Improve Central Compensation

- Supported by Cochrane Review
- **Horizontal head turns** are particularly important to increase the vestibular tone imbalance and thus trigger vestibular compensation
- Active head movements to recalibrate the VOR voluntary eye movements and fixation to improve impaired gaze stabilization.
- Balance training, goal-directed movements, and gait exercises to improve the vestibulospinal regulation of posture and goal-directed motion.
- Voluntary eye movements and fixation to improve impaired gaze stabilization

Pharmacotherapy for the Improvement of Central Compensation (1)

- **There is so far no state-of-the-art placebo-controlled trial that shows any benefit in patients.**

Betahistine

- High daily doses of 50 mg/kg or 100 mg/kg accelerated the time-course of recovery in cats after unilateral vestibular damage
- Co-administration of a lower betahistine dose (0.2 mg/kg/day) and selegiline (1 mg/kg/ day) in this cat model increased the effect on postural recovery compared with betahistine monotherapy

Pharmacotherapy for the Improvement of Central Compensation (2)

N-Acetyl-DL-leucine

- Several studies in cats and rats have shown that N-acetyl-DL-leucine improves and **accelerates postural compensation** after unilateral labyrinthectomy.
- The effect is dose-dependent.
- One observational study described **improvement of postural compensation in patients** after vestibular neurotomy and labyrinthectomy.
- Possible mechanism: rebalancing the abnormal membrane potential in the vestibular nuclei

Pharmacotherapy for the Improvement of Central Compensation (2)

Gingko biloba extract

- Improvement of static and dynamic vestibular symptoms by EGb 761 after a unilateral vestibular lesion in rats, cats, and guinea pigs
- a dose-dependent improvement
- Possible mechanism: neural plasticity, modulation of long-term potentiation, neuronal spine morphology and density, and neuro-genesis mostly by terpene lactones

Pragmatic Therapy

- Causal therapy: steroid given as soon as possible for 2 weeks
- Symptomatic therapy: dimenhydrinate, ondansetron, lorazepam
- **Physiotherapy:**
- When still lying or sitting in bed, they should perform quick head turns to the right and left with fixation of a target in a sitting position.
- Subsequently, vestibular exercises should be performed to improve stance and gait during combined head and body movements.
- We recommend about 15 min three times a day over a period of about 4 weeks.

Follow-up

- We recommend a follow-up examination after 1, 6, and 12 months to evaluate the efficacy of the above measures.
- 15% of those with AUVP develop post-infectious BPPV.
- The patient should be informed about the risk of secondary functional dizziness and the recurrence rate, which is 2–11%.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