NeuroED App

INSELSPITAL
Universitätsklinik für Neurologie

Neuro Pocket

2023

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Emergency and intensive care medicine

Contents and imprint

Contents

Imprint

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Epilepsy

Classification by aetiology

	Structural	Unclear	Genetic
Typical seizure type	Focal, with or without impairment of consciousness, secondarily generalized	Focal, with or without impairment of consciousness, secondarily generalized	Primary generalized
MRI	Epileptogenic structural change ("lesion")	Without epileptogenic structural changes	Without epileptogenic structural changes
EEG	Focal	Focal	Generalized (bihemispheric) epilepsy

General

- **Factors known to provoke seizures**: drug withdrawal, alcohol withdrawal, fever, severe electrolyte imbalance, hypoglycaemia
- **Factors that might provoke seizures** sleep deprivation, stress
- Obtain medical history from others if possible!
- **Driving licence** suspended!

First epileptic seizure

- **Imaging** in the acute stage if possible with MRI
- **EEG** in an emergency situation only if status epilepticus is suspected
- **Driving licence** suspended!
- **Information sheet** for patients with first-time seizure

Follow-up check, usually by the epilepsy centre by phone or in the clinic within 6 months, including EEG

Selection of seizure-suppressing substances for initial therapy

Three important aspects:

1. If the type of seizure (focal or primary generalized) is not known for certain, an agent that is effective against both types must be chosen.
2. Drug therapy can also be started before the diagnosis of epilepsy is certain.
3. For all preparations listed (except Apydan® extent), there are generics available as cheaper alternatives. In patients who are not seizure-free, a change can be evaluated – but it is important that the generic drug is not changed during the course of treatment (because of the sometimes very different bioavailability of the active ingredient in the different preparations).

Epilepsy and pregnancy

General

- Baseline medication blood level (ideally before pregnancy)
- After that, check every 4–6 weeks; adjust the dose if drop > 35%

First epileptic seizure during pregnancy

- Levetiracetam (usual dosage)
- Alternative lamotrigine

Contraindicated: valproate

Status epilepticus during pregnancy

Levetiracetam 2–4 g i.v.

Fitness to drive after an epileptic seizure

Licence suspended for 12 months

- ⇒ possibly longer (this also depends on vehicle categories; stricter regulations apply for lorry drivers, passenger transport drivers, train drivers, pilots, etc.)
- ⇒ in the case of a first unprovoked seizure, the suspension may be reduced to 6 months after consultation with a neurologist
- ⇒ If the seizure is definitely provoked or treatment is started in patients with normal MRI+EEG, it may be possible to shorten it to 3 months after consulting a neurologist

- Condition for lifting suspension: neurological consultation with assessment of freedom from seizures, EEG findings

CAVEAT Ask about activities/hobbies that would also be restricted by epileptic seizures because they are too dangerous (e.g. diving, flying, mountaineering, swimming, etc.)

Seizure-suppressing drugs

		Active ingredient	Mechanism of action						Approved for: **2**	Additional indications	Contra-indications	Systemic side effects									
			Na+	Ca2+	GABA	AMPA	NMDA	SV2A				EKG	Na+ <128 mM 5	HCO3-	Hepatopathy 6	blood count 7	Cholesterol	Osteoporosis 8	Weight	Gastrointestinal	Skin rash 3
Broad spectrum	CLZ	Clonazepam			■						Respiratory failure										
	CLB	Clobazam			■				Adjunct (2nd line)	Anxiety catamenial epi.	Myasthenia gravis										
	LTG	Lamotrigine	■						Monotherapy	Mood stabilizer	Allergy 3, cardiac arrhythmia 4										■
									1. Focal and GGE												
	LVT	Levetiracetam						■	Monotherapy		Depression									■	
	(LEV)								1. Focal and GGE (women)												
	BRV	Brivaracetam						■	Adjunct, only focal												
	VPA	Valproate	■	■	■	■			Monotherapy	Mood stabilizer, migraine	Mitochondriopathy				■	■		■	↑↑		
									1. GGE in men												
	TPM	Topiramate	■	■	■				Monotherapy	Migraine	Kidney stones			■					↓↓		
	ZNS	Zonisamide	■	■	■				Monotherapy (2nd line)		Kidney stones			■					↓		
	PER	Perampanel				■			Adjunct (2nd line)	RLS, insomnia											
Focal epilepsy	PHT	(Fos)Phenytoin1	■						Monotherapy	Neuralgia (V,IX)	Cardiac arrhythmia 4, heart failure 4	■			■	■	■	■			■
	CBZ	Carbamazepine1	■						Monotherapy	Mania, RLS, neuralgia (V,IX)	Allergy 3, MAOI, cardiac arrhythmia 4	■	0.1 (5)		■	■	■	■		■	■
	OXC	Oxcarbazepine	■						Monotherapy		Allergy 3, hyponatraemia	■	0.2 (5)		■			■		■	■
	ESL	Eslicarbazepine	■								Allergy 3, heart 4	■	0.1 (5)								■
	LCM	Lacosamide	Slow type						Zusatz (2. line)		PR-extension 4	■			■						
	CNB	Cenobamate	■		■				Zusatz (3. line)		QT-shortening 4	■									■
	PB	Phenobarbital			■				Monotherapy	Withdrawal therapy	Porphyria, alco. sleep apnea				■			■			■
	GBT	Gabapentin		■	■				Monotherapy	Neuralgia, RLS, anxiolytic								■	↑	■	
	PGB	Pregabalin		■	■				Zusatz (2. line)	Neuralgia, RLS, anxiolytic									↑	■	
Lennox-Gastaut	FBM	Felbamate	■	■	■		■		Zusatz (3. line)		Hepatopathy, blood dyscrasias				■	■				■	
	RUF	Rufinamide	■						Zusatz (3. line)		QT-shortening 4	■				■				■	
	CBD	Cannabidiol	unklar						Zusatz (3. line)						■				↓		
Absence	ESM	Ethosuximide		■					Monotherapy										↓		
Spasmen	VGB	Ethosuximide			■				Monotherapy										↑		

		Active ingredient	Main side effects									Remarks	Trade names	Formulation (mg)	mg/ml	Dose (mg per day)1		
			Suicide	Depression/ Aggressivity	Psychosis	Cognitive effects	Sedation/sleep 9	Headache	Ataxia	Tremor						Initial (mg)	Increase (mg)	Target (mg)
Broad Spectrum	CLZ	Clonazepam					■						Rivotril	Tablet 0.5 2		0.5		
	CLB	Clobazam					■						Urbanyl	Tablet 10		5-10	5/3d	10–40
	LTG	Lamotrigine					↓					Myoklonus 10, asept. meningitis	Lamotrigin	Tablet 25 50 100 200		25	25/2w	100–500
													Lamictal	Tablet 5 25 50 100 200				
	LVT	Levetiracetam	■	■	■	■						Diarrhoea, alopecia	Levetiracetam	Tablet 250 500 1000		1000	500/3d	1000–3000
	(LEV)												Keppra	Tablet 250 500 1000				
	BRV	Brivaracetam	■	■									Briviact	Tablet 25 50 75 100		50	50/3d	50–200
	VPA	Valproate				■		↓↓			■	Alopecia, leukopenia, thrombocytopenia 7, NH3-encephalopathy	Valproat	Tablet 300 500		500	300/3d	1000–2500
													Depakine	Tablet 300 500				
													Orfiril	Capsule 150 300				
	TPM	Topiramate				■		↓↓				Dysgeusia, glaucoma, paraesthesia, anosmia	Topiramat	Tablet 25 50 100 200		50	50/3d	100–600
													Topamax	Tablet 25 50 100 200				
	ZNS	Zonisamide	■	■	■	■			■			Ataxia, anosmia	Zonegran	Capsule 25 50 100		100	100/3d	100–600
	PER	Perampanel	■	■			■					Dizziness, ataxia	Fycompa	Tablet 2 4 6 8 10 12		4	2/2w	4–12
Focal epilepsy	PHT	(Fos)Phenytoin1					■		■			Gingival hyperplasia (60%), hirsutism	Phenydan	Tablet 100		Loading	Level 1	200–400
	CBZ	Carbamazepine1						■	■			Benign leukopenia 7, ↓ T3/T4	Tegretol	Tablet 200 400		200	200/3d	800–1600
													Timonil	Tablet 200 300 400 600				
	OXC	Oxcarbazepine	■					■	■				Apydan	Tablet 150 300 600		300	300/3d	600-2400
													Trileptal	Tablet 150 300 600				
	ESL	Eslicarbazepine						■	■				Zebinix	Tablet 200 800		400	400/w	1200-1600
	LCM	Lacosamide						■	■			Atrial fibrillation	Vimpat	Tablet 50 100 150 200		100-200	100/w	100-400
	CNB	Cenobamate						■	■				Ontozry	Tablet 12.5 25 50 100 200		12.5	25/2w	200
	PB	Phenobarbital				■	■	■					Aphenylbarbit	Tablet 15 50 100		1-3mg/kg	Spiegel1	300
	GBT	Gabapentin				■	■					Oedema	Neurontin	Tablet 600 800, capsule 100 300 400		900	300/3d	900-2400
	PGB	Pregabalin				■	■					Oedema, ↑CK	Lyrica	Capsule 25–300		100	75/3d	150-600
Lennox-Gastaut	FBM	Felbamate					↓		■		■	Ataxia, rhinitis	Taloxa	Tablet 400 600				800-1200
	RUF	Rufinamide					■	■					Inovelon	Tablet 100		400-800		3200
	CBD	Cannabidiol					↓						Epidyolex			5/kg		10-20/kg
Absence	ESM	Ethosuximide	■	■	■		↓					Gingival hyperplasia	Petinimid	Capsule 250		500		1500
Spasms	VGB	Vigabatrin		■			↓				■	Neuropathy	Sabril	Tablet 500, suspension 500		500		1500

Seizure-suppressing drugs

		Active ingredient	Inter-val	T1/2	Women			Mainly metabolized by:									Remarks
			Number of doses/day	T1/2 (hours)	Oral contraceptive	Teratogenicity (RR)3	Schwangerschaft1	Nutrition	Protein binding	Kidneys	UGT 4	CYP1A2	CYP2B6	CYP3A4 5	CYP2C19	CYP2C9	
Broad Spectrum	CLZ	Clonazepam		1		?			0.9								
	CLB	Clobazam	1-2	18	↓	?			0.9					↑			
	LTG	Lamotrigine	1-2	25	↓	1	↓↓		0.6		↑				↓		VPA ↑200%, dose half as fast
				70 VPA													EI5 ↓40%
	LVT	Levetiracetam	2	9	OK	1	↓		0	0.7							
	(LEV)																
	BRV	Brivaracetam	2	9	?	?			0.2	0.1							Rifamp ↓45%, ↑PHT 20%
	VPA	Valproate	2	9-15	↓ VPA	2–9			0.9		↓↓4						Other ASM ↑ NH3 risk
																	Mitochondrial metabolism
	TPM	Topiramate	2	21	↓2	2	↓		0	0.5	-			↑	↓		
	ZNS	Zonisamide	1	70	?	?	↓		0.4	0.4							
	PER	Perampanel	1	100	?	?			0.9								EI↓70%, anti-tonic-clonic seizure activity
focal epilepsy	PHT	(Fos)Phenytoin1	1–3	22	↓	1		↓	0.9		↑			↑↑	↑	↑	Non-linear kinetics – CAVEAT inhibitors!
	CBZ	Carbamazepi-ne1	2–3	30–60	↓	1.5			0.8		↑			↑↑ ↑	↑↑		Auto-induction
				12–17 n. 2 weeks													
	OXC	Oxcarbazepine	2	9	↓	1	↓		0.4					↑↑	↓		
	ESL	Eslicarbazepine	1	15	↓	?	↓		0.3					↑	↓	↑	
	LCM	Lacosamide	2	15	↓	?			0	0.4							
	CNB	Cenobamate	1	30–70	?	?			0.6				↑	↑	↓		↑ CLB 40%
	PB	Phenobarbital	1	80	↓	3.0			0.6	0.3				↑↑ ↑		↑	Very slow reduction
	GBT	Gabapentin	3	6	OK	1		↓	0	1							Weak ASM
	PGB	Pregabalin	2-3	6				↓	0	1							Weak ASM
Lennox-Gastaut	FBM	Felbamate	2-3	22		?			0.3	0.5				↓			No effect on estradiol
	RUF	Rufinamide	2	10		?		↑↑	0.3					↑			VPA ↑ 70%, CAVEAT: tonic-clonic seizures
	CBD	Cannabidiol	2	17		?											↑ CLB 300%
Ab-sence	ESM	Ethosuximide	2-3	60		?			0	0.2							Methosuximide – similar effect
Spas ms	VGB	Vigabatrin	2	10		?			0	1							Optical neuropathy, visual field required

Turn over

Legend for the table

1) Might even increase seizures in primary generalized epilepsies
2) Approved in Switzerland by BAG (www.spezialitatenliste.ch), first choice underlined
3) Cross-allergy between carboxamides (CBZ, OXC, ESL), LTG and PHT, also associated with HLA-B*1502 (Asia) (CAVEAT: Stevens-Johnson syndrome)
4) Perform basic ECG, contraindicated in PR prolongation (higher degree atrioventricular block, LCM) or QT interval shortening (CNB). Cardioplegia possible with i.v. PHT
5) Cross-hyponatraemia (<128 mM) by carboxamide-induced syndrome of inappropriate antidiuretic hormone secretion (SIADH) (carbamazepine (CBZ) 7%, oxcarbazepine (OXC) 22%, eslicarbazepine acetate (ESL) 11%). Risk ↑ with dose (OR 1.2), age (OR 2.5 >40 years), and polytherapy (OR 2.3, Berghuis, Epilepsia, 2017)
6) Liver values including NH3 after 1–2 weeks. Transient elevations in liver enzymes (particularly GGT) are common. Toxicity at >3-fold increase. With VPA, an asymptomatic increase in NH_3 is very common.
7) Blood count: neutropenia or aplastic anemia (CBZ) or thrombocytopenia (valproic acid, VPA)
8) Vitamin D and osteoporosis (densitometry) control for all enzyme inducers and VPA
9) Sedation as an additional NW for all. Insomnia at LTG. Sleep consolidation with GBT, PGB, PER
10) Caveat: possible worsening of myoclonus in JME
11) Na+ channel blockers, especially in combination, can cause dizziness, ataxia, diplopia, and blurred vision. PHT can lead to cerebellar atrophy.

Benzodiazepines: equivalent doses

Active ingredient	Trade name CH	Dose in mg	Max daily dose	h until max plasma conc.	T1/2 (h)	Equivalent doses
Midazolam	Dormicum	7.5–15	15	1	1.5–2.5	7.5
Flurazepam	Dalmadorm	30	30	0.5–2	1–2	15–30
Zolpidem	Stilnox S	10	10	0.5–3	3	20
Oxazepam	Seresta	15–100	150	2–3	7–11	25–30
Alprazolam	Xanax	0.5–4	6	1–2 (5–11)	12–15	1
Triazolam	Holcion	1.125–0.25	0.25	1–2	1.5–5.5	0.5
Flunitrazepam	Rohypnol	0.5–1	2	0.75–2	10–16	1
Lorazepam	Temesta	1–6	7.5	1–2.5	12v16	2
Bromazepam	Lexotanil	1.5–9	36	1–2	15–28	6
Clobazam	Urbanyl	15–60	120	1.5–2	20–50	20
Diazepam	Valium	5–20	20	0.5–1.5	10	10
Clonazepam	Rivotril	1-4	20	2-4	20-60	0.5-2

Valproate levels in hypoalbuminaemia

- **Total VPA target range** 397–693 mmol/l
- 90% protein binding, target range total VPA 350–700 mmol/l (50–100 mg/l), i.e. 35–70 mmol/l free VPA (5–10 mg/l)
- Calculate the individual target range of free VPA depending on albumin according to the table below

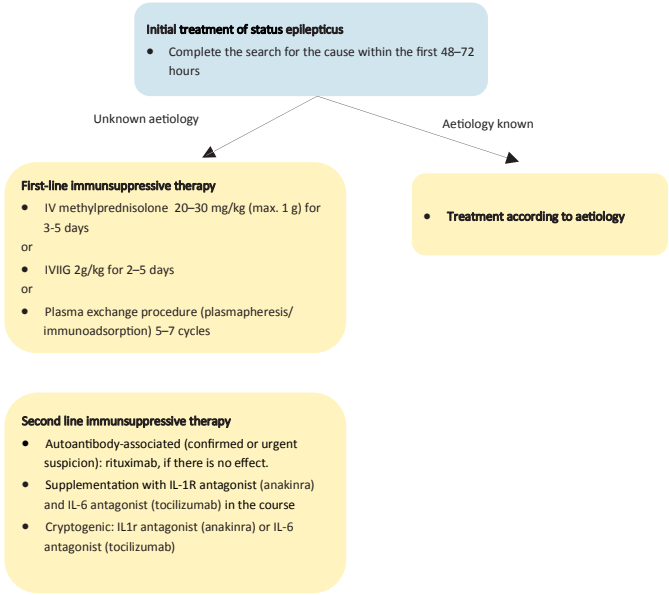
Albumin g/l	Free VPA fraction%	Albumin g/l	Free VPA Fraction%	Albumin g/l	Free VPA Fraction%	Albumin g/l	Free VPA Fraction%
41 g/l	6.8%	35 g/l	10.5%	29 g/l	16.2%	23 g/l	24.9%
40 g/l	7.3%	34 g/l	11.3%	28 g/l	17.4%	22 g/l	26.8%
39 g/l	7.9%	33 g/l	12.1%	27 g/l	18.7%	21 g/l	28.9%
38 g/l	8.5%	32 g/l	13%	26 g/l	20.1%	20 g/l	31%
37 g/l	9.1%	31 g/l	14%	25 g/l	21.6%	19 g/l	33.3%
36 g/l	9.8%	30 g/l	15%	24 g/l	23.2%		

NORSE and FIRES

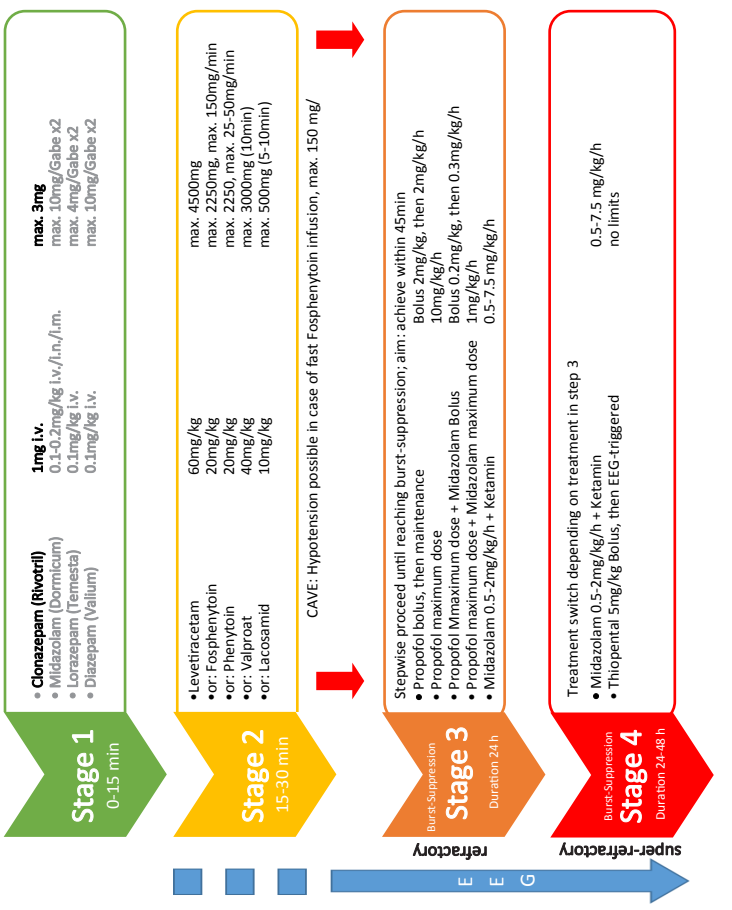
General

NORSE: New onset refractory status epilepticus
Special form: **FIRES**: febrile infection-related epilepsy syndrome

- Search for causes:
  - LP, MRI
  - Early screening for autoimmune antibodies (MOG, GAD65, anti-thyroid)
  - Onconeural Antibodies
  - Rheumatological diseases (esp. SLE, ANA, ANCA)
  - Infectious origin (HIV, HSV, enteroviruses, SARS-CoV2, syphilis, *C. pneumoniae*, *B. henselae*, *M. pneumoniae*, *C. burnetti*, shigella, *C. psitacci*)
  - Toxicological screening
  - If necessary PET, CT thorax/abdomen/pelvis
  - If necessary genetic testing



Adapted from Wickström et al. Epilepsia 2022



Diagnosis	Management	Maintenance therapies	Causal therapy	Status epilepticus without impaired consciousness
• Lab: chemistry, HCG, drugs, medication level • CT oder MRI • Lumbar puncture	• ABCD, BD, HR, O2 •Temp -> antipyretic •Hypoglycaemia thiamine 100 mg IV, then dextrose	•concurrently with non -sedating medications •Choice of 2-3 drugs from stage 2	•Immuntherapy (autoimmune epilepsy) •Epilepsy surgery (focal epilepsy) •Vitamin B6 200 mg/d (pyridoxine-dependent epilepsies) •Thiamine 300–1000 mg i.v. in alcohol abuse	•Generally not life-threatening •Stage 1 and 2, then adapt to the situation (in consultation with epileptology dept.)

Transient loss of consciousness (TLOC)

Definition of TLOC

- Loss of consciousness
- Short duration (usually <5 min)
- Abnormal motor function (loss of tone or tonic/clonic)
- Unresponsive
- Amnesia for duration of loss of consciousness

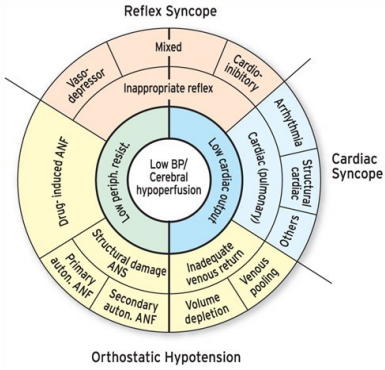
Forms

1. traumatic
2. non-traumatic (syncope, epileptic, functional, rare causes [e.g. SAB, TIA])

Fitness to drive after syncope

Vasovagal, not in sitting position and trigger remediable: given

Details of other forms of syncope: Buser et al. Cardiovasc Med. 2019;22:w02023



Brignole Europ Heart J 2018

History

- **Position during syncope?** Lying, sitting, standing, standing up, moving, physical activity, head rotation/-reclination
- **Trigger?** Pain, micturition, strong emotions (e.g. unpleasant picture), heat, infection, food, medication/noxae (in particular, vasodilators, diuretics, antiarrhythmics)
- **Prodrome?** Dizziness, sweating, visual disturbance, hearing disturbance, nausea/vomiting, epigastric/thoracic pressure, dyspnoea, palpitations, rising emotions, or other aura signs of epileptic seizures, headache
- **Characteristics of the ictus?** Duration of unconsciousness, time to reorientation, convulsions, enuresis/encopresis
- **Recurrence?**
- **Clinical history?** Dyspnoea on exertion, reduced performance, dizziness, cardiac insufficiency
- **Family history?** Sudden cardiac death SCD, PM/ICD, cardiomyopathies, thrombophilia/LE

DD syncope, epileptic seizure, functional seizure

	Syncope	Epileptic seizure	Functional seizure
Typical duration	< 1 min	<2 min	> 2 min
Motor activity	in 80% clonic, partly also rhythmic or tonic phase	possible, rhythmic clonic and/or tonic phase	bizarre movements that can be influenced from the outside, waxing/waning, "no" head movements, pelvis thrusting, twitching of all extremities while conscious
Eyes	open, mostly gaze deviation upwards	open, mostly lateral gaze deviation	mostly closed/squeezed shut
Recovery	quick	slow, amnesia	variable
Tongue biting	seldom, then more likely tip	lateral	seldom, then more likely tip
Enuresis/encopresis	seldom	possible	seldom
Diagnostics	hsTnT+proBNP are predictive of cardiac syncope	EEG (sensitivity highest within 24 hours after event)	

Clarifications – see also Syncope Guidelines, Inselspital

- **Exclusion of urgent conditions** aortic dissection, STEMI, LE, pneumothorax, pericardial tamponade, hypoglycaemia
- **Apparatus** 12-lead ECG/telemetry, blood pressure (left/right), auscultation (systolic?), temperature, echocardiography if necessary, Schellong test if necessary
- **Blood tests** Troponin T, NTproBNP, D-dimer, glucose
- **Red flags?** (see below) – depending on red flags:
  - Consider 6 h cardiac monitoring for emergency or cardiac IMC
  - Consider emergency neurological consultation, EEG
- **Further clarification**

1. Syncope consultation? with red flags/unclear/injury consequences/recurrence
2. Consider echocardiography, Holter ECG/implantable event recorder, coronary angiography, tilt table exam

Red flags → Immediate further clarification, if necessary inpatient (from ESC Guidelines 2018)

Clinical

Major criteria	Minor criteria (Classification as major if additional structural heart disease or abnormal ECG is seen)
• New chest pain, shortness of breath, abdominal pain, headache • Syncope during exertion or lying down • Palpitations before TLOC	• No warning symptoms or only short (<10 sec) prodromes • Family history for SCD at a young age • Syncope while sitting

Personal medical history

Major criteria	
• Severe structural or coronary cardiopathy (heart failure, low LVEF, post myocardial infarction)	

Examination findings

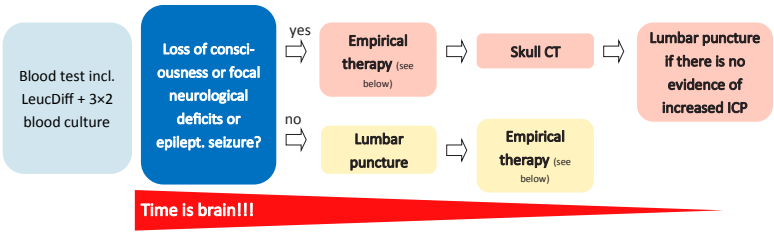
Major criteria	
• Unexplained sys. BP <90 mmHg • Evidence of gastrointestinal bleeding • Persistent bradycardia <40/min while awake and no regular endurance sport • Newly detected systolic • Unclear increase in troponin, NTproBNP, D-dimer	

ECG

Major criteria	Minor criteria (Classification as major if history is compatible with rhythmogenic syncope)
• ECG changes indicative of myocardial ischaemia • Mobitz II or 3rd degree AV block • Bradycardia AF < 40/min • Persistent sinus bradycardia <40/min or repetitive sinoatrial block/sinus pauses >3 sec while awake and no regular endurance sport • Bundle branch block, intraventricular conduction disorder, ventricular hypertrophy, Q waves consistent with ischaemic heart disease or cardiomyopathy • Sustained or non-sustained ventricular tachycardia • Pacemaker or ICD dysfunction • Type 1 Brugada syndrome ECG (typical ST elevations V1-3) • QTc >460 ms on repeat ECGs indicative of LQTS	• longer 2nd degree AV block or 1st degree AV block Wenckebach phenomenon (Mobitz I) • Inappropriate sinus bradycardia/AF 40–50/min • Paroxysmal SVT or AF • Pre-excitation (delta wave, short PQ time) • Short QTc interval ≤ 340ms • Brugada– syndrome ECG • Negative T wave in right precordial leads, epsilon wave indicative of arrhythmogenic right ventricular cardiomyopathy (ARVC)

Pathogen-induced meningitis and encephalitis

	Community-acquired bacterial meningitis	Viral Meningitis/Encephalitis	Meningo/encephalitis Borrelia/ Listeria/TB/fungal
Begin	Fulminant hours to 1–3 days	Acute-subacute over days	Subacute
Clinical CAVEAT Kernig+ Brudzinski sensitivity 5%	Fever (>38°C, 77–97%) headache (87%) meningism (65–83%) qualitative/quantitative disturbance of consciousness (30–69%) focal neurol. sign (15–34%) typical triad (fever, meningism, consciousness) 41–51%	Qualitative/quantitative consciousn. dis. >24h plus ≥ 2 out of fever T ≥38°, new seizures, new focal deficits, CSF CC>4, typical MR-abnormalities (in HSV1 in 95-100% after day 2) , typical findings	Headache, meningism, altered mental status, reduced vigilance , epileptic seizures, neurological deficits, fever.
Isolation	Immediately droplet precautions up to 24 hours after the start of antibiotics or meningococcal PCR (=BioFire®) neg!	None	Tbc: bei V.a. Lungen- oder Miliartuberkulose
Lumbar puncture	Meningitis cell count, glucose, lactate, protein Isoelectric focusing and oligoclonal bands (OCB), CSF/serum glucose ratio (reduction in serum with LP)		
Diagnostics	Blood base, blood count including diff, MiBi: 2x2 BK CSF opening pressure, CSF culture + Gram stain + BioFire® Serology HIV, TBE Serum/CSF index Borrelia, Treponema (TPHA serum, if positive: CSF/serum index) (BioFire® MEP PCR= *N. meningitidis, S. pneumonieae, L. monocytogenes, H. influenzae, Cryptococcus neoformas/gatii*, HSV1+2, VZV, CMV, Enterov., HHV6, Parechov. → Sens 90%, Spec 97%; 1.5% false neg (HSV, EV, Cryptococci) CAVEAT HSV possibly false negative in the first 72 hours		
If BioFire® not possible	CSF PCR: HSV 1+2, VZV	CSF PCR: HSV 1+2, VZV, enteroviruses	Always individual pathogen detection
CSF * number of cells/ml neutrophils%	80%>1000, 14% 100–999, 7%<100 Neutrophils >80%	4–1000, rarely until 4000 Neutrophils: early >50% late <20%	Borrelia 50–100 Neutro <30% Listeria > 100 Neutro ~ 50% TB 50–500 Neutro <30% Fungal 50–500 Neutro <30%
CSF * protein glucose index	> 1g/l ❙ glucose decreased Lactate > 3.5 mmol/l more sensitive than CC!	< 2g/l ❙ Glucose normal lactate < 3.5mmol/l	Borrelia > 1g/l ❙ normal Listeria > 0.5g/l ❙ normal Tbc > 1g/l ❙ depressed Fungal variable ❙ depressed
Pathogen	*St. Pneumoniae*: pneumonia, sepsis, any age *N. meningitidis*: petechiae/ haemorrhages, sepsis, children, adolescents *H. influenzae*: less fulminant, children *Listeria monocytogenes*: sepsis, pregnant women, >50 years, immunocompromised, neoplasia, C2	- HSV PCR false negative up to 4 days after onset in 5% -> continue with aciclovir + repeat puncture after 4 days! - if VZV neg. but clinically suspected -> determine anti-VZV antibodies in the L/S - possibly swab nasopharyngeal. resp. virus multiplex PCR	
Start treatment	Within 1 h (max .3 h)	Within max. 6 h	
Treatment antibiotika.insel.ch	**Empirical therapy** Dexamethasone 10 mg IV 6 hourly for 4 d (up to pneumococci PCR (BioFire®) and *H. influenzae* negative) + Ceftriaxone (Rocephin®) 2×2 g/d i.v. + Amoxicillin (Amoxicillin®) 6×2 g/d i.v. + Aciclovir (Zovirax®) 10mg/kg body weight every 8 hours (with VZV 15 mg/kg) (CAVEAT hydrate well, especially 2 hours after infusion) Consultation with infectiology dept.		Borrelia: Doxycyclin (Doxycyclin®) 200 mg/d p.o. or Ceftriaxon (Rocephin®) 2 g/d i.v. for 14 d Listeria: Amoxicillin (Amoxicillin®) 6×2 g/d i.v. + TMP-SMX 3×5 mg/kg body weight i.v. for 3 weeks Tuberculosis + fungal: consultation with infectiology dept.
Immune deficient?	Consultation with infectiology dept. for diagnosis and treatment		
Recording	ICU or IMC	General award or IMC	General award or IMC
Obligation to report	Meningococci, pneumococci	Tick-borne encephalitis (TBE)	TB
Chemoprophylaxis post-expos.	Meningococci only: Ciprofloxacin 1x500mg (Children: antibiotika.insel.ch)		
Focus search	mastoiditis? endocarditis? spondylodiscitis? splenectomy?		* typical findings



Treatment of intracranial pressure in meningo/encephalitis

In the case of severe courses and possible intracranial pressure, especially if the patient has lost consciousness:

- early monitoring and aggressive therapy
- Target: ICP ≤ 22 mmHg, CPP > 60 mmHg

Treatment options (see also chapter on intracranial pressure)

- Osmotherapy with mannitol 0.5–2 g/kg body weight or hypertonic infusion solutions
- Hyperventilation
- EVD
- Craniectomy

Borrelia burgdorferi

Clinical

- Erythema migrans
- Isolated meningitis
- Meningoradiculoneuritis (Bannwarth syndrome: meningitis plus radiculoneuritis – often cranial nerves, bilateral facial paralysis)
- Radiculitis (often painful!)
- CNS involvement in 4% (chronic course over months–years – encephalitis/encephalomyelitis/myelitis)
- Polyneuropathy/neuritis with acrodermatitis chronica atrophicans: rare
- Cerebral vasculitis: very rare

CSF

- Early >30/µl (50–370) mononuclear, protein elevated >0.6–2 g/l lactate normal
- AQ increased, IgM synthesis 70%, IgG 20%, OKB positive in 70%, lactate <3.5 mmol/l, CXCL13 increased
- CXCL13 increased early on in almost all patients (drops quickly after the start of antibiotics): moderate specificity (also increased in syphilis, lymphoma, cryptococci, for example)
- Late: ZZ 20-300, AQ greatly increased, IgG synthesis 100%, IgM 40%
- Intrathecal AK synthesis begins from the 2nd week of illness and is detectable in 99% after 6–8 weeks.

Diagnosis Typical clinical features and positive L/S antibody index (if only PNS involvement serology; CAVEAT: approx. 20% of the population is seropositive!), or increased CXCL-13 in the early phase.

Treatment Ceftriaxon 2g /d i.v. for 14 d or doxycycline 200 mg/d p.o.

HSV

- Fever in over 90%
- HSV and MRI: from about day 3–5 after symptom onset, MRI in 95–99% pathological and specific (HSV1>>HSV2; FLAIR/T2 > DWI mainly lesions anterior/mesial temporal, frontal, insular)
- HSV PCR false negative in 4–6% if LP within <4 d from symptom onset; rarely and very early, ZZ and protein can be normal; therefore, if there is clinically justified suspicion, re-lumbar puncture after > 4 days after the onset of neurological symptoms and treat until then

Extended diagnostics

Adapted from Boucher et al. 2017

→ immunosuppressed or under anti-fungal therapy: cryptococcus-Ag CSF + enterovirus PCR stool
→ in suspected HSV/EV and BioFire® negative: repeat LP after 2–3 days
→ in suspected listeria (protein>1 g/l, exposure, immun serology,>65): continue amoxi + consult infectiology!
→ Adapt serologies to history: pre-test probability – if the pre-test probability is low, a positive serology result is not helpful (positive predictive value very low)!

Acute meningitis	Common: EV (71), TBE, VZV, HSV-2>1, echoviruses, coxsackie, parechovirus, Toscana (travel history), WNV (travel history), borrelia Rare: HIV, CMV, EBV, HHV-6/7, HSV-1, JEV, LCMV, COVID-19, Adeno, *T. pallidum*, TB, listeria, fungal (cryptococcus), dengue, mumps; uutoimmune: GFAP, seronegative AE
Meningo-/ encephalitis	Common: TICK-BORNE ENCEPHALITIS (TBE), HSV1>2, VZV, EV (70/71) Rare: influenza, adeno, EBV, CMV, HHV-6/7, COVID-19, listeria, mycoplasma, rickettsia, ehrlichia, bartonella, cryptococci, LCMV, adenovirus, parechovirus, Coxsackie, measles, mumps; subacute/ chronic: JCV, PML, CJD, bornavirus, SSPE, T. whipplei, T. pallidum, rabies, TB, brucella
Immunsuppression	All pathogens, more frequently: EBV, CMV, HHV6, VZV, EV, listeria, TB, nocardia, Cryptococcus neoformans, JCV, travel history (WMV, coccidioides), LCMV, HEV, measles, Histoplasma capsulatum, Aspergillus fumigatus, Toxoplasma gondii, Acanthamoeba spp., Balamuthia mandrillaris
Under monoclonal antibody therapy	**Infliximab, Etanercept** VZV, M. tuberculosis, Legionella pneumophila, Listeria monocytogenes, Nocardia, Histoplasma capsulatum **Rituximab** EV, JC virus **Natalizumab** HSV, JC virus **Tocilizumab** VZV, Mycobacterium tuberculosis **Eculizumab** Meningococci
Pathogen after travelling abroad	**Mediterranean** Tuscany, WNV, Rickettsia conorii (Mediterranean spotted fever) **North Africa** dengue, rabies, Rift Valley fever, WNV, Rickettsia conorii **Sub-saharan Africa**: chikungunya, dengue, malaria, rabies, yellow fever, Rift Valley fever, Zika, Rickettsia spp., Salmonella typhi, T. brucei spp. Cryptococcus gattii, lassa fever, Ebola **North America** WNV, La Crosse virus, SLEV, EEEV, WEEV, California encephalitis virus, Colorado tick fever virus, Powassan virus, chikungunya, rabies, EV71, Rickettsia rickettsii, Anaplasma phagocytophilum, Borrelia burgdorferi, Coccidioides, Naegleria fowleri, Acanthamoeba spp., Balamuthia mandrillaris, Baylisascaris procyonis **Central/South America** VEEV, WNV, EEEV, SLEV, chikungunya, dengue, Zika, yellow fever, Rabies, Bartonella bacilliformis, Rickettsia, T. solium, P. falciparum **Asia** JEV, TBEV, Chandipura, Nipah, EV71, chikungunya, rabies, Orientia tsutsugamushi, P. falciparum, Angiostrongylus sp., C. gattii, melioidosis **Australia Oceania**: Murray Valley E, JEV, Hendra, melioidosis
Vectors	**Tick,** TB, Borrelia, (Powassan virus, Colorado tick fever virus, Rickettsia rickettsii, Ehrlichia chaffeensis, Anaplasma phagocytophilum, Francisella tularensis) **Mosquito** JEV, WNV, dengue, yellow fever, chikungunya, La Crosse virus, SLEEV, EEEV, WEEV, VEEV, MVEV, malaria
Food	**Unpasteurized milk** listeria, brucellosis, TBE **Raw sausage/meat** (especially game/pork) HEV **Uncooked meat** Gnathostoma, T. solium, T. gondii
Animals	**Dogs** saliva/bites: Capnocytophaga, Pasteurella, rabies; faeces/aerosol/urine: Salmonella spp., Campylobacter, Toxocara canis, Echinococcus granulosus, Coxiella burnetii (Q fever), brucellosis **Cats** saliva/bites: Bartonella henselae, Pasteurella, (Capnocytophaga), rabies, tularaemia; faeces/ aerosol/urine: Salmonella spp, Campylobacter, Toxoplasma, Coxiella burnetii, Toxocara cati **Hares/rabbits** tularaemia, hep E, rabies **Rodents** leptospirosis, LCMV, Hantavirus, Yersinia pestis, bornavirus **Birds/poultry** psittacosis, cryptococci

DD infectious/autoimmune depending on location

	Infectious	Autoimmune/not infectious
Chronic meningitis	TB, Borrelia, T. pallidum, Throperyma whipplei, Brucella, echoviruses, LCMV, VZV, HIV, fungal (cryptococci, Coccidioides, Histoplasma, Candida, Aspergillus), Acanthamoeba, Taenia solium, Toxoplasma gondii	IgG-4, GFAP, sarcoidosis, SLE, RA, Sjögren, Vogt-Koyanagi, Harada, Behcet's disease, carcinomatous meningeosis, shunt-associated
Recurrent-meningitis	HSV-2>1, EBV, bacterial (portal of entry, immune deficiency, sinusitis/mastoiditis, osteomyelitis, otitis?), fungal (Cryptococcus neoformans, Candida species, Histoplasma capsulatum, Coccidiodes immitis, Blastomyces dermatitidis), Toxoplasma gondii	Epidermoid cysts, craniopharyngeoma, medication (NSAR, Trim-Sulf, cephalopsorin, amoxi, cipro, LTG, CBZ, IVIG, MTX, AZA, TNF blocker, chemo, contrast, Behcet, SLE, Sjögren, sarcoidosis, Vogt-Koyanagi-Harada, GPA, RA
Basal meningitis	TBC, listeria, cryptococci, dimorphic fungi	Sarcoidosis, gliomatosis
Limbic system/ temporal lobe	HSV-1, HSV-2, tick-borne encephalitis, syphilis, WNV, CJD, Bartonella henselae, Mycobacterium tuberculosis, (HHV-6 immunosup.)	Hu, CRMP5/CV2, Ma2, NMDAR, AMPAR, LGI1, CASPR2, GAD65, GABABR, DPPX, mGluR5, AK5, Neurexin-3α, lymphoma, Susac syndrome
Brainstem, rhombencephalitis	Listeria monocytogenes, Mycobacterium tuberculosis, Treponema pallidum, Brucella, Tropheryma whipplei, Blastomyces dermatitidis, HSV1/2, VZV, HIV, PML, EV71, EV (68/71), JE, TICK-BORNE encephalitis (TBE), WNV, Mycoplasma, EBV, HHV6, CMV, EEE, Borrelia, adenoviruses, influenza A, polio, rabies, legionella, salmonella, melioidosis, arboviruses, aspergillus, COVID-19	MS, ADEM, ANNA-1, ANNA-2, PCA-1, Ma1-2, KLHL11, IgLON5, DPPX, AQP4, MOG, Behcet, sarcoidosis, Gq1b/Bickerstaff, CLIPPERS, Susac, SLE, Sjögren, Vogt-Koyanagi-Harada, lymphoma, osmotic demyelination
Thalamus/ basal ganglia	Respiratory viruses (influenza, parainfluenza, adenovirus, RSV), arboviruses, WNV, JE, EV, rabies, CJD, Mycobacterium tuberculosis, toxoplasmosis, Cryptococcus, tick-borne encephalitis	NMDA, CRMP5, ANNA-1, Neurexin 3a, LGI-1, GAD65, anti-phospholipid Ak syndrome, Sjögren
Cerebellum	Tick-borne encephalitis, VZV, WNV, EBV, PML, influenza, rabies, HSV, HIV, CMV, JC, Coxsackieviruses, echoviruses Post-infection: EBV, influenza A/B, mumps, VZV, rotavirus, echovirus, M. pneumoniae	NMO, ADEM, MOG, MS, ANNA-1/2, PCA-1, Tr, CASPR2, KLHL11, NIF, mGluR1, GAD65, VGCC, amphiphysin, SLE, Sjögren, lymphoma
Acute myelitis	Bacterial Borrelia, T. pallidum, TB, mycoplasma, (rarely: Streptococcus A/B, Brucella, Chlamydia, Coxiella, Legionella, Leptospira, Salmonella paratyphi B, Orienta tsutsugamushi, typhus) Viral: Tick-borne encephalitis, VZV, WNV, EV68/71, HIV, HSV2>1, HHV6, influenza A/B, (rarely: coronaviruses, Coxsackieviruses, CMV, EBV, echo, hepatitis A/B/C/E, Parvo B19, LCMV, HTLV-1, chikungunya, dengue, Hanta, measles, rubella, mumps, JE, PML, rabies, polio, Zika) Parasitical Echinococci, Gnathostoma, Schistosoma, Taenia solium, Toxocara, Toxoplasma, Trypanosoma brucei, cysticercosis, Acanthamoeba, malaria Fungal Aspergillus, cryptococci, Blastomyces, Coccidioides	Autoimmune ADEM, GFAP, MS, MOGAD, NMSOD, sarcoidosis Paraneoplastic ANNA-3, amphiphysin, Hu, GAD65, Ma, Ri, Ta, Yo, aquaporin-4, CRMP-5, glycin, NMDA, PCA-2 Substances Benzol, cisplatin, cytarabin, gemcitabin, heroin, ICI, TNF-A-inhibitors, sulfasalazine Neoplastic Metastases, primarily intramedullary tumors
Chronic myelitis	Borrelia, brucellosis, HIV, HTLV-1, TB, T. pallidum, schistosomiasis	Syrinx, tumor, compression, copper (also due to excess zinc), vitamin B12/E, superficial siderosis, CADASIL, ALS, HSP, SCA, Friedreich, adrenomyeloneuropathy
Conus medullaris/ cauda equina	HSV-2, HSV-1, CMV, Treponema pallidum, Mycobacterium tuberculosis, schistosomiasis, mycoses	Neurosarcoidosis
Radiculo-/ neuropathy	VZV, Borrelia, HSV 2>1, Hep C, Hep E, HIV, HTLV, CMV, EBV, tick-borne encephalitis, WNV, TB, brucellosis, Bartonella henselae leprosy, leptospirosis, Chagas, rabies, Zika	GBS (DD post-infectious), CIDP, NF155/186, Contactin1, Caspr1; ANNA1, CRMP5, ANNA3, PCA-1/2, Ma1, amphiphysin, CASPR2, LGI1, MAG IgM k; vitamin B1, B6, B12, E, folic acid, thyroid, copper deficiency vasculitis (EGPA, GPA, NSVN), SLE, Sjogren's, porphyria, toxic/drug

angepasst nach Bradshaw & Venkatesan Semin Neurol 2019

Autoantibody-associated diseases

Antibody cell membrane ass. + synaptic antigens

NMDAR	Psychiatric, epilepsy, movement disorder, dysautonomia	30%, Teratom
DPPX	Encephalitis, sleep disorder, myoclonus, hyperekplexia, ataxia, dysautonomia, gastrointestinal dysmotility	Unklar
GABA AR	Acute encephalitis with seizures/status/epilepsia partialis continua	60%, Thymom
GABA BR	Limbic encephalitis	50%, SCLC
AMPAR	Limbic encephalitis (amnestic disorder and seizures, confusion)	50%, Lunge, Brust, Thymus, Ovarien
CASPR2	Morvan syndrome; limbic encephalitis, cerebellar, neuromyotonia/ myokymia, painful PNP	40% Thymom
MOG	Optic neuritis, longitudinal transverse myelitis, ADEM	Selten
AQP4	NMOSD	<5%, AdenoCa
LGI1	Limbic encephalitis, 60% hyponatraemia, faciobrachial dystonic epileptic seizure, RBD, bradycardia	<10%, Thymom, SCLC
IgLON5	Non-REM parasomnia, RBD, apnoea, stridor, dysphagia, cognitive decline, ataxia, chorea	Unklar
Neurexin-3α	Encephalopathy, encephalitis, seizures	
GlyR	Progressive encephalomyelitis, rigidity, myoclonus, oculomotor disorder, dysautonomia, hyperekplexia, respiratory failure, optic neuritis	Thymom, Mamma-Ca, Hodgkin
mGluR1	Cerebellar (90%) +cognitive/psychiatric	11%, Lymphom
mGluR5	Neuropsychiatric, cognitive, sleep disorder, seizures	60%, Lymphom, SCLC
VGCC	LEMS, LEMS+cerebellar degeneration, ataxia	40%, SCLC (LEMS)
AChR	Muscle: myasthenia; ganglionic: encephalopathy, autonomic dysfunction, seizures, neuropathy	Muskel: Thymom, ganglionär: Brust, Prostata, Bronchial, GIT
MuSK, LRP4	Myasthenia (MuSK generalized MG)	

Antibodies to intracellular antigens

ANNA-1 (Hu)	Sensory neuropathy (sensorimotor/autonomous), cerebellar ataxia, encephalitis, rhombencephalitis, myeloneuropathy	98%; SCLC
PCA-1 (Yo)	Cerebellar degeneration, PNP, myeloneuropathy	90–100%, breast/gynaecological
PCA-2	Sensorimotor PNP, cerebellar degeneration, encephalomyelitis	80%, SCLC, NSCLC, breast
ANNA-2 (Ri)	Cerebellar, opsoclonus/myoclonus, dystonia/Parkinson, trismus, cerebellar deg.	90%, breast/lungs
ANNA-3	Limbic + brainstem encephalitis, sensory + sensorimotor neuropathy, myelopathy	60% SCLC
Ma1 (PNMA1)	Limbic/brainstem encephalitis, cerebellar, PNP	77–100%, lung/pleura, GI, testes, breast, kidney, melanoma
Ma2 (PNMA2)	Encephalitis (limbic 25%), drowsiness, eye movement disorder	90%, testes, Non-SCLC
Amphiphysin	PNP, stiff-person, myelopathy, encephalitis/phalopathy, cerbellar	80%, SCLC, breast
Zic4	Cerebellar degeneration	90%, SCLC
Kelch1	Rhombencephalitis, ataxia (80%), diplopia (60%), vertigo (50%), auditory (40%), dysarthria (30%), epilepsy (20%)	70%, testes, teratoma
GAD65	Limbic encephalitis, stiff-person, cerebellar ataxia	<15%, SCLC
GFAP	Meningoencephalitis	20%, ovary teratoma, adenocarcinoma
Tc/DNER	Cerebellar degeneration	90% Hodgkin
CV2/CRMP5	PNP (asym. painful polyradiculopathy), cerebellar ataxia, chorea, LEMS, myeloneuropathy	90%, SCLC, thymoma
Sox-1	LEMS	20–30%, SCLC (±Hu)
MAR	Night blindness, photopsia, visual field defects, visual disturbances	Melanoma
CAR	Painless vision loss, uveitis	40–60%, SCLC, prostate

Adapted from Binks et al. Pract Neurol 2022

Diagnostics

- **MRI, cerebrospinal fluid diagnostics**
- **1. Clarify DD:** in particular infection-related genesis (e.g. HSV, HHV-6); other DD glioma, neurosyphilis, Whipple, HIV, CJD, mitochondrial disease, SLE, Behcet, Sjögren, cerebral vasculitis
- **2. Antibody diagnostics if the suspicion persists**
  - Laboratory block "limbic encephalitis": LgI1, CASPR2, NMDA, AMPA-R1/R2, GABA-R B1/2
  - Laboratory block "Paraneoplastic antibodies": ANNA-1, ANNA-2, PCA-1, Ma-1, Ma-2
  - Laboratory block "Cerebellum": anti-neuronal nuclear antibodies, Purkinje cell antibodies (monkey cerebellum)
- Determine Ab in CSF + serum (especially NMDA Ab often falsely negative in serum)

Diagnostic criteria

Possible autoimmune encephalitis (if all 3 criteria are met)
1) Subacute onset (<3 months) one or more of: short-term memory impairment, impaired consciousness, lethargy, personality change, psychiatric symptoms
2) One criterion from:
- New focal CNS findings
- Epileptic seizures not explained by known epilepsy
- CSF pleocytosis > 5 cells/mm^3
- MRI findings suggestive of encephalitis

3) Exclusion of DD

Definitive autoimmune encephalitis (if all 4 criteria are met)
1) Subacute onset (<3 months) of short-term memory impairment, epileptic seizures, or psychiatric symptoms consistent with an effect on the limbic system
2) Bilateral FLAIR hyperintensities confined to the medial temporal lobe
3) One criterion of:
- CSF pleocytosis > 5 cells/mm^3
- In the EEG, epilepsy-typical potentials or deceleration focus in the area of the temporal lobe

4) Exclusion of DD

Therapy

Consultation with neuroimmunology team
1. Choice
- **Methylprednisolone** (Solumedrol®) i.v. 1000 mg/d for 5 days, and/or
- **Plasma exchange procedure (plasmapheresis/immunoadsorption)** 5–7 cycles, depending on tolerability daily or every 2nd day and/or
- **Immunglobulin** i.v. 0.4 g/kg body weight/d for 5 d (if possible not before plasmapheresis)

2. Choice: Rituximab i.v. 1000 mg 1× and 1× after 2 weeks or **cyclophosphamide** body surface area × 800 mg i.v.

ICANS/CRES

- Possible complication of CAR-T therapy = gene-modified anti-CD10 chimeric antigen receptor T-cells (YESCARTA®, KYMRIAH®)
- Indication: therapy option for B-cell lymphomas

- CAR-T therapy associated side effects
- CRS (cytokine release syndrome; especially TNF and IFNγ): fever, flu-like symptoms, hypotension, hypoxia (among others)
- ICANS (immune effector cell-associated neurotoxicity syndrome)
- CRES (CAR-T cell-related encephalopathy syndrome)

- Symptoms: encephalopathy with slowing down, headache, aphasia, delirium, reduced vigilance (up to coma), epileptic seizures, global cerebral oedema
- Occurrence: median 5 days after infusion (1–28 days), median duration 13 days
- Classification based on clinical symptoms and CARTOX-10
- Diagnostics: MRI, EEG, possibly LP
- Serious courses: status epilepticus, global cerebral oedema with herniation (evaluate eVD system)
- Therapy: adjusted according to ICANS/CRES stage (see below)
- Early intensive care monitoring

CARTOX-10

• Orientation	5 points: Year, month, city, hospital, a Federal Councilor
• Naming	3 points: 3 objects
• Writing	1 point: Write a sentence; CAVEAT: Note the history, use the same sentence
• Attention	1 point: Counting backwards from 10 to 1 or 100 to 10

CRES Grade 1 CARTOX-10: 7-9 Slowing down Impaired handwriting Fatigue	• MRI • Possibly LP • EEG if suspected	→ Anticonvulsive: Levetiracetam 2 × 750 mg → Restlessness: lorazepam/haloperidol → Steroids: none → Anti-Il6 therapy: Tocilizumub only for CRS
CRES Grade 2 CARTOX-10: 3-6 Delirium Somnolence	• MRI • Possibly LP • EEG every 1–2 days	→ Anticonvulsive: Levetiracetam 2 × 750 mg → Restlessness: Lorazepam/Haloperidol → Steroids: Dexamethasone 10 mg 4 × /d → Anti-Il6 therapy: Tocilizumub only for CRS
CRES Grade 3 CARTOX-10: 0-2 Epileptic seizures Focal cerebral oedema max soporous	• MRI • Possibly LP • EEG daily	→ Anticonvulsive: adjusted → Cerebral oedema: normocapnia, hyperosmolar → Steroids: Dexamethasone 20 mg 4 × /d, if necessary ↑ → Anti-Il6 therapy: Tocilizumub/Siltuximab
CRES Grade 4 CARTOX-10: unarousable Status epilepticus Generaliz. cerebral oedema Coma	• MRI • Possibly LP • EEG daily	→ Anticonvulsive: adjusted → Cerebral edema: possibly EVD, hypercapnia → Steroids: Methylprednisolone 1-2 g burst → Anti-Il6 therapy: Siltuximab

Immune checkpoint inhibitor (ICI) toxicity

Incidence
- after CTLA-4 blockade: 4% (ipilimumab)
- after PD-1 inhibitors: 6% (nivolumab, pembrolizumab, cemiplimab, avelumab, durvalumab, atezolizumab)
- after combination 12%

- **Onset** after 4–13 weeks from infusion

Clinical presentation
- Myositis, myasthenia gravis (2/3 AChR pos), overlap (myositis-myasthenia-myocarditis)
- GBS: demyelinating, classic presentation
- Aseptic meningitis/encephalitis/myelitis
- Other symptoms: Rash, endocrinopathies (thyroid, DM), hepatopathy, cholangitis, pancreatic toxic, enterocolitis, ILD/pneumonitis, sarcoidosis-like, polymyalgia rheumatica, sicca, myocarditis, pericarditis, vasculitis, ACS, arrhythmia, takotsubo, acute interstitial nephritis, conjunctivitis, keratitis , uveitis, orbital myositis, haematological changes. See guidelines: https://doi.org/10.1016/j.annonc.2022.10.001

- Clinically frequent bulbar symptoms (with MG and myositis), therefore check swallowing and VC regularly!
- Determine creatine kinase and troponin T, troponin I to distinguish cardiac vs. myositis!

- For MG: Start with Mestinon 30 mg up to 600 mg/d or neostigmine i.v. (30 mg Mestinon orally = 1 mg neostigmine i.v.)

Grade 1: mild
→ ICI can be continued, but stop ICI in case of encephalitis

Grade 2: moderate, relevant to everyday life
→ pause ICI, prednisone 0.5 mg/kg body weight/d
→ if condition stabilises or improves: taper off steroids over 4–8 weeks
→ if patient deteriorates or relapses: consider methylprednisone pulse and prednisone 1–2 mg/kg body weight/d (slow tapering off over 7 months) + permanent immunosuppression (MMF, AZA, MTX, RTX)

Grade 3: serious + Grade 4: life-threatening
→ stop ICI, methylprednisone 1–2 mg/kg body weight/d
→ if patient stabilizes or improves: taper off steroids over 4–8 weeks
→ if patient's condition worsens, IVI 2 g/kg bw/d and/or PE (5–7 cycles)
→ in case of rapid progression with bulbar/respiratory symptoms and/or myocarditis or persistent bulbar symptoms or lack of response to steroids within 7–14 days: consider methylprednisone pulse and prednisone 1–2 mg/kg body weight/d (slow tapering off over 7 months) + permanent immunosuppression (MMF, AZA, MTX, RTX)

Refractory myositis: infliximab or tocilizumab

Encephalitis: rituximab

Treatment scheme according to Haanen et al. Ann Onc 2022

Multiple sclerosis

McDonald criteria 2017

Basic conditions
- Typical clinical presentation indicative of a first demyelinating event!
- Exclusion of other diseases

Relapsing-remitting multiple sclerosis (RRMS)

Proof of spatial dissemination on MRI
Evidence of at least 1 lesion in at least 2 of the following 4 locations:
- Periventricular (restriction: older patients, consider whether vascular components are more likely)
- Cortical/juxtacortical
- Infratentorial
- Spinal cord

(a lesion is sufficient for clinical 2. (e.g. ON))

Evidence of temporal dissemination on MRI
- Detection of a new lesion compared to a previous MRI scan (regardless of the examination times or their distance)

or
- Evidence of at least one contrast-enhancing and at least one non-contrast-enhancing lesion in an MR examination

or
- Detection of CSF-specific oligoclonal bands (type 2 or type 3 pattern)

There is no need to differentiate between symptomatic and asymptomatic lesions.

Primary progressive multiple sclerosis (PPMS)

Basic conditions
- At least 1 year of disease progression (prospective or retrospective)
- Exclusion of other diseases

In addition, fulfillment of 2 of the following 3 criteria
- ≥1 lesion in ≥1 region (periventricular, juxta-/cortical, infratentorial)
- ≥2 spinal lesions
- detection of CSF-specific oligoclonal bands (type 2 or type 3 pattern)

Note: McDonald criteria are used for early diagnosis and enable proof of spatial+temporal dissemination without waiting for a second relapse event → high sensitivity, lower specificity; if the basic clinical condition is not met there is a high potential for misdiagnosis! The McDonald criteria are not suitable as a differential diagnostic tool.

Standard examinations

- **MRI**
- **Standard BE**:
- **Standard BE:**
- diff blood count
- serum chemistry (liver, kidney, electrolytes, CK)
- CRP
- TSH
- ANA, p-/c-ANCA, APLA (cardiolipin, beta2-glycoprotein IgG/IgM)
- HbA1c
- Vitamin B12 (=HoloTC), folic acid in the erythocyte
- urine status
- hepatitis B+C, HIV, Borrelia, Treponema
- aPTT, INR/Quick (before LP)
- **Standard CSF:** entire routine including OKB and friction scheme for all 3 classes (IgG, IgA, IgM)

Further investigations in patients with red flags

Clinical red flags	• <16 years, >50 years • recurrent mouth ulcers • known rheumatic disease • known tumour disease • known chronic infection, headache	• epileptic seizure • fever • family history of a monogenetic disease • acute onset
Laboratory chemical red flags	systemic signs of inflammation	• pronounced laboratory-detected abnormalities (e.g. hypoglycaemia, electrolyte disorders)
CSF chemical red flags	• >50 cells/µl • granulocytic cell picture • Significant increase in protein (>1 g/l)	• intrathecal IgA synthesis (only 5% in MS) or 3-class reaction (IgG, IgA and IgM synthesis)
MRI red flags	• prominent effect on grey matter • bilateral optic nerve involvement (DD NMOSD)	• spinal lesion of ≥ 3 segment heights (DD NMOSD) • tumefactive lesion (isolated) • Involvement of the meninges/basal meningitis

- **Extension of the examinations depending on the red flags** (possibly also extension of the CSF diagnostics!)
- Laboratory: anti-ds-DNA, "cell nucleus screen", rheumatoid factor, ACE/soluble IL-2 receptor (also in CSF), HTLV-1 and mycoplasma serology, bartonella serology, Quantiferon test, tick-borne encephalitis (TBE) serology, genetics (CADASIL etc., not in an emergency!); in particular, NMOSD (neuromyelitis optica spectrum disease): AQP4 and MOG IgG in the serum, not in the CSF
- Chest X-ray, imaging of other organs
- Consider low-threshold cytology and FACS analysis in CSF diagnostics (can only be done if CSF is in the laboratory/pathology department within 1 hour! Otherwise it is not usable)
- Acute-infectious origin: Don't forget to search for the focus, blood cultures, search for pathogens in the CSF chemistry (e.g. Borrelia, herpes viruses, BioFire® , bacteriology, etc.)!
- Low-threshold consultation with neuroimmunological team!

Relapse Definition

Definition Newly occurring neurological deficit lasting at least 24 hours, independent of an increase in body temperature/the presence of a feverish infection (Uhthoff phenomenon), not explained by another cause. Usually present continuously (with certain fluctuations), rarely also clearly paroxysmal symptoms (e.g. tonic brainstem spasms), but no phenomena that occur in seconds or minutes and are difficult to objectify.

History and diagnostics

- Querying the **onset of symptoms** and documentation of the same is mandatory!
- First diagnosis see above (exclusion of other diseases!)
- With known MS: **Exclusion of acute infection**, possibly search for focus (Uhthoff phenomenon?), contraindication for steroids?
- **Immunotherapy query and risk factors: DD PML to consider?** (especially natalizumab, other immunosuppression outside of MS therapy?)
- **Documentation of relapse severity using EDSS** and functional system scores (see neuroimmunology folder)
- MRI: if the clinical presentation is clear, the flare-up therapy can be started in consultation with the neuroimmunology team without an MRI (and then elective imaging, only contrast medium recording can then no longer be used); in the case of red flags/unclear situation, an MRI of the suspected target region should be performed before flare-up therapy

Continued on the next page

Relapse – treatment and aftercare

Primary therapy

→ **i.v. Steroid pulse with methylprednisolone (SoluMedrol) 1g per day for 3 days** (possibly extension to 5 days over the course) with stomach protection and, if necessary, thrombosis prophylaxis, if necessary also sleep back-up

- Where? Inpatient for first dose; if tolerability is known to be good, then, if possible, on an outpatient basis:
  - ◊ Inselspital: Steroid administration at the weekend in the FastTrack, Mon-Fri in the FANI (registration using the form at L:\NRLK_FORMULARE_AERZTE\ different registrations at fanp@insel.ch, urgent cases Tel 29093; if registration is done at the weekend for Monday, the patient is informed of the appointment by telephone on Monday) or in a hospital close to patient's home/by GP
- CAVEAT Exclusion of contraindications and checks on previous tolerance of high-dose steroids

Alternative and secondary therapy

- bei Kontraindikationen oder vorherigem Nicht-Ansprechen auf Steroidtherapie/n kann ein primäres Austauschverfahren (Plasmapherese, Immunadsorption) in Absprache mit dem neuroimmunologischen Team (Kontakt s. digitales schwarzes Brett) erwogen werden
- in the case of contraindications or previous non-response to steroid therapy/ies, a primary exchange procedure (plasmapheresis, immune adsorption) can be considered in consultation with the neuroimmunological team (contact see digital bulletin board).

Follow-up after relapse event

General: prompt follow-up check during the neuroimmunological department's consultation hours (casemanagement@insel.ch). The urgency depends on the clinical presentation and the individual patient (extended flare-up therapy – plasmapheresis required? When did the symptoms begin? Is there a lot of uncertainty on the part of the patient/family?)

- 1– max. 2 weeks after treatment, depending on the severity of the event; in the case of exchange procedures after the 5th session
- during neuroimmunology consultation hours or, if necessary, via FastTrack Emergency

NOTE The effect of relapse therapy is greatest within approx. 8 weeks after the onset of symptoms (!), therefore, the rapid follow-up check must be handed over to the neuroimmunology consultation from the emergency!

Infection during MS immunotherapy

- **Focus search and infection control** according to internal medicine standards

- Pausing the immunotherapy is usually not necessary and also not useful

Exception: severe systemic infections, possibly with secondary immune phenomena and organ involvement, where a connection to the drug must be assumed. Examples: systemic herpesvirus-associated infections, listeria-associated infections, JC virus-associated progressive multifocal leukoencephalopathy (PML). Especially in the case of PML after therapy with monoclonal antibodies, an accelerated elimination via immune adsorption should be considered (depending on the time of the last administration).

Contacting the neuroimmunological team (for contact details see digital bulletin board) is possible and recommended at any time!

Immunomodulatory therapy

		RRMS	RMS	SPMS	PPMS
Highly active* form	First-line therapy	Cladribine Natalizumab			
	Second-line [1]/ third-line therapy [2]	Alemtuzumab			
Active* form	First-line therapy	Natalizumab** Ocrelizumab Ofatumumab Ponesimod Rituximab***	Interferon-beta 1b Ocrelizumab Ofatumumab	Interferon-beta 1b**** Ocrelizumab Rituximab*** Siponimod	
Designation without specifying the activity	First-line therapy	Beta-interferon Dimethylfumarate Diroximelfumarate Fingolimod Glatirameracetate Ozanimod			Ocrelizumab

alphabetical order, according to the approval text [1, 2]
* There is no general definition of the terms "active" and "highly active", ** Only for JCPyV negative patients. *** Off label. **** Long-term data do not support the use of interferons in active SPMS; Table adapted from [3]; relevant monitoring strategies: aCD20 (ocrelizumab, rituximab, ofatumumab): IgG, lymphocytes, risk of infection; Alemtuzumab: sec. autoimmunity; cladribine: lymphocytes especially before re-exposure; dimethyl fumarate/diroximel fumarate: lymphopenia (sometimes long-lasting), dimethyl fumarate/ diroximel fumarate: lymphopenia (sometimes long-lasting); Glatiramer acetate: liver values; Interferons: liver values, WBC; Natalizumab: JCV; S1PRM (fingolimod, siponimod, ozanimod, ponesimod): VZV, lymphocytes, skin cancer. References: 1. Compendium: https://compendium.ch/; 2. Specialty List. Available online: www.spezialitaetenliste.ch; 3. Friedli et al. 2023 https://doi.org/10.3390/ctn7010002

Radiologically isolated syndrome (RIS)

Definition The term RIS describes MRI changes that meet the criteria of at least spatial and possibly also temporal dissemination in patients who do not have a clinical event that meets the criteria of a relapse event, or a course that indicates PPMS .

Diagnostic criteria

- With the very sensitive McDonald criteria 2017, there are many MRI findings that can be formally classified as RIS. The proposed classification by Okuda (Neurology 2009) is very useful in this context:
- Presence of incidental CNS white matter abnormalities with the following MRI criteria:
  - ◊ ovoid, well-circumscribed, homogeneous foci with or without involvement of the corpus callosum
  - ◊ T2-hyperintensities of at least 3 mm in diameter, which meet the Barkhof criteria (at least 3 out of 4) for spatial dissemination (Barkhof Brain 1997)
  - ◊ the MRI-abnormalities do not correspond to a vascular pattern
- no history of relapsing neurological events
- the MRI abnormalities do not explain any existing clinical impairment
- the MRI abnormalities cannot be attributed to exposure to substances (drug abuse, toxic exposure) or other medical conditions
- exclusion of MRI phenotypes suggestive of leukoaraiosis extensive white matter pathology not involving the corpus callosum
- MRI abnormalities are not better explained by another disease process

Therapy So far there is no evidence to treat patients with RIS.

Follow-up referral for a neuroimmunological consultation (time is determined by the triage of the consultation)

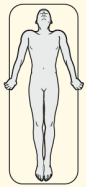
Coma

	Mesencephalic syndrome		Bulbar brain syndrome	
	Early	**Late**	**Early**	**Late**
Pupils	narrow sluggish	medium to wide, not very reactive	expanded, barely or not responsive	wide, rigid
Pain stimulus	flexion-extension syn.	stretch synergisms	Rest stretch synergism	not triggerable
VOR	+/–	weak/–	–	–
Tone	increased	greatly increased	limp	limp

Clinical examination

- **Vital signs** always first: respiration (pattern, saturation, ventilation), circulation, temperature (CAVEAT incorrectly low in case of hypothermia)
- **Inspection** Indications for trauma (indication for immobilization of the cervical spine?), poisoning, jaundice, foetor
- **Brainstem reflexes**
  - pupils: isocoria/anisocoria; narrow wide; light reaction direct/indirect
  - Corneal reflex: positive/negative side difference
  - Oculomotor: spontaneous turn of gaze
  - Vestibulo-ocular reflex: positive/negative
  - Gag reflex
- **Meningism** may be absent in coma/relaxation
- **Motor**
  - Spontaneous movements, side difference
  - Tone, stretch/flexion synergisms (assessment with retromastoidal pain stimulus)
  - Response to pain stimuli: targeted, non-targeted, lateral difference
  - Reflexes, Babinski

Decortication



Decerebration

Most common causes over time

Acute
- vascular – especially basilar artery thrombosis, ICH/SAB
- epileptic – first-time seizure possibly the result of other causes

(Sub)acute
- Meningitis/encephalitis
- Metabolic: Hyper/Hypoglycemia, electrolyte imbalance, endocrine (hypothyroidism, M. Addison, ...), uraemia, hepatic
- Intoxication

Slowly progressive
- Tumour, hydrocephalus

Diagnosis/therapy process

- **Initial examination in the emergency room with anaesthesia (181-8555) and TA/OA medicine (181-7520)**
- **ABCDE**, monitoring
- **If necessary, appropriate stabilization/decision on intubation (under anaesthesia)**
- **Laboratory** glucose, TSH, electrolyte, Ammonia, venous BGA, tox. screening
- **Intoxication? Antagonism?**
- **Temperature measurement – fever →** blood cultures; above all meningitis → empiric therapy (see chapter on meningitis)
- **Evidence of epileptic seizure/non-convulsive status?** If necessary, try Rivotril 1 mg i.v./levetiracetam 1–2 g i.v.
- **Review indication for thiamine dosing** (100–500 mg i.v.,) then consider glucose 40% 50 mL
- **Immediate cerebral imaging** (after stabilization by anesthesia): usually **CT with angio and perfusion** first, if it is still unclear, then, if possible, immediately after MRI
- **If no acute treatment after cerebral imaging** (thrombectomy/OP): admission to IB, organize bed early (181-7770)
- **Further diagnostics on ICU: EEG**, especially if there are indications of status epilepticus (clinically or in perfusion imaging), CSF diagnostics

Intracranial pressure

General symptoms
- Headache
- Nausea/vomiting
- Change of character (RASS)/drive disorder (especially chronic)
- Reduced vigilance (somnolence to coma)
- Cushing's triad: rise in blood pressure, bradycardia, respiratory depression
- Anisocoria

Symptoms of herniation
- VI paresis, papilloedema, divergent globe position
- Loss of light response
- Cheyne-Stokes breathing
- Flexion/extension synergisms

Contact neurosurgery, imaging (if the situation is unclear), eVD system

- **Upper body elevation**
  - 15–30° (caveat: CPP-conrol)

- **Intubation/ventilation/relaxation**
  - normoxaemia (paO2 60–80 mmHg)
  - normocapnia (paCO2 35–45 mmHg)
  - short-term moderate hyperventilation (paCO2 up to 30 mmHg as rescue therapy)
  - PEEP < 15 cmH_2O if possible

- **Sedation**
  - early start
  - deepen over time (including combination of different analgosedatives)
  - barbiturates: in ICP crises (e.g.: 200–400 mg test dose, then 500–2000 mg over 30 min, if necessary escalation to 3–5 mg/kg body weight/hour [EEG control])

- **Securing cerebral perfusion**
  - CPP > 70 mmHg: volume therapy and/or vasopressors (CPP=MAP-ICP)
  - careful lowering of massively hypertensive RR values (RR syst > 220 mmHg), e.g. with urapidil

- **Osmotherapy: mannitol**
  - e.g. 15–20%; 0.25–1 g/kg bw i.v. every 4–8 hours; caution: osmolar gap
  - hypertonic NaCl infusion (e.g. 100 ml 10%; sodium controls)

- **Temperature management**
  - Normothermia (< 36.5°C)
  - Possibly moderate hypothermia (up to 33°C)

Hypoxic ischaemic encephalopathy (HIE)

Requirements and notes

The assessment of the prognosis should not be based on one, but on multimodal (clinical and technical) findings.

- **72 hours after resuscitation at the earliest**
- **at the earliest 24 hours after the end of the therapeutic temperature treatment** (TTM, i.e. normo- or hypothermia)
- **without sedation or relaxation:** CAVEAT effects of benzodiazepines/propofol can last for many hours! CAVEAT in the first 30 hours or after sedation, a suppressed background or burst suppression is not always associated with a poor outcome → never perform an EEG based on questions about indications of a poor prognosis during sedation or TTM (in contrast to questions about a good outcome)

NOTES

- Evoked potentials: useful only when EEG is unreactive and not "highly malignant"
- Myoclonus: A cortical, subcortical and peripheral genesis cannot be sufficiently differentiated on the basis of clinical symptoms alone

Necessary investigations for making a prognosis

24–36 hours after reanimation	
Clinical examination	GCS Pupil reaction Corneal reflex Spontaneous breathing gag reflex CAVEAT Sedation must be stopped at least 1 hour beforehand
EEG	• Reduce/stop sedation if EEG is not continuous (unless EEG already shows epileptiform patterns) • Stimulation by examiner during EEG: 3× pain, 3× acoustic, each with at least 15 seconds interval • Indication for long-term EEG: electroencephalographic seizures, status epilepticus
36-72 hours after reanimation	
MRI	CT as an alternative only if MRI is absolutely contraindicated
EEG if indicated	Indication: detection of steeply configured periodic discharges (spiky or sharp periodic discharges) < 2.5Hz or rhythmic spike waves in the first EEG
NSE	After > 48 hours
> 72 hours after reanimation	
Clinical examination	GCS Pupil reaction Corneal reflex CAVEAT sedation must be stopped at least 3 hours beforehand
EEG	• Stop the sedation at least 1 hour before the EEG if no epileptiform discharges were detected in the pre-EEG • Stimulation by examiner during EEG: 3× pain, 3× acoustic, each with at least 15 seconds interval

Therapy regimen for epileptic activity

Spiky or sharp periodic discharges < 2.5Hz	→ Monotherapy levetiracetam i.v. (40–50 mg/kgKG, max. 4.5 g as bolus; then 2×1.5 g/day) → if the EEG persists: + 1 AED
Rhythmic spike waves	→ Bi-therapy levetiracetam i.v. (40–50 mg/kgKG, max. 4.5 g as a bolus; then 2×1.5 g/day) + lacosamide i.v. (5 mg/kg body weight as a bolus, then 200–400 mg/day p.o.; caveat contraindications: AV block) or topiramate p.o. (200–400 mg as a bolus; then 200–400 mg/day; beware of metabolic acidosis) or valproate i.v. (20 mg/kg body weight in max. 10 mg/kg/min) as a bolus, then 2×900 mg/day), then albumin-corrected level (see scheme p. 6), KI: severe hepatopathy and mitochondriopathy → if the EEG persists: + 1 AED
Elektroencephalographische Anfälle (wiederholte Entladungen > 2.5 Hz oder Entwicklung wie in den ACNS Kriterien definiert)	→ bolus benzodiazepine → + bi-therapy as above → if after 2 hours status/serial seizures not broken through, then therapeutic/drug burst suppression for 48 hours (i.e. up to 72 hours after reanimation)
Status epilepticus (wie ↑elektroencephalographische Anfälle, über > 5 Minuten)	

Barbella score (only for patients with epileptiform EEG within <72h)

Barbella et al. Neurology 2020

EEG 24–36 hours	No epileptiform discharges	1 point
	Continuous background ≥ 50%	1 point
	Reactivity	1 point
EEG 72 hours	Normal background amplitude	1 point
	Stimulus-induced rhythmic periodic or ictal discharges	1 point
	Reactivity	1 point
Evaluation: > 4 points are associated with a good prognosis		

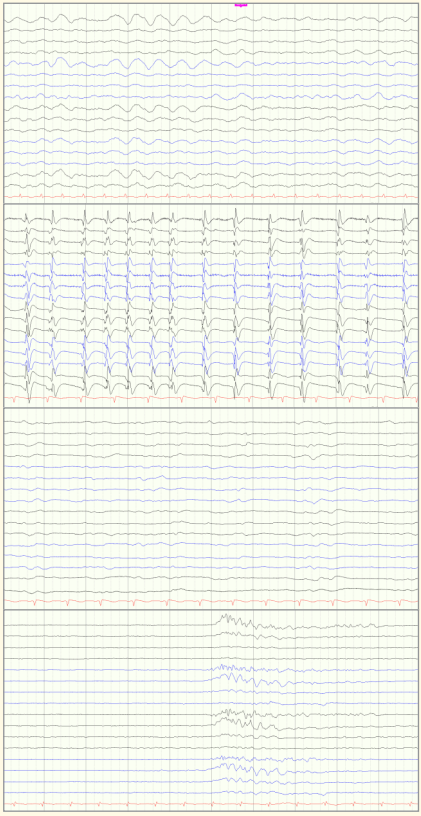
Hypoxic ischaemic encephalopathy (HIE)

Indicative of a good prognosis	Indicative of a poor prognosis
Course • clinical improvement in the last 24 hours	**Brainstem reflex** • absent bilateral pupillary reflexes after 72 hours, without sedation, have a high specificity and low sensitivity for a poor outcome (CAVEAT in the first hours the specificity is lower) • absent bilateral corneal reflexes are somewhat less specific
Pain stimulus • targeted reaction to pain stimulus (≥ M5 in the GCS)	**Pain stimulus** • absent reaction or extension response to pain stimulus (M1 or M2 in the GCS) sensitive but not specific (CAVEAT up to 20% false positives!)
EEG (high positive predictive value for a good outcome in the first 24 hours after resuscitation, but possibly no longer after >72 hours) • responsive and continuous (very specific but not sensitive to good outcome) • insb. with an anterior-posterior gradient • without periodic discharges • NREM II sleep elements	**EEG** • highly malignant pattern according to Westhall: very specific for poor outcome on the 3rd day ◊ suppressed background (<10uV) with or without periodic discharges ◊ Burst suppression (<10uV during >50% of the trace): very specific for poor outcome on day 3, especially with identical bursts • malignant pattern according to Westhall: high specificity for poor outcome if at least 2 items from two different categories ◊ lack of responsiveness ◊ malignant periodic or rhythmic patterns (periodic discharges, rhythmic polyspike-/spike-/sharp-and-wave, definite electroencephalographic seizure) ◊ malignant background activity (discontinuous, low-voltage, reversed anterior-posterior gradient; caution: according to Fenter et al. Resuscitation 2023, the absence of "malignant background activity" is not necessary for "benign EEG") CAVEAT Epileptiform activity is not always associated with poor prognosis (see Barbella Score)
Neuron-specific enolase (NSE) < 30 mcg/l after 48 hours CAVEAT not specific for neuronal loss (e.g. also increased with haemolysis), optimal time for measurement unclear, limit values disputed, not usable under ECMO (since increased by haemolysis)	**Neuron-specific enolase** (NSE) > 33 mcg/L according to older studies, probably not very specific > 66 mcg/L after 48 hours: probably more specific > 90 mcg/l : DGN guidelines
	MRI • pronounced DWI lesions, cortical in all lobes or in 3 lobes plus one subcortical structure (BG, hippocampus, thalamus, brainstem) CAVEAT no prospective study, specificity probably lower than with the EEG!
	SSEP • Absence of N20 after 72 hours specifically for poor outcome, assessment complicated by artefacts

Discontinuation of therapy for HIE

- **Prerequisites for discontinuation of HIE therapy**
  - ◊ **Presence of at least 2 features for bad prognosis**
  - ◊ **+ Lack of any evidence of good prognosis**
  - ◊ if these conditions are not met, the situation should be re-evaluated the following day
- Decision to discontinue therapy to be made individually and following assessment of the overall context; Discontinuation may be indicated for reasons other than encephalopathy, e.g. living will or comorbidity (heart failure, sepsis, etc.) – the decision rests with the treating intensive care physician

EEG example



A. Continuous background with rhythmic delta activity (G-RDA); responsiveness to pain stimuli ("benign" according to Westhall et al.)

B. Rhythmic spike waves, equivalent to an NCSE; the background cannot be assessed.

C. The same patient as in B. after administration of 0.5 mg Rivotril: regression of the epileptic activity and appearance of a discontinuous background (therefore formally "malignant" according to Westhall et al).

D. Burst suppression on day 3, without sedation, has a poor prognosis ("highly malignant" according to Westhall et al). CAVEAT can also be indicated by sedation or TTM

Toxic syndromes

Syndrome	Trigger	Vital signs	Pupils	Other symptoms	Treatment
Neuroleptic malignant syndrome (NMS)	Start/dose change of neuroleptics, MCP, lithium, carbamazepine, dehydration, condition after MNS, age etc.	Hyperthermia, tachypnoea, tachycardia, hypertension	Normal	Rigor, dystonia, hyporeflexia, disturbance of consciousness up to coma, mutism	STOP neuroleptics, volume administration, temperature management; if necessary try amantadine (200 mg/d), lorazepam or dantrolene (2.5 mg/kg i.v., then 7.5 mg/kg over 24 hours
Malignant hyperthermia (MH)	Complications of anaesthesia, predisposition: myopathies, trigger: succinylcholine, inhalation anaesthesia (including isoflurane, desflurane)	Up to 24 hours after anaesthesia: hyperthermia, tachycardia, hypotension, initially: increase in endexp. $paCO_2 > 45$ mmHg	Normal	Generalized increase in tone (despite relaxation)	Discontinue substance, dantrolene 2.5–10 mg/kg i.v. over 15 min, then 7.5–10 mg/kg over 24 h (at least 1 day), induced hyperventilation, therapeutic heparin; CI: verapamil, digitalis, alpha/beta mimetics
Serotonin syndrome	Serotonergic medication (combinations!), e.g. MAOI, SSRI, SNRI, triptans, tricyclics, tramadol, lithium, grapefruit juice, etc.	Hyperthermia, tachypnoea, tachycardia, hypertension	Mydriasis	Tremor, hyperreflexia, clonus/myoclonus, hallucinations, diarrhoea, sweating	Discontinuation of the triggering agent, volume administration, if necessary benzodiazepines Possible complications: DIC, ARDS, rhabdomyolysis (then CK increase)
Anticholinergic syndrome	Antihistamines, tricyclics, scopolamine, atropine	Hyperthermia, tachypnoea, tachycardia, hypertension	Mydriasis	Agitation, hypervigilance, possible coma, delirium, flushing, anhidrosis, urinary retention	Symptomatic, possibly physostigmine (if peripheral **and** central symptoms), benzodiazepines
Sympathomimetic toxidrome	Cocaine, amphetamines, pseudoephedrine, adrenaline, dobutamine, dopamine	Hyperthermia, tachypnoea, tachycardia, hypertension	Mydriasis	Agitation, psychosis, tremor, epileptic seizures, sweating	Symptomatic

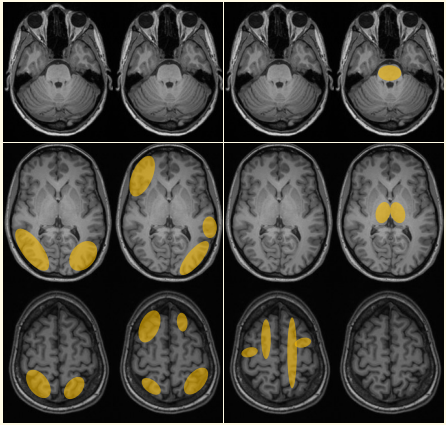
(Posterior) reversible encephalopathy syndrome (P)RES

Diagnostic criteria

1) Clinical, at least 1 of:
- Epileptic seizure, encephalopathy/confusion, headache, visual disturbances

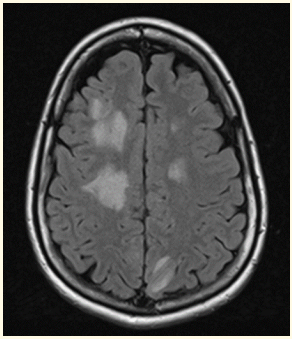
2) Risk factors, at least 1 of:
- marked hypertension or strong BP fluctuations, renal failure, immunosuppressive therapy, chemotherapy, eclampsia, autoimmune disease, administration of contrast media containing iodine

3) Radiological findings
- bilateral vasogenic oedema, cytotoxic oedema, normal



classical 20–55% | holohemispheric 15–25% | Sulcus front. sup. 15–25% | central 5–15%

Distribution pattern (adapted from Eberhardt Forsch NeurolPsych2018)



Typical FLAIR-hyperintensities

Therapy: treat/eliminate triggers; after that the outcome is usually good

Electrolyte disorders

Na^+ Hyponatraemia <135 mmol/l, clinically relevant mostly from <125–130 • Confusion, delirium to coma • Epileptic seizures, cerebral edema • Focal deficits incl. paresis • CAVEAT slow recovery due to the risk of central pontine myelinolysis	**Hypernatraemia** > 140mmol, symptoms mostly from >160 mmol/l • Altered mental status, delirium to coma • epileptic seizures • rigor, tremor, myoclonus, chorea, asterixis • CAVEAT slow compensation max. 0.5 mmol/l/h and 10–12 mmol/day due to the risk of cerebral oedema
K^+ hypocalaemia <3.4 mmol, life-threatening < 3.0 mmol/l • 3–3.5: mild muscle weakness, myalgia, fatigue • 2.5–3: marked muscle weakness (proximal emphasis), muscle spasms, confusion • 2–2.5: rhabdomyolysis, coma	**Hypercalaemia** >5.2 mmol/l, symptoms mostly from 6 mmol/l • usually ventricular fibrillation or asystole before the onset of neurological symptoms • at most slight muscle weakness, paraesthaesia, confusion, coma, hearing and taste disorders
Ca^{2+} hypocalcaemia < 2.2 mmol/l total, <1 mmol/l ionized • tetany, blepharospasm, photophobia	**Hypercalcaemia** > 2.7 mmol/l total • confusion, delirium to coma • proximal paresis

Hyponatraemia compensation max. 12 mmol/24 h

Hypovolaemia ?urine sodium	urine sodium: >20 mmol/l: renal Na loss, cerebral salt wasting syndrome <20 mmol/l: extrarenal Na loss	correction of volume deficiency 0.9% NaCl
normovolemia urinary osmolality?	urine osmolality: <100 mosm/kg: psychogenic polydipsia >100 mosm/kg: inadequate ADH effect	fluid retention < 1l/d
Hypervolaemia ?urine sodium	urine sodium : >20 mmol/l: chronic renal failure < 20 mmol/l: heart failure, hepatic failure, nephrotic syndrome	Treatment for underlying disease, fluid retention, diuretics
Clinical assessment of the volaemia is often difficult, if necessary, ultrasound of the inferior vena cava (<2cm hypovolaemia)		

Osmotic demyelination/central pontine myelinolysis

- Aetiology: too rapid correction of hyponatraemia (limit value: < 125 mmol/l; maximum correction: 10 mmol/l over 24 h)
- Symptoms: impaired consciousness (coma), tetraparasis, loss of brainstem function (oculomotor function, respiration, dysphagia, dysarthria, etc.) up to locked-in syndrome
- Typically onset is 2–6 days after correction of hyponatraemia
- Detection of the lesion in the MRI, sometimes only after up to 4 weeks
- DD basilar artery thrombosis, Wernicke encephalopathy, hyponatraemic encephalopathy

- Therapy: supportive, no specific therapy known

B1 deficiency – Wernicke encephalopathy

- Symptoms: encephalopathy with quantitative and qualitative impaired consciousness (up to coma), oculomotor disorders, (gait) ataxia
- DD: (brainstem) encephalitis, meningitis, Miller-Fisher syndrome, Bickerstaff encephalitis, osmotic demyelination
- Korsakoff syndrome: late sequelae of WE (85%, anterograde and retrograde amnesia, confabulations, mostly with gait disturbance and nystagmus)

Manifest Wernicke encephalopathy: Benerva i.v. 500 mg over 30 min 3×/d for 2 d, then 250 mg/d for 5 d other substitution 100 mg/d early (!) at the slightest suspicion

B12 deficiency

- Funicular myelosis (subacute PNP + spinal with surface + deep sensory disorder + spinal ataxia, paresis, missing or increased reflexes) even without hemat. changes possible; depression, irritability, insomnia, cognitive retardation, psychosis, macrocytic anaemia, glossitis, oral ulcers
- Laboratory: holo-TC (if > 25 pmol/l (also note methylmalonic acid and NI!), DD copper deficiency/zinc overdose), hyperhomocysteinaemia

Substitution initial parenteral 1000 µg/d i.v. several times/week, after the 10th dose 1×/week

Thyroid dysfunction and steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT)

Hypothyroidism

- Cognitive impairments: slowing down, difficulty concentrating and short-term memory impairment
- CTS (carpal tunnel syndrome) (25–30%!); PNP: especially sensitive and painful (often in the course)
- Myopathy (common): asymptomatic CK elevation to myalgia/spasms with proximal muscle weakness
- Myxoedema coma: rare! Bradycardia, hypothermia, hypotension, hyponatraemia, hypoglycaemia plus altered mental status (confusion, lethargy, coma)

Hyperthyroidism

- Encephalopathy (subacute behavioural problems/personality disorder, psychosis, agitation, depression) insomnia, cognitive impairments (mild to agitation/delirium, rarely coma)
- Generalized tonic-clonic seizures (in thyrotoxic crisis encephalopathy)
- Tremor (high frequency, small amplitude, action tremor)
- Stroke (usually cardioembolic in thyrotoxic-induced aFib)
- Myopathy (normal CK, proximal paresis, acute or chronic for weeks)
- PNP (axonal sensitive, rarely demyelinating), CTS
- Rarely myasthaenia gravis, periodic paralysis, chorea (also acute unilateral), headache
- Graves disease: proptosis, restricted globe motility, GBS

SREAT: (Hashimoto encephalopathy)

Diagnostic criteria (certain if all 6 criteria are met)

1) Encephalopathy with epileptic seizures, myoclonus, hallucinations, stroke-like episodes
2) Subclinical or mild symptomatic thyroid disease (usually hypothyroidism)
3) MRI brain normal or non-specific findings
4) Detection of thyroid peroxidase or thyroglobulin Ab (Caveat! positive in up to 20% normal population!)
5) Lack of evidence of other known neuronal Ab in serum and CSF
6) Exclusion of DD (important: LP: lymphocytic pleocytosis (up to cell count 170) in 25%)

Functional neurological disorders (FNS)

General

- **FNS is not a diagnosis of exclusion, but a diagnosis based on positive signs!**
- Psychological factors/exertion/stress are often present but are NOT a diagnostic criterion!

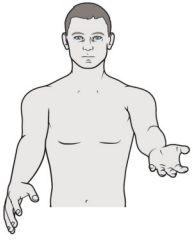
Diagnosis

- **History** often acute onset of symptoms (optional in connection with trauma, medical intervention, drug-related adverse events, etc.), fluctuating course (with alternation between symptomatic and symptom-free intervals, possibly patient had similar symptoms in the past already with spontaneous resolution), rarely progressive symptoms
- **Clinical examination** specifically for positive signs (see below); video recordings may be helpful (especially for paroxysmal or fluctuating symptoms)
- Search specifically for positive characters (see below); video recordings may be helpful (especially for paroxysmal or fluctuating symptoms)
- Referral to psychiatry/psychiatric consultation only if additional psychiatric symptoms exist/are in the foreground (anxiety, depression, PTSD, psychotic symptoms, etc.)

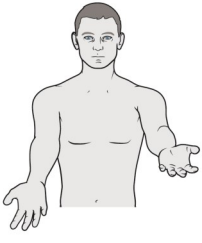
A. One or more symptoms of altered voluntary motor or sensory function
B. **Positive signs** (see below) in the clinical examination
C. The symptom or deficit is not better explained by another physical or mental disorder, or even if another neurological disorder is present, it does not explain the symptoms (e.g., coexistence of epileptic and non-epileptic seizures)
D. The symptom or deficit causes clinically significant distress or impairment in social, occupational, or other important areas of functioning, or requires medical evaluation

Procedure

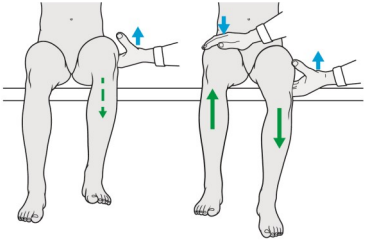
- **Explain suspected diagnosis or diagnosis, using the term "functional" (not "psychogenic" or "conversion"): "**A functional neurological disorder is suspected but needs further observation/testing/etc." / "You have an FNS"
- If necessary, submit a protocol (deposited in ED) so that the patient can describe the symptoms precisely
- Ask patients/relatives to make a video of the symptoms
- **Register for a follow-up check with a consultant for functional neurological disorders (neuropsychosomatik@insel.ch) or with the neurologist who has been treating the patient so far**



Organic paresis with pronation



Functional paresis without pronation



Hoover sign

Positive signs

adjusted according to Espay JAMA Neurol 2019 www.neurosymptoms.org

Functional over movements

Tremor

- Variable frequency
- stops with contralateral movements (e.g. finger-nose test) or divided attention (e.g. arithmetic)
- *Entrainment* (taking of an externally specified frequency, e.g. by clapping)) or total cessation

Myoclonus

- Variability of duration/distribution/latency in stimulus sensitivity
- Mainly axial or facial jerks

Dystonia

- Fixed dystonia from onset (see figure)
- Variable resistance to passive flexion
- Lack of sensoric trick/no "geste antagoniste"
- Face: tonic distortion of the lip or jaw to one side (see fig.); squinting at passive opening

Tics

- Not quite stereotypical
- Interference with speech or voluntary movements
- Lack of urge to move
- Not voluntarily suppressible

Functional sensory disorders

- Sharp midline delimitation face/trunk/back or also circular on the extremities
- *Tuning fork sign* (asymmetrically perceived vibration of the tuning fork on the right and left half of the forehead)
- Non-anatomical boundaries (pattern of sensory disturbance does not correspond to a dermatome and/or area served by a peripheral nerve)

Functional (non-epileptic) seizures

Ictal

- Closed eyes
- Squinting at passive opening
- Duration > 2min
- Waxing and waning (increase and decrease in movements with pauses)
- Opisthotonus
- Asynchronous limb movements
- Side-to-side head shaking ("no" motion)/pelvic movements
- Crying/moaning

Postictal

- Rapid reorientation (CAVEAT also in frontal lobe epilepsy)

Functional movement restrictions

General signs

- Extreme slowing down and tiredness
- *"Give-way weakness"* ("loss" of strength during examination)
- Inconsistency between automatic movements and movements during explicit examination

Leg symptoms

- Hoover sign (see illustration)
- Hip abductors sign (abduction weakness that disappears with contralateral abduction)
- Tiptoe/heel stand possible despite weakness during examination while lying/sitting (motor inconsistency)

Arm symptoms

- Falling without pronation (see figure)
- Functional use in spontaneous movements discrepant with individual strength test (motor inconsistency)

Face

Lip pulling sign (tonic downward tucking of the lip spontaneously and/or when prompted to smile, see figure). *Sternocleidomastoid sign* (weakness when turning the head to the side of the functional motor hemi-syndrome instead of to the anatomically explainable contralateral side)

Parkinson symptoms

- Lack of frequency/amplitude decrease in repetitive finger and hand movements
- Variable counterhold during passive movement

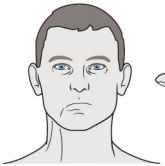
Functional axial manifestation

Gait

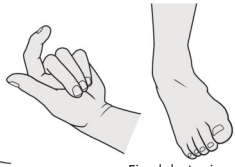
- Buckling in the knees
- Delayed gait with forefoot dragging on the ground
- Unergonomic gait pattern
- Excessive slowing down or "walking like ice"
- *"Huffing and puffing sign"* (Grimacing/moaning while walking)
- No or controlled falls despite excessive gait instability
- Reduction of swaying/unsteady gait with divided attention (e.g. arithmetic), walking backwards or sideways, running

Speech

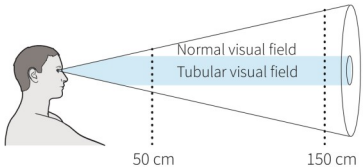
- Variability over longer periods of observation/ conversation
- Extreme slowness and effort when speaking



Lip pulling sign

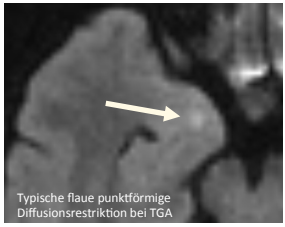


Fixed dystonia



Amnesia DD

- transient global amnesia
- encephalitis
- transient epileptic amnesia
- Ischemia/haemorrhage/inflammation thalamic/hippocampal
- Wernicke encephalopathy
- venous thrombosis
- post traumatic
- functional



Typische flaue punktförmige Diffusionsrestriktion bei TGA

Transient global amnesia (TGA)

- Acute onset of anterograde amnesia, usually retrograde amnesia occurs gradually over time
- Attention and orientation to the person maintained
- Resolution within 24 h (at least of the major deficits >7d detectable in detailed neuropsychological testing)
- Aetiology unclear, DD ischaemic, epileptic (consider especially in case of recurrence), venous congestion
- CAVEAT Identical clinical symptoms also possible with thalamic and temporal lobe infarction and encephalitis (then usually slower/no regression) → discharge only when regression is clear
- CAVEAT Do not miss the onset of encephalitis

Clarifications

- 8-or 10-word learning list **and follow-up examination after hours, discharge only after clear regression, otherwise consider inpatient admission and LP**
- **MRI to rule out DD** (circumscribed weak diffusion disorders hippocampal* are possible; 35% after 0–6h, 60% 6–12 h)
- EEG in case of recurrence

* Stroke risk in typical TGA patients with typical weak diffusion disorders hippocampal appears not to be increased, but the studies are not yet conclusive with regard to safety → if several risk factors are present, consider outpatient standard stroke clarifications

Testing

Normal neurostatus +
- orientation
- digit span
- backward spelling

- Calculation incl. Serial 7
- visuospatial testing
- language testing

8 word list

	Pass 1	Pass 2	Pass 3	Recall after 10 min	Cue	Recognition
Carnation					Flower	Carnation, tulip, rose
17					Number	13, 17, 19
Belt					Garment	Trousers, belt, shoe
Toyota					Car make	Mercedes, Honda, Toyota
Hail					Weather	Lightning, hail, cloud
Back					Body part	Back, neck, nose
Pigeon					Bird species	Duck, tit, pigeon
Spruce					Tree species	Spruce, maple, fir

Delirium

General

- Screening: CAM (Confusion Assessment Method)
- Assessement during course: **RASS** (Richmond Agitation Sedation Scale):

+4 combative	+3 very agitated	+2 agitated	+1 restless	0 alert and calm
−5 unarousable	−4 deep sedation	−3 moderate sedation	−2 light sedation	−1 drowsy

Diagnostic criteria ICD-10

1. **Impaired attention** → reduced awareness of the environment
2. **Thought disorder**, manifest as
   - impaired short-term memory
   - disorientation (place, time, person)
3. **Psychomotor abnormalities**, at least 1 out of
   - rapid, unpredictable shifts from hypo- to hyperactivity
   - prolonged reaction time
   - changed speaking speed
   - startle reaction
4. **Sleep disorder**, at least 1 of
   - insomnia with and without daytime sleepiness
   - nocturnal worsening of symptoms
   - nightmares (can sometimes continue as hallucinations/illusionary misjudgment)
5. **Acute onset** and **fluctuating** during the day
6. Evidence of an organic or systemic brain disease (jointly) responsible

Therapy

1. **Eliminate/treat cause**
2. **Non-drug therapy measures**
   - Circadian rhythmization (window seat, clock, minimize night-time checks)
   - Stimulus reduction (earplugs, reduce irritating non-perception or false perception of the environment)

Symptomatic treatment

Alcohol withdrawal delirium
primarily benzodiazepines! + thiamine substitution

Delirium associated with stroke (see also stroke guidelines Bern)
Step 1: Pipamperon (Dipiperon®) 20 mg stepwise(maximum dose 360 mg/d) p.o.
or **Quetiapin** (**Seroquel®**) 12.5 mg weise (maximum dose 800 mg/d) p.o.
or Risperidon (Risperdal®) 2×0.5 mg/d (maximum dose 16 mg/d) p.o.
or Haloperidol (Haldol®) 0.5–1 mg weise (maximum dose 60 mg/d) p.o. oder i.v. oder 5 mg i.m.
CAVEAT: Arrhythmias → i.v. only administer in exceptional cases and under monitoring
Step 2: **Diazepam** (**Valium®**) 5 mg weise i.v. (increase possible up to 10mg weise) i.v.
or **Midazolam (Dormicum®)**: 2.5–5 mg stepwise as a bolus (maximum dose 10 mg) i.v., then if necessary 2–5 mg/h via Perfusor (maximum dose 10 mg/h); antidote: Flumazenil (Anexate®)
Step 3: Clonidin (Catapresan®): 25–50 µg bolus, then 25–150 µg/h via Perfusor (maximum dose 150 µg/h)
Step 4: **Dexmedetomid (Dexdor®)** or **Propofol** (administration only on ICU/IMC)

Delirium associated with Parkinson
Quetiapin (Seroquel®) 25–100 mg p.o., max. 300 mg/d
Clozapin (Leponex®) 6.25–12.5 mg, max. 100 mg/d; 2/3 of the dose at night, 1/3 spread over the day

History

See headache questionnaire for details

Type	How many headache types are there? (differentiated medical history for each)	**Accompanying symptoms**	Accompanying symptoms ? Cranial autonomic symptoms? Aura symptoms?
Timeline	When did it start? How quickly did it start? How often does it occur? How long does it last?	**Causes/trigger**	Trigger factors? Comorbidities? Family history?
Localization	Where? Spread?	**Behaviour**	What makes it worse? (cough, position, ...) What relieves it? (location, rest, ...) What does the patient do during attack?
Character	Pain characteristics? Pain severity (NRS)?	**Medication**	What type? How often? Dose? Use?

Red flags for secondary headache

History of headaches

- thunderclap headache
- first headache
- changes of known headache
- positional headache
- aggravated by sneezing, coughing, exertion
- first-time or altered aura Increasing headache
- nw permanent headache
- severe unilateral headache
- strictly circumscribed headache

General medical history

- neurological deficits
- Cranial autonomic symptoms
- vomiting on an empty stomach
- epileptic seizures

History systemic

- age >50
- oncological history
- immunosuppression
- pregnancy
- new drugs
- **tumor symptoms**

Clinical findings

- Systemic signs including fever
- vigilance disorder
- confusion
- meningism
- neurological deficit
- papilloedema
- unilateral eye redness
- blisters on the face
- Horner syndrome

Diagnosis

- **Acute imaging if a potentially acute dangerous cause (see Red flags)**
- **Thunderclap headache: CT within 6 hours (**sensitivity decreases after that; CAVEAT false negative results associated with reduced haematocrit) or **MRI; if imaging is negative** (false negative in 2–5%!): **lumbar puncture**
- **Lumbar puncture** to rule out inflammatory cause + to rule out increased CSF pressure after normal imaging 12 hours after headache started with cyto (erythrophages?) and ferritin
- Repeat imaging for known headaches and appearance of new red flags

Follow-up checks

- Always give a headache calendar
- Follow-up checks:
  - ◊ first time, benign: general practitioner
  - ◊ repeated headache < 4 months: neurologist
  - ◊ repeated headache > 4 months: headache consultant
  - ◊ unclear diagnosis, complex picture: follow-up after 2 weeks (headache consultant or emergency fellow and supervision by headache consultant)

Migraine

Diagnostic criteria

Migraine without aura

- At least 5 headache attacks with:
  - ◊ duration 4–72 h
  - ◊ 2 of: unilateral, pulsating, moderate to very severe (VAS 4–10), aggravated by physical activity
  - ◊ 1 of: nausea/vomiting, photophobia/phonophobia

Migraine with aura

- At least two attacks with:
  - ◊ at least 1 reversible aura symptom from: visual, sensory, language/speech, motor, brainstem, retinal
  - ◊ at least 3 of: spread of aura symptoms over ≥5min, two or more aura symptoms occur one after the other, duration of the aura 5–60min, at least one aura symptom is unilateral, at least one aura symptom is positive, aura is accompanied or followed by headache within 60 min

Acute therapy in emergencies

- Acetyl salicylate 1000 mg i.v. or metamizol (Novalgin®) 1000 mg i.v.
- Sumatriptan (Imigran®) 6 mg s.c. or 10–20mg nasal or Zolmitriptan (Zomig®) 5 mg nasal
- Status migrainosus: prednisolone (Spiricort®) 100 mg 1-0-0 p.o. for 3 days

Prophylaxis + treatment for attacks at home

Acute treatment

Acetylsalicylate 1000 mg or ibuprofen 400–800 mg + domperidone (Motilium®) 10 mg

Triptan: e.g. sumatriptan 50 mg p.o., zolmitriptan (Zolmitriptan®, Zomig®) 2.5 mg p.o., almotriptan (Almogran®) 12.5 mg p.o.

Prophylaxis (if more than 3 attacks or 5 days/month, severe or prolonged attacks)

- Aerobic endurance training at least 3 times a week for 45 minutes, relaxation exercises
- 1st-line medication: beta blockers (e.g. propranolol 40–240mg/d), topiramate 2×50mg/d, flunarizine 5–10mg/d

Tension headache

Diagnostic criteria

Episodic tension headache

- A minimum of 10 headache attacks with:
  - ◊ duration 30 min. to 7 days
  - ◊ 1 of: bilateral, pressing or pulling quality, mild to moderate, not aggravated by routine physical activity
  - ◊ no nausea or vomiting
  - ◊ max. 1 from: photophobia, phonophobia

Acute treatment in emergencies

- Acetylsalicylate 1000 mg i.v. or metamizol (Novalgin®) 1000 mg i.v.

Prophylaxis + treatment for attacks at home

Acute treatment: acetylsalicylate 1000 mg, ibuprofen 400–800 mg

Prophylaxis: endurance sports, biofeedback, relaxation exercises; amitriptyline 25–150 mg/d, venlafaxine 75–150 mg/d

Cluster headache

Diagnostic criteria

- A minimum of 5 headache attacks with:
  - ◊ severe or very severe pain, unilateral orbital, supraorbital or temporal, duration 15–180 min
  - ◊ ipsilateral to headache 1 of: conjunctival injection, nasal congestion/rhinorrhea, lid oedema, sweating, miosis/ptosis
  - ◊ feeling restless or agitated
  - ◊ occurs daily up to 8 times/day

Acute therapy in emergencies

- Inhalation 100% O_2 via mask 10–12l /min, for 10–15 min
- Sumatriptan (Imigran®) 6 mg s.c., zolmitriptan (Zomig®) 5 mg nasal
- Shortening of episodes: prednisolone (Spiricort®) 100/75/50/25 mg p.o. per day for 5 days

Prophylaxis + treatment for attacks at home

Acute treatment
- sumatriptan (Imigran®) 20 mg nasal, zolmitriptan (Zomig®) 5 mg nasal
- home oxygen

Prophylaxis
- verapamil 240–720 mg/d (ECG control)
- topiramate 100–200 mg/d

Trigeminal neuralgia

Diagnostic criteria

Classic trigeminal neuralgia
- Paroxysmal pain attacks involving one or more branches of the trigeminal nerve with:
  - A. duration fractions of a second up to 2 minutes
  - B. strong Intensity
  - C. like an electric shock, shooting, stabbing, or sharp
  - D. triggerable by harmless stimuli in the trigeminal area

Symptomatic trigeminal neuralgia
- As above, additionally: with or without constant pain between paroxysms
- evidence of causative lesion other than vascular compression

Acute therapy in emergencies

- Fosphenytoin loading i.v., followed by phenytoin p.o. 100–300 mg/d
- in individual cases, if necessary, steroid high dose or Rivotril using a perfusor pump under inpatient conditions, fosphenytoin saturation i.v., then phenytoin p.o. 100–300mg/d

Prophylaxis + treatment for attacks at home

- Carbamazepine (after HLA testing): 200–400 mg (elderly patients: 100–200 mg) delayed (Tegretol CR®, Timonil ret®), increase by 100–200 mg every 5 days or 50 mg daily (compliance!) up to 800 mg, if necessary up to 1600 mg or tolerance limit (serum level monitoring)
- Oxcarbazepine (Apydan extent®, Trileptal®): increase dosage as for carbamazepine; target dose 900–1800 mg/d, CAVEAT hyponatraemia (monitoring necessary, mainly in the first 3 months)

Idiopathic intracranial hypertension

Diagnostic criteria

A. symptoms of increased CSF pressure, usually with papilloedema
B. elevated CSF pressure in lateral position with legs not fully flexed > 25 cmH_2O
C. normal CSF biochemistry and cellular findings
D. exclusion of structural or vascular lesions on MRI
E. no relevant medication or any other identifiable cause

Investigations

- Medication history, particularly tetracyclines, nitrofurantoin, nalidixic acid, retinoids (vitamin A deficiency and overdose), danazol, lithium, tamoxifen, indomethacin, growth hormone, alpha-interferon, cyclosporine, cimetidine and amiodarone
- Weight gain? endocrine disorder? sleep apnoea?
- MRI: drainage disorder? fistula?
- Optical coherence tomography if possible before LP, if necessary optic nerve sheath sonography

Treatment options

Step 1: weight reduction + acetazolamide (2×500 mg/d, max. 2000 mg/d, if necessary + furosemide 30–80mg/d); alternatively topiramate (25–100 mg/d)
Step 2: repeated LP until CSF pressure <20 cm H_2O
Step 3: consider: stenting venous stenosis, optic nerve sheath fenestration, VP shunt

CSF hypotension syndrome

Diagnostic criteria

A) 1 of: decreased CSF pressure (<6 cm H_2O), imaging evidence of CSF leak
B) development of headache associated with time or leading to evidence of low CSF pressure or CSF leak
C) no other explanation

Score MRI *Dobrocky JAMA Neurol 2019*

Findings	Probability of CSF leak detection
• Vein-like enlargement of the superior sagittal sinus, 2 pts • Pachymeningeal enhancement 2 pts • Subdural fluid accumulation FLAIR 1 pt • Suprasellar cysts ≤ 4 mm 2 pts • Prepontine cysts ≤ 5 mm 1 pt • Mamillopontine distance ≤ 6.5 mm	3–4 points: intermediate probability ≥ 5 points: high probability

Treatment options

1. Conservative: Strict! Bedrest at least 24 hours, caffeine N 200 mg 3 times/day p.o.
2. Epidural blood patch by NRAD
3. Possible surgical closure if a leak is detected

Movement Disorders and DBS

General

CAVEAT Medication to be avoided in Parkinson's disease: metoclopramide and haloperidol (dopamine receptor antagonist → increase in extrapyramidal symptoms);
Alternatives: domperidone, clozapine

Stimulators and pumps

Neurostimulators for queries see instructions at **thalamus.insel.ch**, manufacturer Medtronic, 24 h emergency call 0800 633 333. Operations on patients with neurostimulators: diathermy is strictly forbidden! Cauterization only bipolar between two cautery tips; Grounding between the site of cauterization and the implanted material as far as possible from the implant; only minimal energy required; neurostimulator should be turned off shortly before surgery for safety reasons and turned on again in the exit
Duodopa-Pump manufacturer Abbvie +41 399 15 00, 24 h emergency 0800 20 40 88
Apomorphin-Pump manufacturer Licher MT +49 5130 5833 100, 24 h emergency +49 172 670 02 72

Acute hyperkinesia

Dyskinesia with Parkinson's
→ Fractionation of L-DOPA: Reduction of the single dose to the minimum effective dose, shorten the administration interval to 2 hours (lack of dopamine stores with increase in disease → serum level of L-DOPA correlates with dopamine concentration in the synapse), MAO-B inhibitors and COMT inhibitors, stop L -DOPA slow-release preparations (since resorption unreliable), amantadine (antidyskinetic effect), if necessary apomorphine pump (with involvement of the ZfB team)

Status dystonicus possible triggers: infection, changes in medication, defect in the neurostimulator
→ Eliminate possible secondary causes, check neurostimulator
→ Anticholinergics, BZD, baclofen, CBZ, if there is insufficient improvement, consider intrathecal baclofen/sedation

Acute dystonia → biperiden (Akineton®) 5 mg i.v., then p.o. for 3–7 days

Myoclonus → clonazepam (Rivotril®) i.v., valproate (Orifil®) i.v., levetiracetam (Levetiracetam®) i.v.

Chorea/ballismus
Exclusion of secondary causes, especially in hemichorea (hypoglycaemia or hyperglycaemia, lupus erythematosus, antiphospholipid syndrome, Sydenham's chorea, HIV, focal basal ganglia lesion due to stroke)
→ short-term haloperidol if there is a risk of falling (ballismus usually time-limited), long-term tetrabenazine (CAVEAT may induce depression)

Akinetic crisis

WARNING Life-threatening condition (CK increase in patients with renal insufficiency, thrombophlebitis, pulmonary embolism, pneumonia, urinary tract infection, sepsis) → treatment under intensive care conditions

Triggers dehydration, infection, ingestion error, administration of neuroleptics (except clozapine), absorption disorders

Treatment

General

- thrombosis prophylaxis
- hydrogenation
- treatment of hyperthermia
- stool regulation
- arrhythmic day/night cycle treated with clozapine (Leponex®) start 12.5 mg

Specific

In the case of elective surgery, swallowing disorders, etc.: valculate the L-DOPA equivalent dose according to the scheme at thalamus.insel.ch

Madopar LIQ via nasal or gastric tube every 2 hours, dosage 150% of the calculated L-dopaequivalent dose.

Alternatively/if there are obstacles to gastrointestinal absorption: parenteral drug administration R

⇒Rotigotine (Neupro®) transdermal + Domperidon 3×20 mg bis 3x30 mg (CAVEAT QT-time↑, Torsade de pointes)

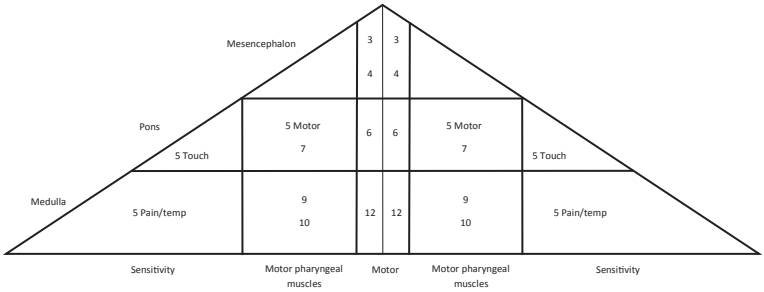
⇒ Amantadin (PK-Merz®) 1×500 ml i.v. over 3 h (max. 55 drops/min) CAVEAT delirium risk QT-Zeit↑

L-Dopa equivalent doses

		Einzeldosen (mg/100 mg L-Dopa)
L-dopa	L-dopa	100
	retarded L-dopa	133
	Duodopa	90
COMT-inhibitors*	Entacapone	LD x 0.33
	Tolcapone	LD x 0.5
Dopamine agonists (non-ergot)	Pramipexole	1 mg Salz
	Ropinirole	5
	Rotigotine	3,3
	Piribedil	100
Dopamine agonists (ergot)	Lisuride	1
	Bromocriptine	10
	Pergolide	1
	Cabergoline	1.5
	DHEC	20
MAO-B inhibitors	Selegiline 10 mg (oral)	10
	Selegiline 1.25 mg (sublingual)	1.25
	Rasagline	1
Others	Amantadine	100
	Apomorphine (Infusion or injection)	10

*To calculate the equivalent dose of COMT inhibitors, the total L-dopa dose (including sustained-release L-dopa) is multiplied by the corresponding value. For Stalevo, the dose is calculated separately for L-dopa and the COMT inhibitor. In the British National Formulary, selegiline 10 mg orally is given as equivalent to 1.25 mg sublingually. From the DGN S3 guideline "Idiopathic Parkinson's Syndrome".

Cranial nerves



CN I hyp-/anosmia, parosmia, cacosmia

- Hyp-/anosmia, parosmia, cacosmia
- Examination with forced multiple choice e.g. using Sniffin' Sticks/trigeminal irritant ammonia

CN II anisocoria

- Anisocoria in the light more clearly than in the dark (constriction deficit) → oculomotor nerve paresis, mydriasis of local causes or pupillotonia
- Anisocoria more obvious in dark than in light (dilatation deficit) → Horner syndrome or physiological anisocoria

- pre-existing/new?
- trauma?
- intracranial pressure?
- oculomotor disorders, cranial nerve failures?
- toxins or drugs in the eye/systemic?
- disease of the iris?

Anisocoria more evident in the dark (narrower pupil is abnormal)

Horner syndrome

Hypohidrosis ipsilateral redness only half of the face, ipsilat. conjunctiva

ja / nein

preganglionic
1.Neuron: hypothalamus/ brainstem/cervical cord: CVI, trauma, tumour, demyelination
2.Neuron: apical pulmonary lesion, SD malignancy

Anisocoria the same in the light and the dark

Sudden LR <1mm

Physiological

Ganglionic/post-ganglionic 3. Neuron: dissection, trauma, aneurysm (ICA), cavernous sinus (thrombosis, tumour aneurysm)

Anisocoria more evident in the light (dilated pupil is abnormal)

- Consensual LR reduced
- Convergence miosis preserved

- Pupillotonia (Adie)
- Argyll-Robertson
- Parinaud
- Pharmacological – Differentiation is only possible pharmacologically

- Consensual LR reduced
- Convergence miosis absent

Internal oculomotor paresis
DD Ciliary ganglionitis?

Causes of acute (transient) visual disturbances

Monocular

- Retinal stroke (e.g. occlusion of the ophthalmic artery)
- Retinal TIA*
- Ischemic optic neuropathy
- Vitreous haemorrhage
- Symptomatic posterior vitreous detachment (flashes, soot rain)
- Refractive disorder (e.g. dry eye, slipped lens, keratoconus)
- Glaucoma attack
- Retinal detachment
- Obscurations (blackouts lasting only seconds and greyout with papilloedema)

Binocular

- Retrochiasmal lesions
- Lesions of the chiasma
- Intracranial pressure with congestion papillae and the associated impairment of vision and field of vision
- Epileptic hypoglycaemia
- PRES CO intoxication
- Stroke, SAB, reversible cerebral vasoconstriction syndrome (RCVS) migraine

*2 forms:
1. amaurosis fugax: sudden onset uninfluenced by external factors
2. retinal insufficiency (e.g. in haemodynamically caused ischaemia with e.g. high-grade ICA stenosis/ICA occlusion): usually recurrent and only transient dark vision/blindness when looking at bright light, recovery in dark surroundings

Diplopia

- with slight squint deviation only blurred vision (often with decompensated exophoria)
- monocular double vision: usually ophthalmological cause, but also possible with occipital lesions

Hallucinations of neurological origin

Charles Bonnet syndrome
- Disinhibition phenomenon with severe visual impairment

Peduncular hallucinosis
- Pseudohallucinations, optical misinterpretations and complex optical phenomena (e.g. metamorphopsia, 180° spatial tilt)
- Cause: lesions in the ascending reticular activating system (ARAS) (mainly brainstem, thalamus)
- Therapy: usually rapidly regresses spontaneously, symptomatically with neuroleptics

Epileptic

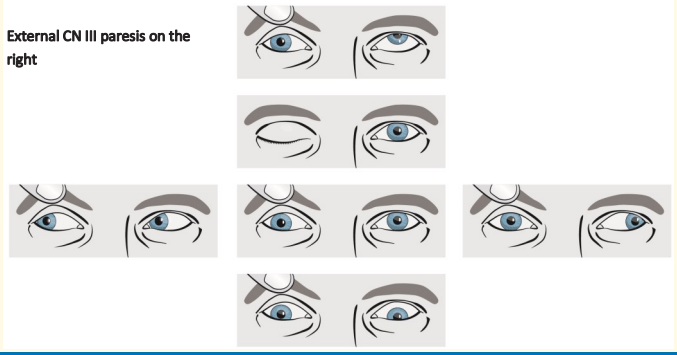
Sleep-associated
- hypnagogic/hypnopompic hallucinations, e.g. also in narcolepsy

Medicament-related
- especially dopaminergic therapy

Encephalitis/encephalopathy etc.

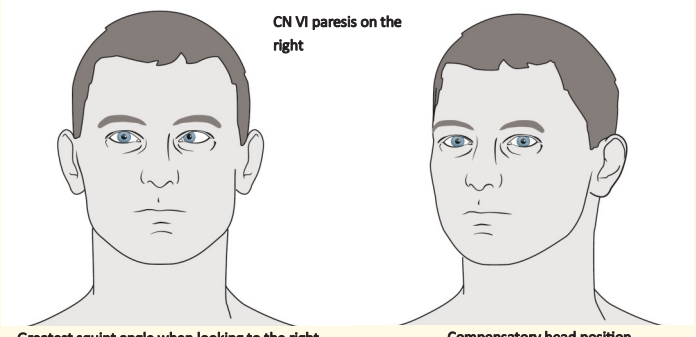
CN III oculomotor nerve palsy

- **Causes** with internal ophthalmoplegia**:** often compression aneurysm of the posterior communicating artery (PCOM), basilar artery, PCA or ICA; without internal ophthalmoplegia: often painful and microvascular (ipsilesional)
- **Lesion nuclear** ipsilesional III paresis, contralesional eye gaze paresis + ptosis
- **Lesion of intramesencephalic nerve segment** possibly +contra-lesional paresis/ataxia/tremor/rigor
- Incomplete: affects mesencephalon rather than nerve
- LP of suspected infectious origin or B symptoms (malignant cells)
- If ischemic origin is most likely: aspirin 100 mg long-term therapy



CN VI abducens nerve palsy

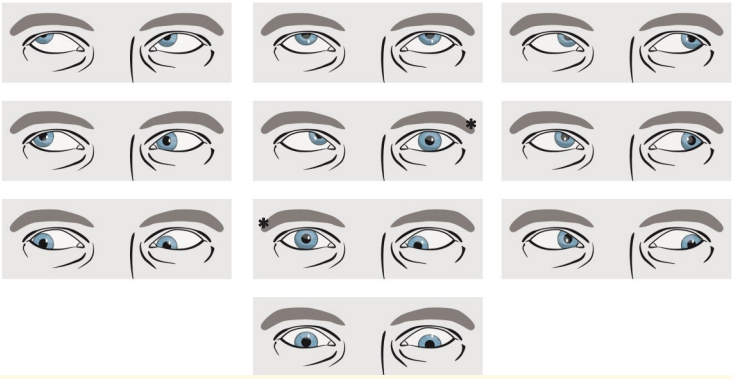
- **Causes** tumour > microvascular (ipsilesional) > trauma > intracranial pressure
- **Nuclear lesion** not abduction paresis but ipsiversive horizontal gaze paresis, possibly + ipsilesional CN V, VII, contralesional paresis, hypaesthesia
- **Lesion of intrapontine nerve segment** possibly contra-lesional paresis, hypaesthesia, ipsilesional CN VII, Horner
- lumbar puncture if suspected infectious origin or B symptoms (malignant cells)
- If ischemic origin most likely: aspirin 100 mg long-term therapy

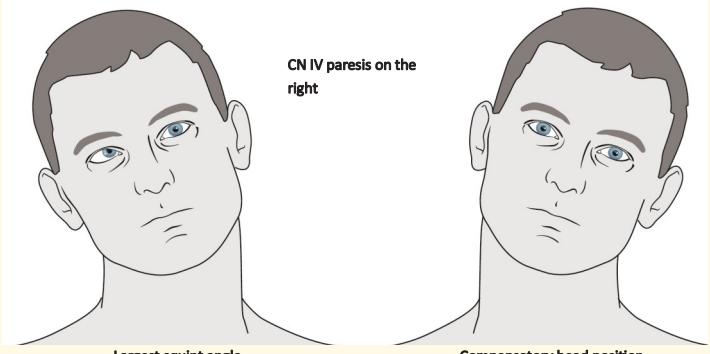


CN IV trochlear palsy

- **Causes** trauma > microvascular contralesional > tumour
- **Function** internal rotation of the eye (deficit max. in abduction; diplopia oblique with rod held horizontally) > prolapse (deficit max. in adduction; diplopia parallel with rod held horizontally)
- **Mesencephalic lesion**, possibly ipsilesional IV paresis, Horner, ataxia, INO, contra-lesional pain/temp
- Partial paresis: descending deficit may be absent
- LP if suspected infectious origin or B symptoms (malignant cells)
- If ischemic origin most likely: aspirin 100 mg long-term therapy

CN IV Paresis on the right *fixed eye when looking straight ahead





Largest squint angle

Bielschowsky Phenomenon +

Compensatory head position

CN VII facial paralysis

Diagnosis

- Even in the case of idiopathic paresis, there is at most a slight sensory disturbance on the face and slight pressure pain in the ear/mastoid area (no red flag)
- **Clinical examination**
  - further HN failures (tumour? polyradiculitis?), loss of reflexes (Miller-Fischer?)
  - always otoscopy: ?zoster oticus
  - Dysfunction M. stapedius: hyperacusis low frequencies
  - hemiplegic taste disturbance – tongue?
- **Severity** House-Brackmann scale
  - grade I normal
  - grade II mild paresis
  - grade III moderate, not disfiguring, active closure of the eyes possible
  - grade IV eyelid closure incomplete
  - grade V in addition, hardly any movement of the corners of the mouth
  - grade VI complete paralysis
- **BE:** CRP, Lc, HbA1c, **Borrelia serology always, VZV serology with clinical suspicion** (reddening, swelling, blisters in the ear canal or eardrum, pain in the ear region) or swab and PCR from blisters if present
- MRI for any atypical clinical findings or red flags (e.g. hypoacusis, tinnitus, sensory deficits, diplopia, recurrence, bilateral, other deficits)
- **CSF diagnostics** for red flags (e.g. severe pain, any indication of infectious origin, immunocompromised patient, recurrence, progression)
- Bilateral → Borrelia? sarcoidosis (Heerfordt syndrome)? GBS/Miller-Fischer? Syphilis?
- Pain → borrelia? VZV?
- Recurrence → Melkersson Rosenthal Syndrome?

Central versus peripheral

- Frontal branch affected → peripheral or nuclear (nuclear: often also abducens palsy)
- Frontal branch not affected → supranuclear or peripheral incomplete
- If situation is unclear: neurophysiological examination in the early phase (day 1–3) (canalicular hypoexcitability?)

Treatment

- **Prednisolone (Spiricort®) 60 mg 1-0-0 for 10 days**
- Begin prednisolone if possible within the first 3 days
- **If eye closure is incomplete (**test at rest, eyes not actively squinting **): watch glass bandage + dexpanthenol eye ointment**
- In the event of VZV detection/suspicion, definitely and in individual cases (in the case of severe HB V/VI) consider: additional Famvir® (famciclovir) 3×500 mg p.o. for 7 days, alternatively valaciclovir 3x1000 mg/d for 7 days, or brivudine 1x125 mg/d for 7 days. For eye involvement, headache, other cranial nerves aciclovir i.v. 10 mg/kg body weight every 8 hours for 7 days
- Physiotherapy: can be prescribed, evidence is slim, but there is definitely a psychological factor

The same procedure applies to pregnant women, inpatient steroid administration

Follow-up check

- Short-term follow-up if no MRI/lumbar puncture in the acute phase: after 5–7 days of querying findings + telephone consultation via emergency fellow → if Borrelia serology is positive → LP
- Medium-term: if there is no significant clinical improvement within 6 weeks: facial neurography (registration in ENGM via 23098)

CN V

- Testing: corneal reflex, sensitivity, pain on pressure at the nerve exit points, motor function (m. masseter, m. temporalis on both sides)
- Clinical: sensory disturbances, neuroparalytic keratitis possible when V1 affected

CN IX

- Ageusia in posterior third of the tongue
- Lack of gag reflex
- Anaesthesia and analgesia in the upper part of the pharynx, in the tonsil area and at the base of the tongue
- Mild dysphagia
- Drooping soft palate on paralysed side

CN X

- Speech and swallowing disorders
- Nasal language
- Hoarse voice with recurrent nerve paresis
- Dyspnoea with bilateral recurrent nerve paresis
- Tachycardia and arrhythmia

Multiple cranial nerve deficits

	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	Horner
Orbital apex	X	X	X	V1	X							
Cavernosus sinus		X	X	V1 +2	x							
Petrous apicitis (Gradenigo's syndrome)				x	x							
Cerebellopontine angle syndrome				x		x	x	(X)	(X)			
internal auditory canal						x	x					
Jugular foramen								x	x	x		
Jugulare foramen/intercondylar space (Collet Sicard)								x	x	x	x	
Retropharyngeal space								x	x	x	x	x
Brainstem	Depending on the location											
Meningitis/meningeosis carcinomatosa	Variable											

Mimics

- Guillain Barré/Miller Fisher
- Motor neuron disease
- Myasthenia gravis
- Oculopharyngeal muscular dystrophy

Examination for dizziness and oculomotor function

History

- **Temporal course/duration** acute/episodic/chronic
- **Character** rotating/swaying dizziness, feeling of drowsiness, unsteadiness when walking/standing
- **Spontaneous triggers,** change of position, sitting, standing, running, eyes closed/open, Valsalva manoeuvre, stress, time of day
- **Accompanying symptoms** oscillopsia, hyperacusis, tinnitus, feeling of pressure in the ears, headache, sensitivity to light/noise, double vision, paresis, ataxia, nausea/vomiting, other pain
- **Medicaments**

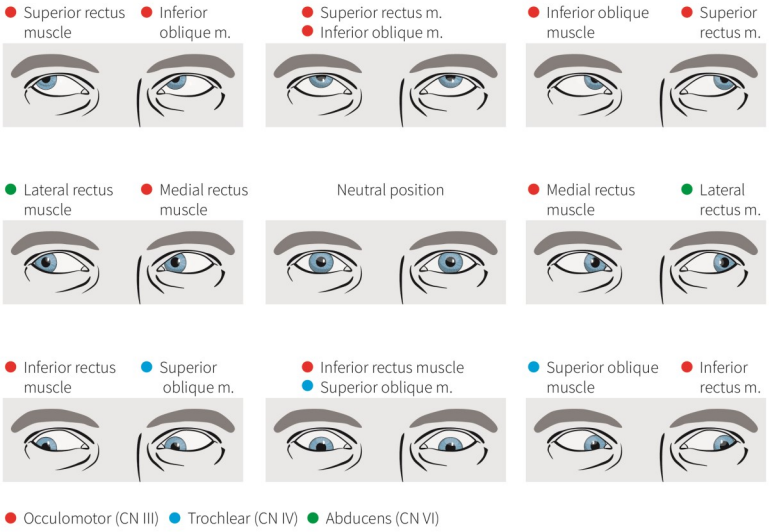
Standard examination (always!) for dizziness/eye movement disorders

adapted from Strupp Deut. Ärzteblatt 2011 & Bremova-Ertl 2019

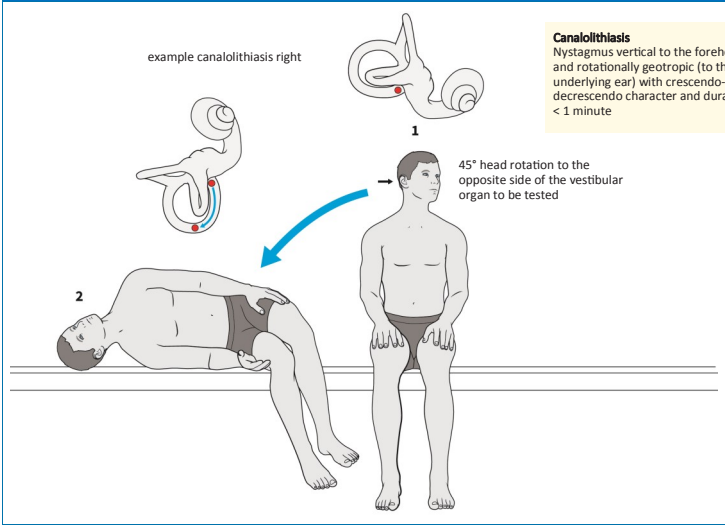
Examination	Ask about/pointing to
Body and head position	Head tilt (nose in direction of pull of paretic muscle)
Vertical head movements	Compensatory head movements in vertical supranuclear saccades/gaze palsy (focal midbrain lesions, M. Niemann-Pick type C (NPC), GM2 gangliosidosis)
Horizontal head movements	Horizontal supranuclear saccade/gaze palsy (compensation by vestibulo-ocular reflex (VOR), so-called "head thrusts", e.g. oculomotor apraxia in spinocerebellar ataxia, Cogan syndrome, neuronopathic Gaucher disease)
Increased blinking	Saccadic palsy, hypometric and slowed saccades (NPC, lid apraxia, but **not** in PSP and other atypical parkinsonian syndromes)
Horizontal forehead wrinkle	Vertical upward supranuclear gaze palsy
Position of eyelids/bulb	• Exophthalmus, chemosis, eyeball pain, failure II, III, IV, V, VI: thrombosis S. cavernosus • Ptosis, enophthalmos: Horner's syndrome → anhidrosis/erythrophobia? miosis? • Ptosis unilateral/bilateral: ocular MG?
Eye position/motility (primary position of the eyes)	
Position eyes looking straight ahead	Primary misalignment, spontaneous, fixation nystagmus
Cover test	Horizontal or vertical misalignment (skew deviation), latent nystagmus
Eight end positions (right, left, up, down, four diagonal) (binary and monocular)	Range of motion? (eye motility disorder?), terminal position nystagmus?
Gaze holding function	
10° to 40° horizontally or 10° to 20° vertically and back to 0°	Gaze nystagmus horizontal or vertical? CAVEAT: terminal nystagmus is **physiological** (higher frequency, fine-tuned, no oscillopsia, approx. 30 seconds duration, then suspension) Rebound nystagmus (beats in opposite direction when returning to 0° position; cerebellar origin)
Slow following movements (also eye following)	
Horizontal or vertical/ everywhere	Smooth versus saccaded (fine/coarse)
Saccades	
Horizontally and vertically when looking around and when specifically requested	**Latency** (impaired initiation or oculomotor apraxia), **speed** (saccadic slowdown: riMLF/ PPRF), **targeting** (hypermetric: cerebellum), **unconjugated movements** (INO?)

Standard examination (continued)

Optokinetic nystagmus ("2-in-1"; tests saccades AND gaze tracking together)	
Horizontal and vertical with OCN - drum, strip tape, app	**Auslösbarkeit** (Sakkaden-/Blickparese?), **Schlagrichtung und Phase** (Umkehrung: Nystagmuslatenz/kongenitaler Nystagmus) (App: z.B. OptoDrum)
Peripheral vestibular function	
Vestibulo-ocular reflex (VOR) of the horizontal semicircular canal	Unilateral or bilateral peripheral vestibular lesion (especially involving the superior part of the N. VIII) CAUTION: Always switch the testing sides, it must not be predictive, otherwise false negative
Visual fixation suppression of the VOR	
Fixation test	**Absent suppression of VOR** (Vestibulo-Ocular Reflex)? → Sign of a central (usually cerebellar) disorder
Examination using Frenzel goggles	
Looking straight ahead, left, right, down and up	**Spontaneous nystagmus**? (typically suppressed by fixation)
Head shake test	**Head-shaking nystagmus**? (Destabilization of the pre-existing peripheral vestibular lesion) or 'perverted head-shaking nystagmus' (cerebellar lesion)
Positional manoeuvres	Positional vertigo in BPPV, central positional/positional nystagmus
Other neurostatus including gait test	

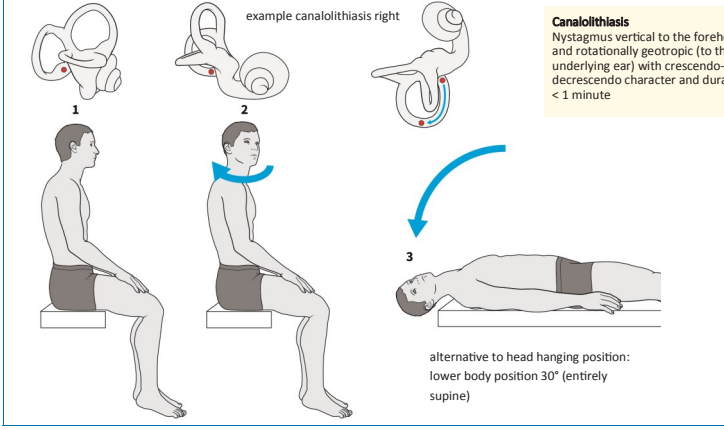


Diagnosis right posterior semicircular canal (lateral position)



Canalolithiasis
Nystagmus vertical to the forehead and rotationally geotropic (to the underlying ear) with crescendo-decrescendo character and duration < 1 minute

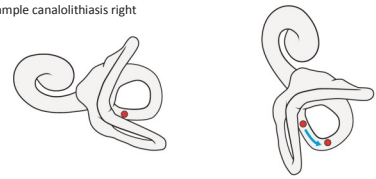
Diagnostic posterior right semicircular canal (Dix Hallpike)

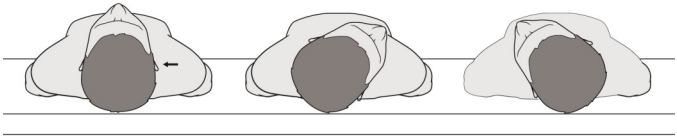


Canalolithiasis
Nystagmus vertical to the forehead and rotationally geotropic (to the underlying ear) with crescendo-decrescendo character and duration < 1 minute

Diagnosis lateral semicircular canal on both sides (supine roll)

example canalolithiasis right





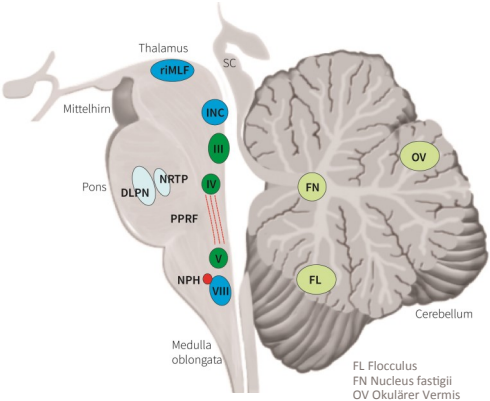
Canalolithiasis

- Geotropic nystagmus (towards the lower ear) in both lateral positions of the head with crescendo-decrescendo character and a duration of 10–30 seconds
- The side with the higher intensity of the nystagmus is affected

Cupulolithiasis

- Apogeotropic nystagmus (to the upper ear), can last for a very long time, sometimes > 60 seconds
- The side with the less intense nystagmus is affected

Okulomotor centres

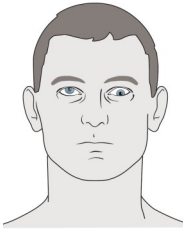


riMLF	Rostral interstitial nucleus of the medial longitudinal fasciculus	Vertical saccade paresis
INC	Cajal interstitial nucleus	Vertical gaze nystagmus
DLPN	Dorsolateral pontine nucleus	Horizontal saccadic follow-up movements. ipsi
NRPT	Tegmental pontine reticular nucleus	Disruption horizontal saccades+following movement+ vergence
PPRF	Paramedian pontine reticular formation	Horizontal saccadic paresis ipsiversive
NPH	Nucleus praepositus hypoglossi	Horizontal gaze nystagmus
MLF	Medial longitudinal fasciculus	Internuclear ophthalmoplegia

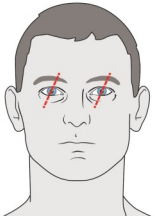
See also Table showing types of nystagmus and eye movement disorders

Ocular tilt reaction, INO, diplopia

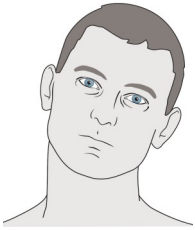
Ocular tilt reaction
Lesion site: ipsiversive vestibular core/contraversive MLF



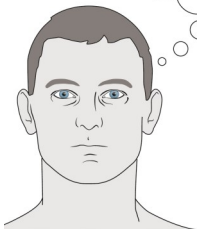
Skew deviation



Excyclorotation OS
Incyclorotation OD



Head tilt

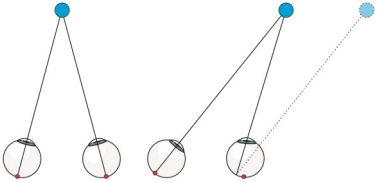


Tilting of the subjective visual vertical SVV > ±2.5°

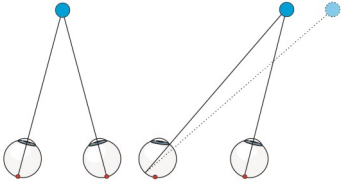
Internuclear ophthalmoplegia on the right

INO right
adduction deficit right +
dissociated nystagmus on the left

Double images (un)/crossed



Uncrossed doubles



Crossed doubles

Classification of dizziness

Episodic/positional vestibular syndrome: seconds – minutes	Acute vestibular syndrome: days – weeks
• Benign paroxysmal positional vertigo BPLS (<1 min) • Vestibular paroxysmia (<1 min) • Anterior semicircular canal dehiscence • TIA	• Acute unilateral vestibulopathy (formerly vestibular neuritis); DD inferior vestibular neuritis (CAVEAT horizontal VOR normal) • Brainstem/cerebellar infarction (AICA: possibly with hearing impairment)
Episodic vestibular syndrome: minutes – hours	**Chronic vestibular syndrome: months – years**
• Vestibular migraine (5 min – 72 hrs) • Meniere's disease (20 min – 12 hrs) • Episodic ataxia type 2 (minutes – days) • TIA	• Bilateral vestibulopathy • Persistent postural perceptual dizziness (including phobic postural dizziness) • Cerebellar or extrapyramidal problems

Episodic position-dependent vestibular syndromes

	Posterior semicircular canal diagnosis: lateral position or Dix-Hallpike	**Therapie**
BPLS	• Nystagmus vertical to the forehead and rotationally geotropic with a crescendo-decrescendo character and a duration of less than one minute	Epley oder Sémont (Plus) Manöver
	Horizontal semicircular canal diagnostic: supine roll manoeuvre	
	Canalolithiasis • Nystagmus geotropic (towards the lower ear) in both lateral positions of the head with cresecendo-decrescendo character • The side with the higher intensity of the nystagmus is affected	Gufoni Manöver
	Cupulolithiasis • Apogeotropic nystagmus (towards the overlying ear), can last for a very long time • The side with the less intense nystagmus is affected	Gufoni plus Manöver
Central	**Central postural or positional nystagmus**	
	• A similar nystagmus can be triggered in different head positions (right, left, head hanging position); this does not match the level of the respective semicircular canal (often beating down towards the nose)	
	Red flags (indicative of central genesis of dizziness) • accompanying headache • ataxia, inability to walk freely • atypical nystagmus: downbeat, nystagmus begins immediately after provocation, duration >90 seconds, lack of a crescendo-decrescendo character • prominent nystagmus with little or no vertigo • poor response to positioning manoeuvres • repeated vomiting during positioning manoeuvres • frequent recurrence	

Acute vestibular syndrome: peripheral vs central (HINTS+)

		Peripheral	Central
H I	**Head-impulse test**	ipsilateral pathological with insertion saccade	normal (but pathologically possible if the vestibular core is affected)
N	**Nystagmus** (when looking straight ahead and turning left/right)	dominantly horizontally directional, beating away from failed vestibular organ	- dominantly vertical and/or torsional - dominant horizontally changing direction when looking left/right - lack of suppression by fixation
T S	**Test of skew** (alternating cover test)	normal	Skew deviation (vertical corrective movement when covering, in 30% of all central origin)
+	**Hearing loss**	normal	ipsilateral pathological (e.g. AICA infarction)
++	**Neurostatus**	normal	pathological (ataxia extremities, dysarthria, CN paresis, paresis, sensory disturbance) possible triggering of dizziness by turning the head to the side/up (hemodyne due to compression of the vertebral artery)
++	**Gait and core stability**	can walk freely but doesn't want to "won't walk"	Cannot stand/walk freely, possible trunk ataxia "can't walk"

Acute unilateral vestibulopathy

Criteria

1. Acute vestibular syndrome with acute/subacute rotary vertigo, which, untreated, lasts at least 24 hours
2. Peripheral vestibular horizontal torsional spontaneous nystagmus with beating direction to the healthy side
3. Video HIT: VOR gain <0.7 and/or reduced calories on the affected side
4. No hearing loss and no tinnitus
5. No central oculomotor disorders (skew deviation, gaze nystagmus)

Therapy Methylprednisolone 100 mg/day for 3 days; reduce dose by 20 mg every fourth day until stopped, targeted balance training accelerates and improves central vestibular compensation (→ prescription)

Bilateral vestibulopathy

Criteria

1. Chronic vestibular syndrome with unsteadiness while standing and unsteady gait and at least 1 of:
   - Motion-dependent visual disturbances or oscillopsia when walking or rapid head/body movement
   - Poor balance in the dark and/or on uneven ground
2. No discomfort while sitting or lying down
3. Reduced or absent VOR on both sides: v-HIT on both sides with reduced gain (<0.6) and/or reduced caloric response (<6°/sec)

DD Consider Cogan syndrome as the cause of bilateral vestibulopathy

Therapy vestibular rehabilitation + case-by-case depending on the cause (e.g. meningitis/ototoxic medication), chronic course without progression

Vestibular migraine

Criteria
1. At least 5 episodes of vestibular symptoms lasting 5 minutes to 72 hours
2. Positive personal history of migraine with or without aura according to ICHD criteria
3. At least 1 concomitant migraine symptom in >50% of vestibular episodes
   - migraine-typical headaches or
   - sensitivity to light or noise or
   - visual aura

Therapy see chapter on Headache

Vestibular paroxysmia

Criteria
At least 10 vertigo attacks, duration: seconds – max. 1 min., usually occurring when the head is turned (spontaneously possible), good response to "sodium channel blockers" (e.g. carbamazepine), often tinnitus, hearing loss
Diagnosis MRI with CISS-sequence (vascular-nerve contact N. VIII/vascular?)

Therapy Carbamazepine (after HLA testing) (Tegretol CR®, Timonil ret®) 200–600 mg/d or oxcarbazepine (Apydan extent®, Trileptal®) 300–900 mg/d

Meniere's disease

Criteria
1. 1 or 2 attacks of vertigo lasting 20 minutes to 12 hours (intense rotary vertigo with nausea and vomiting)
2. Audiometrically documented hearing loss <2000 Hz >30 db during the vertigo episode (+/−24 hours)
3. Fluctuating tinnitus or pressure in the affected ear

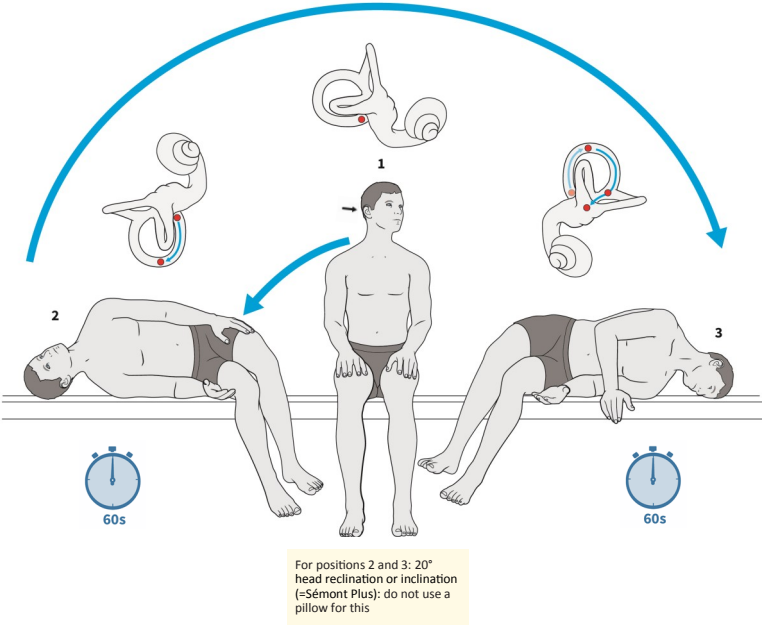
Diagnosis audiometry, caloric, vHIT, o-/c-VEMP

Therapy Betahistine dihydrochloride (Betahistin®, Betaserc®) 3×24 mg/d, if necessary expansion to high-dose therapy by the vertigo centre. As soon as 6 months have been free of attacks, the daily dose can be slowly reduced (depending on the course, by 1 tablet every 3 months)

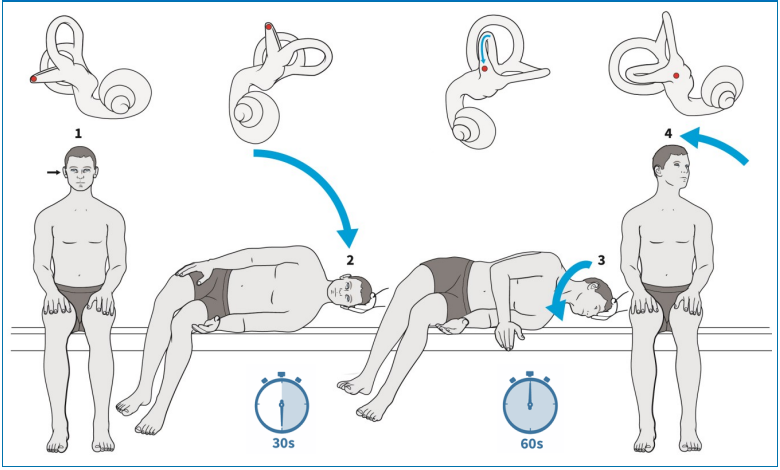
Follow-up checks

- Always give patient a dizziness calendar (Base A).
- BPLS: provide exercise instructions, check-up with the dizziness consultant in 2–4 weeks
- Acute unilateral vestibulopathy: dizziness physiotherapy for 4 weeks (provide prescription), follow-up in 6 weeks with the dizziness consultant, with v-HIT, caloric, and o-/c-VEMP
- Referral to the dizziness consultant via ANZ casemanagement@insel.ch

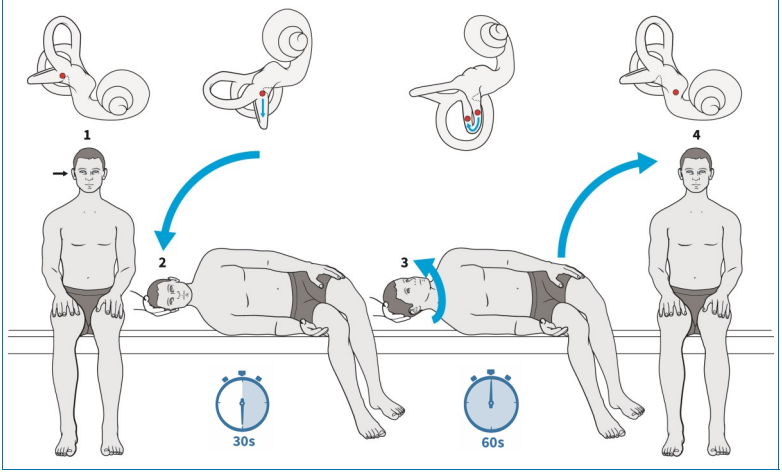
Therapy for right posterior semicircular canal (Sémont Plus)



Therapy geotropic horizontal semicircular canal on the right (Gufoni)



Therapy ageotropic/horizontal semicircular canal on the right cupulolithiasis (Gufoni Plus)



Nystagmus and eye movement disorders

Nystagmus forms adapted from LMU Pocketguide Okulomotorik Kremmyda, Büttner, Strupp

Nystagmus	Position	Direction	Lesion	Comments
Spontaneous nystagmus	looking straight ahead	horizontal-rotatory	- peripheral vestibular (labyrinth, CN VIII) - central (pons, cerebellum)	Contralateral to the lesion, pathol. Halmagyi ipsilateral, towards fast phase ↑, with fixation ↓ Plus central oculomotor dysfunction, possibly purely horizontal
Fixation nystagmus		downbeat	Flocculus, in 40% unclear origin	looking away, sideways and during fixation ↑
		upbeat	pontomedullary/ pontomesencephalic	when looking up and in fixation ↑
		rotatory	Mesencephalon (INC), medulla (Wallenberg)	INC only: ipsilateral to the lesion, INC+riMLF: contralateral to the lesion, + OTR
		pendelförmig	Pons (Guillain-Mollaret triangle)	with fixation ↑ [+palatine tremor]
Gaze direction nystagmus	sideways/ upwards	in direction of view	NPH, flocculus (horizontal) INC, flocculus (vertical)	non-exhaustive
Positional nystagmus	Looking straight ahead	rotatory top horizontal	posterior semicircular canal horizontal semicircular canal	exhaustive with accompanying vertigo exhaustive with accompanying vertigo
Position nystagmus	Looking straight ahead	horizontal/ down	cerebellum (usually nodulus)	inexhaustible or exhaustible, not correlating well with dizziness
Congenital nystagmus	any	mostly horizontal	none	usually no oscillopsia, increase with fixation, zero zone

Eye movement disorders

	Direction	Core	Disorder
Saccades	horizontal	PPRF	Ipsilateral slowing, horizontal gaze palsy
	vertical/tors	riMLF	Vertical slowdown + gaze paresis, contral. torsion
Gaze holding function	horizontal	NPH/FL	Gaze nystagmus ipsilateral to the lesion
	Vertical/ tors	INC/FL	Vertical/torsional gaze nystagmus, torsional spontaneous nystagmus
Slow eye movements		NRTP/DLPN/FL	Ipsilateral saccadic gaze
OCN	similar to slow Blickfolge		Reduction
Vergence		Mesencephalon RF, posterior commissure	Exophoria, pseudo-abducens nerve palsy, convergence retraction nystagmus
VOR		VIII (nerve, nucleus) FL, Nod, uvula	Spontaneous nystgamus, pathological ipsilateral Halmagyi, downbeat, periodically alternating nystagmus, positional nystagmus

Central supranuclear gaze palsy

Horizontal	
Pons lesions: ipsilesional horizontal gaze palsy, contralesional gaze turn	
Abducens nucleus ("pontine gaze centre")	• usually all types of horizontal eye movements are affected • ipsilesional abduction palsy • contralesional adduction palsy
Isolated damage to the pontine paramedian reticular formation (PPRF)	• disruption of horizontal saccades (prolongation of latency, slowing down and fluctuations in saccade velocity)
Isolated damage to the dorsolateral pontine nuclei (DLPN)	• disturbance of slow following movements
Bilateral PPRF lesions	• Loss of horizontal saccades in both directions plus temporary disruption of vertical saccades
Midbrain lesions: due to damage to the descending pathways to the DLPN and PPRF ipsilesional paresis of the horizontal following movements and the horizontal saccades **and/or** contralesional horizontal saccade paresis (before vs after fibre crossing)	
Extensive hemisphere lesions contralesional horizontal gaze palsy, often with ipsilesional (head and) gaze turn	• horizontal VOR often omitted (at least partially) • more common in right than left brain lesions • frontal and parietal areas with oculomotor functions as well as regions that are important for visual attention are affected • no permanent disorder, resolution within days to weeks
Thalamus lesions: contralesional gaze deviations with ipsilesional gaze palsy (wrong way eyes), vertical gaze palsy	
Internuclear ophthalmoplegia (INO)	• adduction palsy: damage to the MLF on the side of the adduction palsy (better or preserved with convergence) • abduction nystagmus • slowed abduction saccades
One and a half syndrome	• complete ipsilesional horizontal gaze palsy (lesion of the abducens nucleus) • + "half" contralesional horizontal gaze palsy (ipsilesional internuclear ophthalmoplegia, lesion ipsilesional MLF)
Vertical	
Rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) (saccade generator vertical/torsional)	• slowing down to complete saccade paresis, lengthening of saccade duration, lengthening of latency
interstitial nucleus of Cajal (INC) (gaze hold function/integrator, generation of slow following movements, involved in vertical VOR)	• vertical gaze palsy (all types of vertical oculomotor disorders), downbeat nystagmus (leaky integrator)
Posterior commissure (CP) (Crossing of the fibres of riMLF and INC to Ncl. III.)	• vertical gaze paresis (all types of vertical oculomotor disorders), convergence retraction nystagmus
Bilateral riMLF lesion	• isolated vertical saccadic paresis • lower saccades more affected than upper ones

Peripheral nerve lesions

Carpal tunnel syndrome

- **Motor deficit**/atrophy abductor pollicis brevis (push thumb 90° from palm level)
- **Sensory disturbance** hypaesthesia digits I–IV ½ (recess ball of thumb); sometimes whole hand and up to upper arm); 2-point discrimination (side comparison)
- **Typical triggers**: driving/telephoning/sleeping, improvement by shaking out hand
- Tinel sign on the wrist, Phalen test may trigger symptoms
- **Mild therapy** (no permanent impairments): avoid triggers, wrist splint (overnight), possibly 20 mg prednisone for 2 weeks; in the case of a sensorimotor deficit also ad ENMG (?OP ?steroid injection); pregnancy: conservative treatment, if the clinical symptoms are pronounced, steroid injections into the canal by the hand surgeons!!

Sulcus ulnaris syndrome

- **Motor** claw hand, Froment's sign (adduction of the thumb paretic, compensation: flexion of the distal phalanx of the thumb when trying to pinch a piece of paper between the thumb and the index finger)
- **Sensory disturbance** hypaesthesia digits V and IV ½, ulnar edge of the hand
- Tinel sign in the sulcus ulnaris (compare with the opposite side!)
- Nerve may be dislocated from the sulcus
- **Therapy** Rest/avoid repetitive elbow flexion/supporting elbow; possibly padded elbow splint; in case of failures ENMG (?OP)

Radial pressure lesion

- **Motor**
  - ◊ typical lesion on the upper arm: weakness of the hand/finger extensors
  - ◊ proximal lesion: triceps paresis, TSR failure, sensory disturbance on the radial forearm/upper arm

  CAVEAT Test finger spread on a surface, otherwise impression of an additional ulnaris paresis
- **Sensitivity disorder** possibly supply area R. superficialis on the back of the hand
- **DD** central drop-hand: von Wartenberg's sign (extension in the wrist when clenching a fist; flexion in the wrist tends to be increased in the case of a peripheral lesion), other hand functions are also restricted
- **Investigations** none with typical clinical features and history, otherwise radial neurography; with normal sensitivity and insidious onset DD MMN
- **Therapy** finger extension splint in case of severe symptoms (Plaster cast room, Tel 22476)
- **Check** ENMG if the cause is unclear, in severe clinical cases after 2–3 weeks

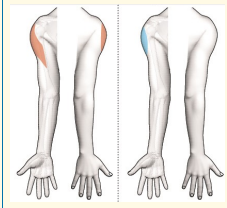
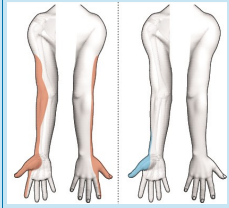
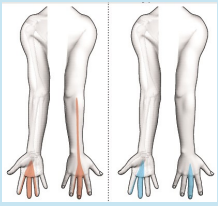
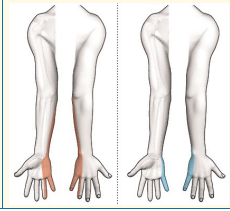
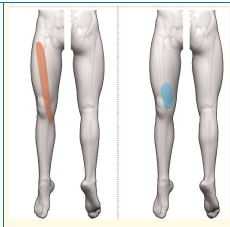
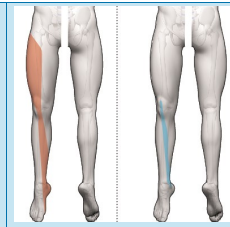
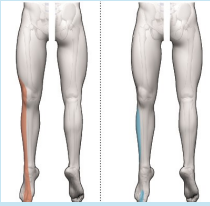
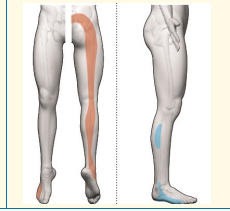
Peroneal tendon disorders

- **Motor** paresis, foot and toe dorsiflexion, foot eversion
- **Sensitivity disorder** N. peroneus superficialis and profundus, can also be normal
- Tinel sign on the neck of the fibula?
- **Investigations** evidence of nerve conduction block in peroneal neurography; if necessary, imaging in suspected Baker's cyst or similar.
- **Therapy** foot lifter splint at dtl. clinic (Plaster cast room, Tel 22476, prescription for orthopedic specialist supplier)

Important DDs radicular/peripheral nerve lesion

- **L5/Peroneal**: at L5
  - radicular pain
  - additional paresis, leg abduction and foot inversion
  - Trendelenburg sign (DD cause – Trendelenburg weakness caused by superior gluteal nerve lesion, gluteal insufficiency)
  - mostly paresis Ext hallucis longus > tibialis anterior (equally affected in case of peroneal neuropathy) (tibialis posterior reflex weakened)
- **C8/ulnar nerve**: in the case of an ulnar nerve lesion, loss of sensitivity is limited to the middle of digit IV; at C8 also thenar muscles and flexion thumb terminal paretic (m. flexor poll. longus, medianus)

General: Radicular pain, weakened Kenn reflex, flaccid paresis, hyposensitivity (primarily hypoalgesia!), possibly Laseguè sign, pain often does not strictly follow the dermatome

	Pain	Hypoesthesia	Comment		Pain	Hypoesthesia	Comment
C 5			Paresis deltoideus arm abduction 30–90° > biceps BTR weakened	C 6			Paresis biceps and brachioradialis (palpate when tense) BTR > RPR absent/ weakened
C 7			Paresis triceps> finger flexors (and pectoralis major/ pronator teres syndrome) TTR weakened	C 8			Paresis of hypothenar muscles, e.g. abductor digiti minimi Possibly weakened TTR and Trömner reflex (Horner syndrome?)
L 3			Paresis knee extension > leg adduction PTR > adductor reflex weakened	L 4			Paresis knee extension (climbing on chair) PRR weakened
L 5			Paresis M. tibialis anterior < extensor hallucis longus (lift big toe longer when standing/heel walk), M. gluteus medius/ leg abduction (test Trendelenburg sign or in lateral position) (tibialis post Rflx ↓)	S 1			Paresis triceps surae (toe stand/ walk/jump) + paresis hip extension (for DD tibial paresis) ARR weakened (if necessary, test while kneeling with feet over the edge of the bed)

Cauda equina syndrome

Jodhpur anaesthesia, paresis triceps surae and small foot muscles; bladder and rectal dysfunction (can be absent initially/in the case of slow process) → neurosurgical emergency!

Guillain-Barré syndrome, Miller-Fisher

Diagnosis

- **Blood exam** routine laboratory, if necessary GM1-AK, GM2-AK, anti-GQ1b-AK, hepatitis E, CMV, EBV, campylobacter stool culture, *Mycoplasma pneumoniae*, Zika virus, COVID
- **Clinical examination** rarely initially normal to increased reflexes (especially axonal variant, according to *C. jejuni*)
- **Lumbar puncture** to rule out DD (ZZ >50: search for pathogens; 10-50: consider searching for pathogens, especially Borrelia, VZV, HIV, CMV, EBV), cytalbumin dissociation in the 1st week only in 50%
- **Imaging** MRI of the spinal axis to rule out DD, especially if the clinical picture is not quite typical, if necessary MR neurography to objectify the plexus involvement
- **Elektrophysiology** (often largely normal initially, maximum changes usually after 2 weeks): delayed or absent F waves, possibly intermediate responses; over the disease course demyelinating/axonal changes
- Autonomous parameters and vital capacity! (VC sitting vs lying -> cervical paralysis?)
- Determine GBS disability score mEGOS und EGRIS (GBS respiratory insufficiency score)!
- **Always measure vital capacity** when sitting and lying down (big difference → diaphragmatic paresis?), respiratory rate, ECG

Red flags indicative of other DD

- Fever, signs of infection in the laboratory tests
- Respiratory problems with otherwise only minor paresis
- Sensitive > motor, clear sensitivity level
- Bladder/rectal dysfunction at the beginning or persistent during the disease course
- Clear asymmetry of paresis
- LP pleocytosis >50/µl, polynuclear pleocytosis
- Nadir of paresis > 4 weeks after onset (e.g. CIDP?)

Monitoring

- **Monitoring IB** for rapid progression, severe autonomic involvement, dysphagia, accessory respiratory muscle involvement (VC <1l), EGRIS >4
- **Monitoring** BP/pulse min 4/d, ECG, more often in the case of great variability
- **Respiration** Vital capacity lying down, respiratory rate initially every 2–4 hours, if clinical conditions are stable every 6–12 hours; low-threshold, call in ABGA/MET team (when using auxiliary respiratory muscles, AF>25, shallow/paradoxical breathing, see respiratory insufficiency on the next page) **WARNING increased risk of CO_2 anaesthesia with respiratory involvement** → O_2 administration/opiate therapy only after/under ABGA control

Treatment

- Before IvIG or PLEX: 2–3 tubes of zero serum ad immunoserology for preservation
- Mild GBS: GBS Disability Score ≤2 (10 m ambulatory unaided) – IVIG not mandatory
- **IvIG 0.4 g/kg body weight over 5 days**
- **Replacement procedures (plasmapheresis, immune adsorption)** as a therapy option, consider as initial therapy in severe cases (no evidence)
- 40% without relevant response within 4 weeks: no evidence for 2nd IVIG cycle
- Thrombosis prophylaxis Clexane 1×40mg or 10,000 IU heparin; in case of immobility Clexane 2×40mg or 15,000 IU heparin
- **Pain management** analgesic ladder , often fentanyl plaster necessary, early use of pregabalin/gabapentin
- Low-threshold laxative medication, possibly possibly residual urine sono/DK
- > 4 weeks after onset: no therapy/DD CIDP (possibly IvIG/steroids?)
- **Miller Fisher**: ophthalmoplegia, sensory ataxia, areflexia. GQ1b, mostly benign course, IVIG
- **Bickerstaff**: ophthalmoplegia (also nystagmus, opsoclonus, ptosis), cranial nerve deficits V, VII, IX–XII, ataxia (>90%), loss of consciousness (74%), paresis (60%), areflexia/hyperreflexia, pyramidal signs (40%), ventilation required (20%); MRI lesions pons/midbrain/thalamus in 40%, GQ1b (66%), pleocytosis (50–70% up to 250/ul), treatment with IVIG, possibly plus steroids

Myasthenia gravis

- **Antibodies**:
  - AChR antibodies (80%); muscle-specific receptor tyrosine kinase (MuSK antibodies) (3%)
  - in AChR antibody- and MuSK antibody-negative patients: lipoprotein-related protein 4 (LPR4) (1%)
  - seronegative (15%)
  - paraneoplastic in thymomas: anti-titin antibodies (MGT-30), only in patients <50 years -> association with thymomas + difficult treatment with little response to thymectomy
- 70% thymic hyperplasia, 15% thymoma
- **Examination**: Simpson test (upwarts gaze 1 min), ice pack test, myasthenia score
- **Tensilon test**: Edrophonium 2 mg i.v. as a test dose, after 1 minute if tolerated (CAVEAT: bradycardia, hypotension, bronchospasm) administration of a further 3 mg, if necessary a further 5 mg; Alternative: test with Mestinon 60 p.o. (response after 2–5 hours)
- **Instrumental**: EMG (repetitive stimulation); CT chest
- **BE**: acetylcholine receptor antibodies; Anti-MuSK, possibly anti-Titin, LRP4 (if other antibodies neg.). LEMS: anti-VGCC (calcium channels), possibly paraneoplastic antibodies (especially Sox1, Hu, CV2)
- **Classification**:
  - class I purely ocular myasthenia
  - class II mild to moderate generalized myasthenia often involving the ocular muscles
  - class III moderate generalized myasthenia
  - class IV severe generalized myasthenia
  - class V requiring intubation

- **Treatment**
  - Pyridostigmine (Mestinon®): dosage according to effect, e.g. 30–60 mg p. o. every 4–5 hours, maximum daily dose 360 mg
  - Methylprednisolone start at 15–20 mg/d, target dose approx. 0.5–1.5 mg/kg body weight/d, increase 5 mg/week (do not forget: Bactrim and calcium/vitamin D3 with long-term steroid therapy >20 mg/d
  - Azathioprine (Imurek®): 2–3 mg/kg body weight/day, maintenance dose 1–2.5 mg/kg body weight
  - Azarek, MTX, MMF
  - Thymectomy
    - If patient has a thymoma
    - without thymoma for patients AChR+ <50 yrs with generalized MG or ocular poor response
    - small thymectomy in patients with MuSK+ or LRP4+, seronegative, >65 years, purely ocular

Myasthenic crisis

- Worsening of myasthenia, especially dyspnoea (dyspnoea of speech, shallow breathing, increased respiratory rate) and bulbar symptoms (nasal speech, dysphagia)
- **Investigations** exclusion of infection, medication history (reduction of immunosuppression? change in dose of cholinergic drugs?, deterioration due to various antibiotics, antiepileptic drugs, anaesthetics, see UpToDate for complete list), vital capacity, ABGA

- Monitoring in IMC (possibly NIV therapy, if VC <15–20 ml/kg possibly prophylactic intubation))
- aBGA, nasogastric tube, NIV, or intubation
- **Ist choice: plasma exchange** (plasmapheresis or immune adsorption) 4–6× every 2nd day (CAVEAT: not possible in patients with sepsis)
- **2nd choice: IVIG** 0.4 g/kg body weight/d over 5 d (CAVEAT: not in patients with hypercoagulability, severe NI)
- Prednisone 60–80 mg/d (worsening in approx. 30% after 4–6 d, 10% requiring intubation)
- Possibility of lack of response or relapse within 4–6 weeks -> Consider 2nd cycle (PE/IVIG) or eculizumab (Soliris).
- Treatment with cholinesterase inhibitors in crisis patients is secondary (promotes bronchial secretion! pyridostigmine (Mestinon) 30 mg up to 600 mg/d or neostigmine 0.15–0.3 mg/h i.v .(30 mg Mestinon p.o. = 1mg neostigmine i.v.)

Myasthenia, respiratory failure

DD myasthenic crisis/cholinergic crisis

	Myasthenic crisis	**Cholinergic crisis** (rare, above all with pyridostigmine > 120 mg every 3 hours)
Pupils	Normal/Mydriasis	Miosis
Pulse	Tachycardia	Bradycardia
Musculature	Paresis	Paresis + fasciculations
Respiration	Insufficiency	Less in the foreground
GI tract	Normal	Diarrhoea, cramps
Amelioration by:	Cholinergics	Atropine

Medications causing myasthenia gravis List not comprehensive

Group	Myasthenia-enhancing drugs	Alternatives
Analgesics/ anti-rheum.	Chloroquine, D-penicillamine, metamizole	Acetylsalicylic acid, diclofenac, indomethacin, gold
Muscle relaxants	Chlormezanone, gallamine, pancuronium bromide, succinylcholine; effects can last for days or weeks with MG	Carbamazepine, valproic acid, lamotrigen, vigabitrin, gabapentin
Antibiotics	Aminoglycosides, ampicillin, clindamycin, colistin, D-penicillinamine, erythromycin, fluoroquinolones, imipenem, lincomycin, macrolides, polymyxin B, quinine, telithromycin, tetracyclines	Cephalosporin, chloramphenicol, nitrofurantoin
Cardiovascular	Antiarrhythmics (quinidine), beta blockers, calcium channel blockers (verapamil), procainamide, statins	ACE-He, digitalis prep, ipratropium bromide, oxyfedrine, tocainide
Effective on the central nervous system	Amantadine, antidepr. tricyclic, anticonvulsants (phenytoin, trimethadone, barbiturates), benzodiazepines, chlorpromazine, lithium, antipsychotics highly potent, trihexyphenidyl	
Others	Botulinum toxin, quinine, curare, diuretics (via hypokalaemia), glucocorticoids, desferrioxamine, active vaccinations, interferons, iodinated contrast media, magnesium-containing drugs, nicotine patches, tiopronin	

Respiratory failure

- **Clinical findings** lethargy/difficulty concentrating, speech dyspnoea, use of auxiliary respiratory muscles, increased respiratory rate (>25) with shallow breathing, counting after maximum inspiration (normal up to >50 possible, dtl.
- dyspnoea at <15), cyanosis, weak coughing, orthopnoea with diaphragmatic paresis, aspiration/hoarse voice after eating/drinking in patients with bulbar palsy
- **Vital capacity** (CAVEAT false low values in patients with facial paresis if there is a leak around the mouthpiece)
  - ◊ Set point for males 5.76 body weight−0.026A−4.34 ± 1.00
  - ◊ Set point for females 4.43 body weight−0.026A−2.89 ± 0.71
- Decrease in vital capacity when lying down vs upright position >25%: indication of clear diaphragmatic paresis
- **Monitoring vital capacity respiratory rate** frequency depends on the the disease
- **Management** respiratory physiotherapy, possibly Cough-Assist if it is difficult to cough up secretion (through PT), O_2 administration only 1–2l under ABGA controls because of the risk of CO_2 anaesthesia
- Nocturnal hypopnoea: waking up with a feeling of suffocation, headache in the morning, daytime sleepiness → ABGA on waking, consider NIV if necessary
- Notify the MET team if respiratory rate >30, vital capacity <1 L or less than 15–20 ml/kg body weight, or decrease >50% from admission
- SNIP >60 women and >70 men rules out relevant insufficiency

Dying phase consult the palliative care team 181-5040

Indications of dying phase

- Changes in breathing (especially reduced depth of breathing , pauses between breaths or irregular breathing)
- Worsening of the general condition with permanent confinement to bed (Karnofsky Performance Status: 10–20, ECOG 4)
- Altered level of consciousness (increasingly somnolent to comatose)
- Inability to take in food, medication or fluids
- Changes in skin

Measures

- **Clinical assessment:** attention to shortness of breath, pain, bronchial secretion/rattling, nausea, delirium
- **Discontinuation of medications and measures** that cannot help improve current symptoms; prescribe the remaining drugs (also reserve drugs) i. v. or s.c.
- **Stop diagnostics + routine measurements (**blood pressure, pulse, weight, etc.)
- **Disable ICD** if used
- **Reserve medication** for dyspnoea, pain, restlessness/confusion, nausea and rattling, see below
- Inform relatives and possibly the family doctor about the high probability of imminent death
- If desired, actively involve relatives in the care
- Check autopsy status or other legacy (organ donation)?
- Identify spiritual/religious needs, inform pastoral care if necessary
- Offer relatives the opportunity to stay overnight. At the same time, ask about their stress situation and discuss options for distance/relaxation; check who to call

Medication

Dyspnoea

- Morphine 2.5–5 mg s.c. or 2.5 mg i.v. up to every 30 min
  in the case of previous treatment with opioids: 10–16% of the daily dose in reserve up to every 20 min
- Midazolam (Dormicum®) s.c. or i.v. 0.5–1 mg up to every 30 min in addition to morphine

Restlessness/confusion (Caution: treatment only needed in the case of severe agitation)

- Haloperidol (Haldol®) 0.5–1 mg s.c. or i.v. up to hourly in reserve – if unsuccessful chlorpromazine (Largactil®) 6.25 to 12.5 mg
- Rattle breathing: positioning, butylscopolamine (Buscopan®) 20 mg s.c. or i.v. 3–6 times per 24 hours only if the patient is unconscious and without hypervolaemia

Nausea

1. Metoclopramide (Primperan®) 10 mg s.c. or i.v. up to 4 ×/d 2. haloperidol (Haldol®) 0.5–1mg s.c./i.v. up to 5 mg/d

Pain

Morphine 2.5–5 mg s.c. or 2.5 mg i.v. up to every 30 min or in the case of previous treatment with opioids 10% of the daily dose usally up to every 30 min. or continuously 30 mg/24 h s.c. or 20mg/24 h i.v., increase as required reserve dose

Reanimation, palliation, determination of death

Reanimation

- **The decision** on the REA status is a medical decision based on the patient's will, if there is a living will AND medical findings/prognosis (e.g. living will reanimation "yes" for patients with poor prognosis/short life expectancy → Reanimation no
- **The goal** of successful resuscitation: **return to a self-determined life**
- If the patient refuses attempts at resuscitation, they must not be carried out
- REA status NO is independent of intensive care yes/no and intubation yes/no
- **Attention: REA status NO often leads to worse treatment/outcome** (=cognitive error)
- The **REA status should be constantly updated**
- See also under E-learning at neuronews.ch

Determination of death

- **Certain signs of death**: postmortem lividity (after 30–60 min), rigor mortis (after 2–3 h beginning at the temporomandibular joint)
- Fill in the death certificate (in the folder "Handbuch Totenfall", Register 11, to be found under Nursing)
- Autopsy?
- Cornea donation? Registration via intranet form + Tel. eye clinic (office hours 28538, otherwise DA 27367)

General

Diagnosis by neurology and intensive care (both independent of organ transplantation), at least one qualified (FA before 11/17 or 5x brain death diagnosis under supervision), carried out jointly

Guidelines/forms https://www.samw.ch/de/Publikationen/Richtlinien.html

Requirements

Exclusion of other causes of coma	• Metabolic (also normocapnia, no hypercapnia during clinical assessment except apnoea test) • Hypothermia <35 degrees • Especially CNS infection, polyradiculitis cranialis • Circulatory shock • Drug/toxin stop sedatives sufficiently early; CAVEAT in the case of thiopenthal, the clinical assessment is too uncertain due to slow degradation and additional diagnostics are mandatory • Coma adequately explained by cerebral imaging
Clinical determination of death	• Absence of brainstem reflexes ◊ Pupils wide without light reactivity ◊ Oculocephalic reflex absent (if not possible, ice water rinse) ◊ Corneal reflexes absent ◊ Lack of reaction to trigeminal pain stimulus (triggering centrally, preferably retromastoidal; spinal reflexes would be possible on the extremities) ◊ Lack of cough reflex (e.g. when suctioning)
Absence of spontaneous breathing in the apnoea test	• Preserved neuromuscular function as a prerequisite • Output BGA with normal $PaCO_2$/pH • Lack of spontaneous breathing for more than a minute with documented $PaCO_2$>60 mmHg, pH<7.30 (parallel O_2 administration via catheter in the tube allowed)
Additional technical diagnostics for the detection of cerebral perfusion failure	Only required for non-assessable cranial nerves or non-assessable apnoea test with pre-existing hypercapnia • Transcranial Doppler with pendulum flow/systolic spikes • CT angiography/perfusion • MR angiography • DSA

Organ donation

Prerequisite for organ donation

- Organization/consultation with intensive care physicians
- Documented patient consent
- If not available: consent of relatives/appointed trusted person

Types

- Organ donation after primary brain death (**DBD: donation after brain death**)
- Organ donation after prolonged cardiac arrest (**DCD: donation after cardiac death**)
  - ◊ planned cardiac arrest with subsequent onset of brain death
  - ◊ with advance notice, usually terminated at 9 a.m. the following day
  - ◊ Procedure: Patient is in the operating room, is extubated, waiting for cardiac arrest (neurologist is waiting in the operating area), exactly 5 minutes after cardiac arrest, brain death diagnosis according to protocol
  - ◊ conducted by Konsil-OA, usually by background service at weekends

Lumbar puncture

General

- **Standard**
  - ◊ Glucose serum
  - ◊ always zero serum
- CSF: 1 tube each for haematology (ZZ, Ery) + chemistry (protein, glucose, lactate) + depending on the investigation(usually 1–2 tubes to preserve (see below) for any subsequent prescriptions) (higher required volume esp. for TB culture, cytopathology and FACS analysis)
- Between 3 and 5 lumbar spinous process (conus medullaris extends to LWK 1/2 in 94%)
- with ultrasound control or under fluoroscopy in NRAD if not possible
- **Flat position after LP** No evidence on length of stay for the prevention of post-puncture headache
- **Pressure measurement** in lateral position with legs not fully bent, otherwise incorrectly high

Special examinations in the CSF

- **Reserve/keep CSF for repeat orders** *xserv body fluids > liquor > sterile vessel > corresponding clinical information* note "PCF" or "reserve" + if necessary "culture" (cannot be reordered) *"Zero CSF"* is storage of only supernatant after centrifugation
- Also remove **oligoclonal bands** from zero serum (automatic prescription in xserv)
- **Bacterial culture** *xserv Körperflüssigkeiten > Liquor > steriles Gefäss > Bakterien > Bakt Mikr/Kult*
- **Mycobacteria** *xserv Körperflüssigkeiten > Liquor > steriles Gefäss > Mykobakterien > Myc Mik/Kult*
- **BioFire®** Mon–Sun 8 a.m. - 6 p.m.: register via the on-call doctor for microbiology 181-6720; xserv (6 p.m. to 8 a.m. only via xserv, but the sample will only be processed from 8 a.m. the following day) includes: *N. meningitidis, S. pneumoniae, L. monocytogenes, H. influenzae, Cryptococcus neoformans/gatii*, HSV 1 and 2, VZV, enterovirus, cytomegalovirus, HHV 6, parechoviruses
- **Cytopathology** Mo–Fr until 16 Uhr: an extra tube ad pathol; sxserv *Patholglgie > klinische Zytopathologie*; samples must be examined within 4 hours due to cell decay (rate of false negatives increases)
- **Flow cytometry** Mo–Thurs until 14:30 and Fri until 12:00 p.m. an extra tube for hematology → pre-registration via 29657, at the *xserv Zentrum Labormed > Flowzytometrie: Immunzelltypisierung (=CD 4/8 Ratio) oder Hämatol. Immunphänotypisierung (?Tumorzellen)*

DD SAB DD iatrogenic blood transfusion

SAB indicative/proving:

- Xanthochromia: certainly positive only 12 hours after the onset of the headache, assessed visually or, better, spectrophotometrically
- Ferritin > 15 ng/ml
- Cytology: detection of siderophages

Assessment CC in case of SAB/blood contamination

Withdraw 1 cell per 1000 erys if not already done by lab! (see remarks result) (applies primarily to granulocytes)

Restart (D)OAC/heparin after LP

- **Heparin**: Heparin- UFH and NMWH after 4 hours
- **VKA**: oral restart can be done immediately after LP (therapeutic effect is expected after 2–3 days, evaluate bridging with heparin if there is a high embolic risk)
- **DOACs with once-daily dosing** (rivaroxaban/edoxaban): dosing on the same day about 4 hours after LP (therapeutic effect occurs about 4 hours after dosing), normal dosing from the morning of the following day
- **DOACs with twice-daily dosing** (apixaban/dabigatran): dosing on the same day about 4 hours later, if this is BEFORE 12:00 p.m., then the evening dose can also be taken normally; if LP AFTER 12:00: skip the evening dose and continue as normal the next day (unless there is a very high risk of embolism; then consider bridging with heparin)

Emergency LP urgency rating

In principle, the diagnostic benefit must always be weighed against the potential risk (in many cases it makes sense to delay the LP, e.g. start empirical treatment in cases if suspected bacterial meningitis and LP later)

LP in thrombocytopenia

- Platelets 10,000 – 50,000/ml: relative contraindication → decision on an individual basis
- Platelets < 10,000/ml: absolute contraindication

LP under antiplatelet therapy

- Monotherapy (aspirin, plavix, etc.): harmless
- Dual therapy: no data, risk of bleeding probably increased, no contraindication if there is a clear emergency indication; in the case of elective LP, switch to monotherapy 7 days before LP
- Triple therapy: contraindication

Elective LP under (D)OAC

- VKA: depending on the INR, discontinue several days (usually >3 days) in advance, INR control on the day of LP (limit values see right)
- DOAC: pause 48 hours beforehand, schedule LP for the next day; bridge with heparin

Emergency LP under (D)AOC or INR increase

INR > 1.4 spontaneous or Marcoumar/Sintrom ingestion	INR < 1.4	LP possible
	INR 1.4–1.8	LP possible, but slightly increased risk of bleeding probable
	INR > 1.8	**Contraindication** Reversion Absolute emergency indication: prothrombin complex (Prothromplex®): 50 U/kg body weight i.v. (if <50 kg body weight: 30 U/kg body weight) => INR measurement after 15 minutes, if still increased => repeat administration (target INR <1.5) Relative emergency indication: discontinue medication, possibly vitamin K (Konakion i.v.), measure INR e.g. again after 12 hours or prothrombin complex if spontaneous INR increase
DOAC intake	Plasma level* <30 ng/ml or last intake before >48h+normal kidney function	LP possible
	Plasma level* 30–100ng/ml	LP möglich, aber leicht erhöhtes Blutungsrisiko wahrscheinlich
	Plasma level* >100 ng/ml	**Contraindication** Reversion Dabigatran: PRAX BIND® 2×5g i.v., LP possible after 5 minutes Apixaban, edoxaban, rivaroxaban: CAVEAT no data on safety; therefore only in the case of an absolute emergency Consider prothrombin complex (Prothromplex®): 50 U/kg body weight i.v. (if <50 kg body weight: 30 U/kg body weight); once andexanet alfa (ANNEXA®) becomes available this may be used at levels >75 ng/ml

*** = Substance-specific factor anti-IIa or anti-Xa activity, taking into account:**

- if last intake <6 h: activity can still increase after determination!
- relatively rapid change in activity, therefore often a relevant drop within hours → in the case of increased activity (>30 ng/ml) evaluation, repeat measurement after 6 hours

MRI

General

- **Renewal of the MRI safety questionnaire for each examination** prescribed by the BAG + MR manufacturer
- **No emergency MRI for active implants and for unspecified implants (**if vitally indicated: individual case decision exclusively by LA NRAD; discussion with 23460)
- **Clarification of MRI suitability if active implants takes at least 24 hours** (expenditure of time + legal requirement that the patient has 24 hours to think about it)

MRI suitability

Type	Suitability	Procedure
Jewellery cannot be removed	suitable	Inform MTRA
Joint prosthesis **Spondylosis** **Bypass**	suitable	Inform MTRA
Stent **Coil** **Clip**	suitable	Inform MTRA
Heart valve prosthesis **Tympanic tubes** **PFO/ASD closure Thoracoabdominal stents and vascular prostheses**	type dependent	→ OP report with exact implant identification to NRAD together with registration **CAVEAT** also with bio-valves, as some of these are implanted in metal rings that are not suitable for MRI
Pacemaker **Shunt** **Pump** **Stimulators**	type dependent **Clarification mandatory together with rhythmology or NCHI**	→ OP report with exact implant identification to NRAD together with registration **CAVEAT** also pacemaker cable identifier, as these may not be MRI-compatible either

MRI and pregnancy

- **Usually no gadolinium contrast agent during the entire pregnancy;** visualization of extracranial arteries and veins using time of flight (TOF) angiography; gadolinium administration only with vital indication
- **1st trimester**: strict indication
- **2nd to 3rd trimester**: possible if clearly indicated
- **Lactation**: if possible, discard breast milk for 48 hours after gadolinium administration

MRI and renal failure

- **GFR < 15 ml/min:** no gadolinium contrast agent; vascular imaging of extracranial arteries and veins using time of flight (TOF) angiography

Medications during pregnancy: www.embryotox.de

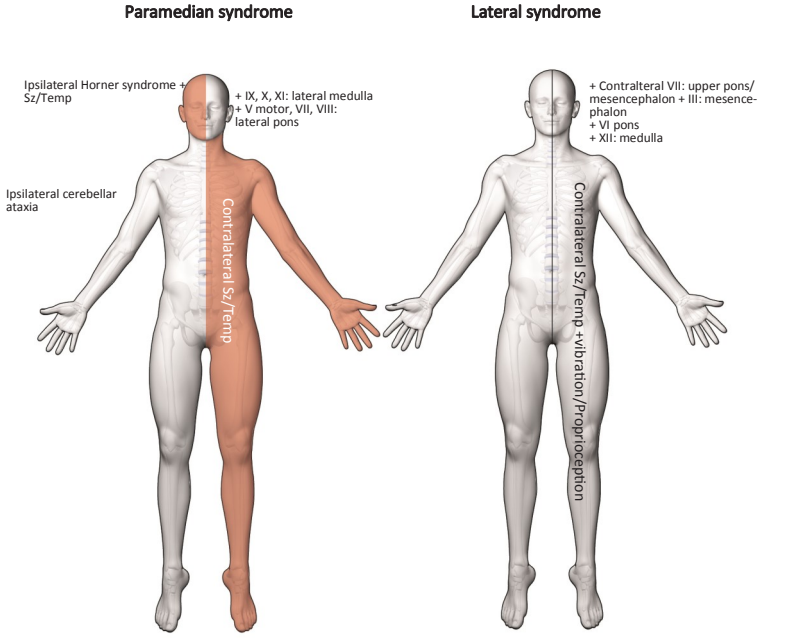
Lab blocks

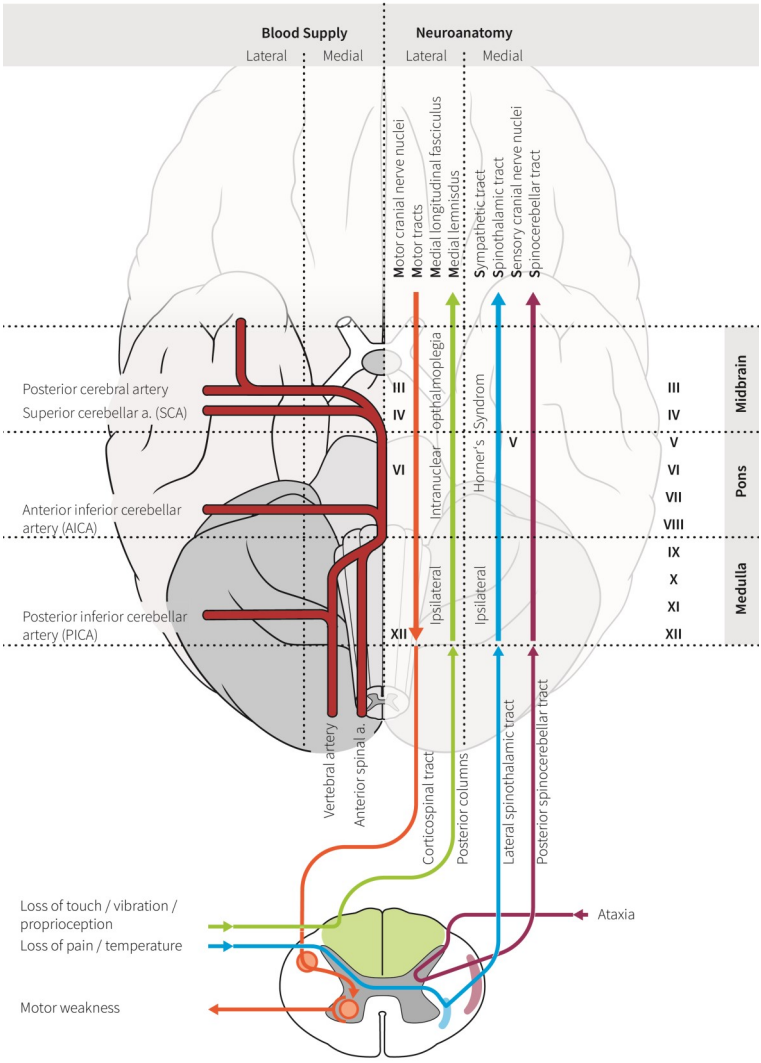
Polyneuropathy	**Stage 1** CRP, differential blood count, fasting glucose, electrolytes, liver/kidney values, TSH, serum protein electrophoresis and immunofixation, serum free light chains kappa/lambda, HbA1c, vitamin B12, urine status **Stage** 2 lumbar puncture with routine incl. IEF, ACE and IL2 receptor in the CSF/serum, CDT, holotranscobalamin, infection serology (HIV, Borrelia, syphilis, hepatitis B/C, CMV, VZV, EBV, mycoplasma), cryoglobulins, vasculitis antibodies (RF, ANA, p-/c-ANCA, cardiolipin Ab), paraneoplastic antibodies, vitamin B1/B6/E **Immune neuropathies:** possibly ganglioside block, anti-MAG (for IgM paraprotein), if necessary paranodal AK: neurofascin 155/186, contactin 1, CASPR 1, etc. (in consultation with a neuroimmunological laboratory). **Additional serology in acute and dysimmune PNP** hepatitis E virus, *C. jejuni*, anti-ganglioside antibodies, possibly Zika virus abs
Myelopathy	Cu, holotranscobalamin, NMO-AK, MOG-AK, vasculitis block, SS-A, SS-B, possibly paraneoplastic AK, ACE, sIL2-R, infection see Neuropocket (including mycoplasma, tick-borne encephalitis, enteroviruses, herpes viruses)
Muscle	CK, CK-MB, hs troponin T, (in exceptional cases troponin I; external), LDH, Ca2+, anorg. phosphate, 25-hydroxy-vit D
Myositis	HMGCR, myositis-screen (Jo-1, PL-7, PL-12, EJ, SRP, Mi-2, MDA-5, TIF1-gamma, Ro 52 kDa, SAE-1, SAE-2, NXP-2EJ)
Polymyositis overlap	(PM-Scl 100 und 75, U1-RNP (A,C,70kDa), Ku)
Dementia	• Standard laboratory including kidney and liver values; Ca, phosphate, albumin, TSH, holotranscobalamin, folic acid, syphilis, HIV, Borrelia; HbA1c, lipid status (< 80 years) • If necessary ferritin, transferrin; PTH; vasculitis screening, immune fixation including light chains; TRAK, anti-Tg, anti-TPO; fasting cortisol; vitamin B1, vitamin B6; Pb, Hg, CDT, drug screening, drug levels; Cu (possibly in 24-hour urine), ceruloplasmin; autoimmune/paraneoplastic encephalitis antibodies • If necessary, CSF analyses: standard parameters, amyloid b1-42, total tau, phospho-tau (Alzheimer's); protein 14-3-3, RT-QuIC (prionopathy); encephalitis antibodies
RLS	Ca, HbA1c, TSH, holotranscobalamin, folic acid, transferrin, ferritin
CNS lymphoma	In serum and CSF FACS analysis (see below), CSF cytology (at least 10 ml), HIV screening test, if necessary IL-10/IL-6 ratio in the CSF; if necessary EBV-PCR in the CSF

Brainstem anatomy

Rule of 4 (adapted from P. Gates)

1. 4 **M**edial structures
   - **M**otor pathway
   - **M**edial lemniscus
   - **M**edial longitudinal fasciculus
   - **M**otor cranial nerves
2. 4 lateral structures beginning with s
   - **S**pinocerebellar pathways
   - **S**ensory nucleus of trigeminal nerve
   - **S**ympathic pathway
   - **S**pinothalamic pathways
3. 4 cranial nerves in the medulla oblongata, 4 in the pons and 4 above the pons (including 2 in the midbrain)
4. 4 medial motor CN nuclei (each integer quotient of 12: XII, VI, IV, III (not I+II))




Blood Supply
Lateral
Medial
Neuroanatomy
Lateral
Medial
Motor cranial nerve nuclei
Motor tracts
Medial longitudinal fasciculus
Medial lemnisdus
Sympathetic tract
Spinothalamic tract
Sensory cranial nerve nuclei
Spinocerebellar tract
Posterior cerebral artery
Superior cerebellar a. (SCA)
Anterior inferior cerebellar artery (AICA)
Posterior inferior cerebellar artery (PICA)
III
IV
VI
XII
Ophthalmoplegia
Intranuclear
Ipsilateral
Horner's Syndrom
V
Ipsilateral
III
IV
V
VI
VII
VIII
IX
X
XI
XII
Midbrain
Pons
Medulla
Vertebral artery
Anterior spinal a.
Corticospinal tract
Posterior columns
Lateral spinothalamic tract
Posterior spinocerebellar tract
Loss of touch / vibration / proprioception
Loss of pain / temperature
Motor weakness
Ataxia

Brachial plexus

	C 4	C 5	C 6	C 7	C 8	Th 1	
Serratus anterior N. thoracicus longus							Arm/shoulder elevation, winged scapula with increase in anteversion and wall support (auxiliary respiratory muscle)
Pectoralis maj. Clavic Anteil C5							Anteversion, adduction, internal rotation (auxiliary respiratory muscle)
Supraspinatus N.suprascapularis							Arm abduction 0-15°
Infraspinatus N. suprascapularis							Main external rotator
Latissimus dorsi							Adduction, internal rotation (retroversion, cough muscle)
Teres major N. thoracodorsalis							Internal rotation, adduction, retroversion (apron grip)
Deltoideus N. axillaris							Abduction (ante/retro version)
N. musculocutaneus							
Biceps							Elbow flexion in supination, strongest supinator
Brachialis							strongest flexor in the elbow (pronation and supination)
N. radialis							
Triceps							Extension elbow
Brachioradialis							Flexion elbow in pronation/neutral position
Nervus interosseus posterior							
Supinator							Supination
Ext. carpi radialis							Extension wrist, radial abduction
Ext. carpi ulnaris							Extension wrist, ulnar abduction
Ext. dig. comm.							Extension wrist and fingers II-V
Ext. poll. longus							Spread thumbs by hand (tendon palpate radial back of hand), radial abduction
Ext. indicis propr.							Extension index finger
Abd. poll. longus							Spread thumbs by hand, radial abduction, supination
N. medianus							
Pronator teres							Pronation, less flexion elbows
Flex. carpi radialis							Wrist flexion, radial abduction
Flex. dig. superficialis							Flexion to the middle phalanx dig. II-V
Abd. poll. brevis							Push the thumb out from the palm of the hand towards the palmar side. Typical atrophy in CTS at the proximal-lateral thenar
Opponens pollicis							Opposition of the thumb
Nervus interosseus anterior							
Flex. poll. longus							Flexion and opposition of the thumb
Flex dig prof, dig II III							Flexion to the end joint
Pronator quadratus							Pronation forearm
Flex pollicis brevis (C. Superf.)							Flexion thumb metatarsophalangeal joint opposition + flexion in saddle joint
N. ulnaris							
Flex. carpi ulnaris							Flexion + ulnar abduction wrist
Flex dig. prof, dig. IV V							Flexion to the end joint
Abd. dig. minimi							Abduction little finger
Adductor pollicis							Adduction + opposition movement thumb
Flex pollicis brevis (C. prof.)							Flexion in the metatarsophalangeal joint
Interossei palmar/dorsal							Palmar: finger adduction, dorsal: finger spreading

	L 1	L 2	L 3	L 4	L 5	S 1	S2	
N. femoralis								
M. iliopsoas								Hip beugung
Quadriceps femoris								Knee extension, climb onto a stool
N. obturatorius								
Adductor magnus								Hip adduction
Adductor longus								Hip adduction
N. gluteus sup.								
M. gluteus med. and min.								Hip abduction/internal rotation, Trendelenburg sign
M. tensor fasciae latae								Hip abduction
N. gluteus inf.								
M. gluteus maximus								Hip extension, stepping onto a stool
N. ischiadicus								
Medial hamstrings								Knee flexion (possibly test in prone position)
Biceps fem. caput longus (tib)								Knee flexion
N. peroneus								
Cap. brev. biceps fem.								Knee flexion
M. tibialis anterior								Foot dorsiflexion, palpate on the the tibia
M. extensor digitorum longus								Toe extension, tendons on the back of the foot
M. extensor hallucis longus								Big toe extension, distal phalanx
M. extensor digitorum brevis								Toe extension (dist. phalanx), palpated on the lateral dorsum of the foot
M. peroneus longus/brevis								Foot eversion, tendon on the lateral edge of the foot
N. tibialis								
M. gastrocnemius/soleus								Plantar flexion + supination foot
M. tibialis posterior								Foot inversion, 90° in the ankle
M. flexor digitorum longus								Toe flexion
Intrinsic foot muscles (excl. EDB)								Toe flexion/adduction

Key muscles

Movement	Root	Re-flex	Nerve	Muscle
Shoulder abduction	C5		Axillaris	Deltoideus
Elbow flexion	C5/6 C6	+ +	Musculocut. Radialis	Biceps Brachioradialis
Elbow extensions	C7	+	Radialis	Triceps
Wrist dorsal ext	C6		Radialis	Ext. Carpi radialis longus
Finger stretching	C7		Interosseus posterior	Ext. dig. comm.
Finger flexion	C8	+	Interosseus anterior Ulnaris	Flex. poll. Longus + dig. profundus (Index) Flexus dig. Prof (Dig IV+V)
Finger abduction	Th1		Ulnaris	Interosseus dors I

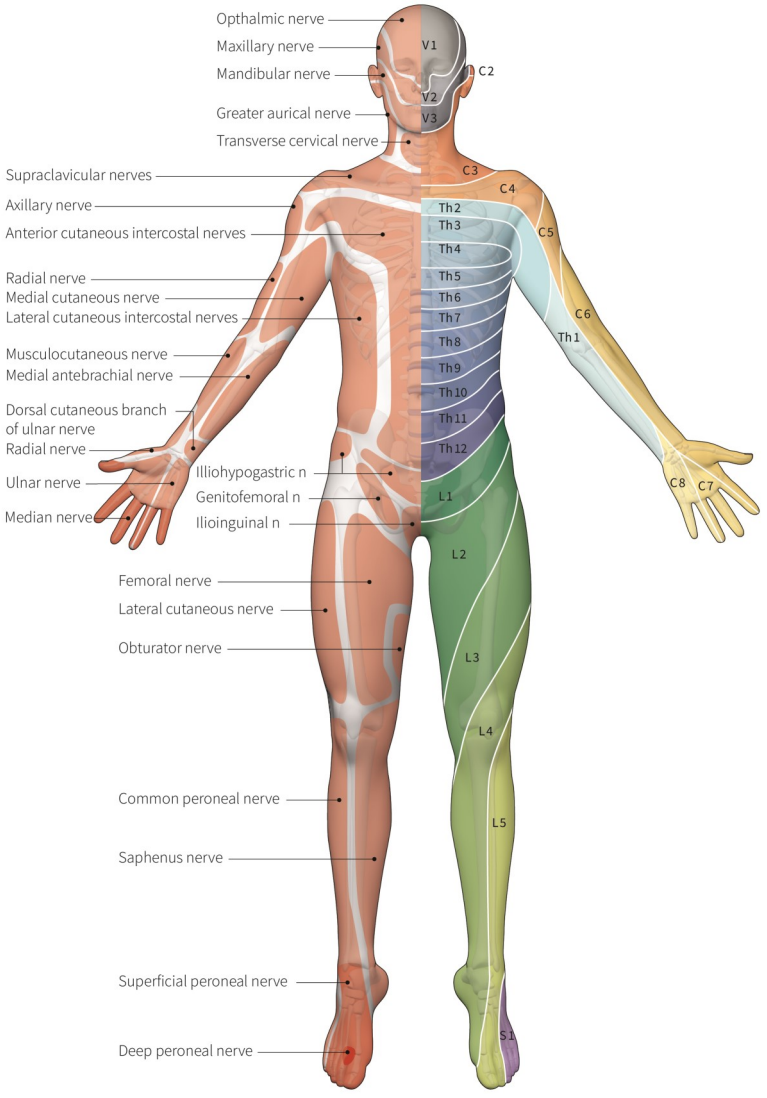
Movement	Root	Re-flex	Nerve	Muscle
Hip flexion	L1/2		Femoralirs + Plexus	Iliopsoas
Hip adduction	L2/3	+	Obturator	Adduktoren
Hip abduktion	L4/5		Gluteus superior	Gluteus medius
Hip extension	L5/S1		Gluteus inferior	Gluteus maximus
Knee flexion	S1		Ischiadicus	Kniebeuger
Knee extensor	L3/4	+	Femoralis	Quadriceps femoris
Knee flexor	L5/S2		Ischiadicus	Biceps femoris
Foot dorsal extension	L4		Peroneus prof.	Tibialis anterior
Foot eversion	L5/S1		Peroneus sup.	Peroneii
Foot inversion	L5		Tibialis	Tibialis posterior
Foot plantar flexion	S1/2	+	Tibialis	Gastrocnemius/soleus
Big toe extension	L5		Peroneus prof.	Extensor hallucis longus

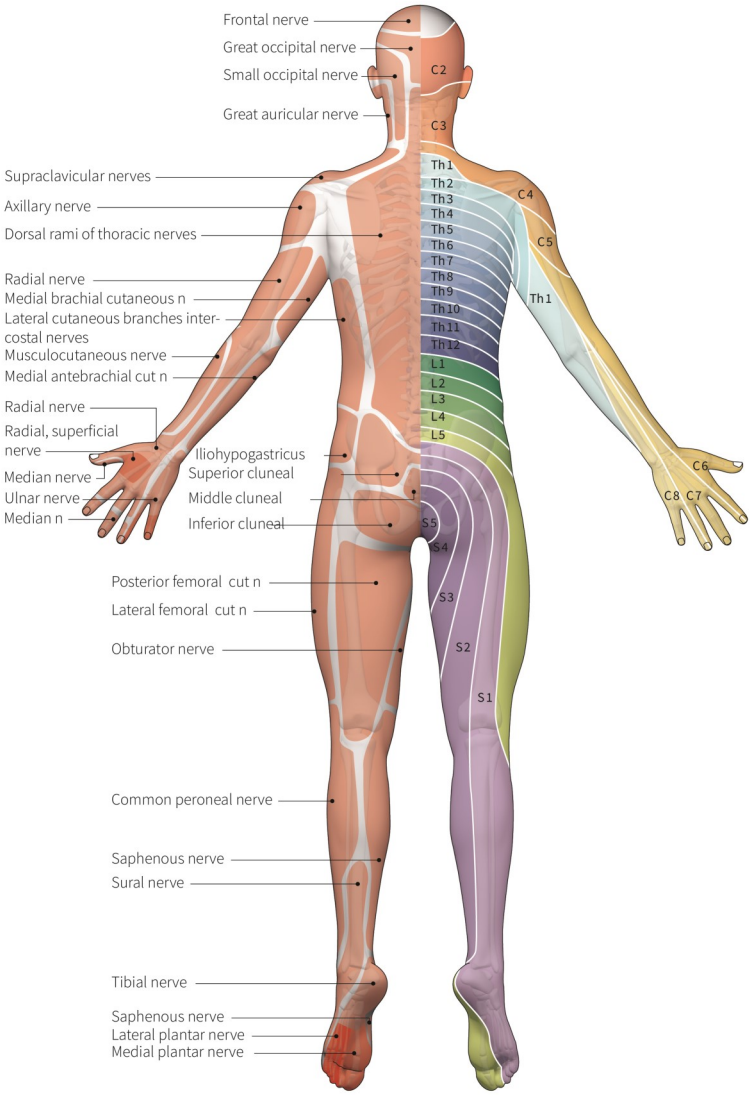
Upper arm
Musculocutaneous nerve C5–7
Coracobrachialis
Biceps brachii
Brachialis
Median nerve C5–Th1
Ulnar nerve C8–Th1
Medial cutaneous nerve
Me antebr cut n
Posterior cutaneous
Radial nerve C5–Th1
Axillary nerve C5–7
Lat cut nerve
Deltoid
Teres minor
Intercostobrachial nerve
Triceps brachii
Anconaeus
Brachiorad
Ext carp rad longus
Supraspinatus
Infraspinatus
Suprascapularis nerve
Lateral cord
Posterior cord
Medial cord
Thor long n
Subclavius n
C5
C6
C7
C8
Th1
Serratus ant
Subclavius

Forearm
Hand
Lateral antebrachial cutaneous nerve
Pronator teres
Flex carp rad
Palmaris longus
Flex dig sup
Flex dig prof I + II
Flex poll long
Pronator quad
Interosseous ant nerve
Abd poll br
Oppon poll
Flex poll br
Flex poll br
Add poll
Lumbrical
I + II
Inteross
lumbr III + IV
Median/ulnar palmar branch
Palm br
Abd V
Flex V br
Oppon V
Flex carpi
ulnaris
Flex dig prof IV + V
Palmar hand
Dorsal br.
Posterior antebrachial cut
Superficial branch
Profund branch
Supinator
Ext dig comm
Ext carp rad br
Abd poll long
Ext carp uln
Ext dig V propr
Ext. poll long
Ext poll br
Ext indicis propr
Dorsal hand

TIgh
Scrotal / labial branch
Cremaster
Cutan branch
tor tracts
Femoral
Cutaneous lat L2–3
Saphenous
Anteriour cutaneous
Quadriceps f
Sartorius
Pectineous
Quadratus lumb
Intercostal lumb
Iliopsoas
Abdominal
Iliacus
Iliohypogastricus
Ilioilingual
Genitofemoral
Femoral nerve L2–4
Obturator L2–4
Obturator ext
Adductor mag
Posterior ramus
Anterior ramus
Adductor br
Add long
Gracilis
Semimembr
Semitend
Biceps fem cp l:g
Quadratus fem
Biceps fem cp h
Common peroneal n
Lumbar plexus L1–4
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Co1
Sciatic nerve L4–S3
TIbial ner
Sacral plexus L4–S3
Inf gluteal L5–S2
Sup gluteal L4–S1
Cutan
Inf lat cluneii
Perineal
Pudendal
Ocygeal
Obturator int
Gemelli
Piriformis
Tensor fasc lat
Gluteus med
Gluteus min
Gluteus max

Lower leg
Foot
Ext hallucis brev
Ext dig brev
Medial crural cut
Deep peroneal n
Infrapatellar
Ext hall + dig long
Anterior tibial
Superf. peroneal n
Peronei
Sural, lat dorsal cut
Communicans ramus
Calc lat rami
Crural inteross nerve
Sural nerve
Gastrocnemius
Soleus
Plantar
Popliteus muscle
Dorsum of foot
Abd V
Quadr plant
Flex V
Opp V
Medial calcaneal
Lateral plantar n
Lumbrical III + IV
Interossei
Medial plantar
Posterior tibial
Flex dig long
Flex hall long
Abd hallucis
Flex dig brev
Flex hall br cp med
Lumbrical I + II
Add hall
Flex hall brev
Plantar region


Opthalmic nerve
Maxillary nerve
Mandibular nerve
Greater aurical nerve
Transverse cervical nerve
Supraclavicular nerves
Axillary nerve
Anterior cutaneous intercostal nerves
Radial nerve
Medial cutaneous nerve
Lateral cutaneous intercostal nerves
Musculocutaneous nerve
Medial antebrachial nerve
Dorsal cutaneous branch of ulnar nerve
Radial nerve
Ulnar nerve
Median nerve
Illiohypogastric n
Genitofemoral n
Ilioinguinal n
Femoral nerve
Lateral cutaneous nerve
Obturator nerve
Common peroneal nerve
Saphenus nerve
Superficial peroneal nerve
Deep peroneal nerve
V1
V2
V3
C2
C3
C4
C5
C6
C7
C8
Th1
Th2
Th3
Th4
Th5
Th6
Th7
Th8
Th9
Th10
Th11
Th12
L1
L2
L3
L4
L5
S1
S2


Frontal nerve
Great occipital nerve
Small occipital nerve
Great auricular nerve
Supraclavicular nerves
Axillary nerve
Dorsal rami of thoracic nerves
Radial nerve
Medial brachial cutaneous n
Lateral cutaneous branches inter-costal nerves
Musculocutaneous nerve
Medial antebrachial cut n
Radial nerve
Radial, superficial nerve
Median nerve
Ulnar nerve
Median n
Iliohypogastricus
Superior cluneal
Middle cluneal
Inferior cluneal
Posterior femoral cut n
Lateral femoral cut n
Obturator nerve
Common peroneal nerve
Saphenous nerve
Sural nerve
Tibial nerve
Saphenous nerve
Lateral plantar nerve
Medial plantar nerve
C2
C3
Th1
Th2
Th3
Th4
Th5
Th6
Th7
Th8
Th9
Th10
Th11
Th12
L1
L2
L3
L4
L5
S5
S4
S3
S2
S1
C4
C5
Th1
C6
C8 C7

UKN patient registration & triage 23636 *7808
UKN Fax 031 - 632 42 69 ukn@insel.ch

ESI Triage level

Level 1	Immediate life-saving measures required
Level 2	High risk situation, confused, lethargic, disoriented, strong Sz
Level 3	Not level 2 but vital parameters in the danger zone HF > 100, AF > 20, SpO2 < 92
Level 4	Not level 2, one resource is required
Level 5	Not level 2, no resource needed

MRI Regist./result	**21377 /23460**
CT Neuro Regist./Fax/ result	**28272**/ 28283/ *5563
CT Notfall MTRA/result	46201/**6201+NRAD*5563
NeuroAngio	22448 / **23484**

REA Alarm/MET Team	***9999 / *5588**
Anaesthesia incl. advance warning	***8555**
MR advance/NF regist. Anmeldung.Neuroradiologie@	**26200**
IB Shift management	***7770**
Stroke Unit	***7483 / *5887**
Bettenstation	***8792 / *6445**
UNZ OA Medicine/surgery	***7520 / *7510**
ACN Acute Care Nurse	***7968**

Care: shift management	***8130**
Care base A / B	23725 / 22441
FTN FastTrack care	*8213 / 23414
NCH TA / OA	***6310 / *7310**
Cardiology TA / OA NF	***6248 / 22005**
KAIM TA	*6360
Infectiology TA / Hygi.	*6666 / *6699
HNO TA	*6230
Haematology	*6220
Ophthalmology	27367

Sekretariat NeuroNF	**21644** notfallzentrum-neurologie@
Fax base A / B	24269 / 25731
Stationsdienst	*6442
StrokeUnit Dienst	*4876
WoEn Station	*4875
Notfall Fellow	*6441
Dienst-OA	*6009 / *4012/ 21702
Konsil-OA	***5488 / Fax 20371**
Student früh/spät	*4873 / *4874
Palliativ Team	*5040

Diagnostik

Notfall-CT Auskunft	*6203
Neurodoppler	***6032** / Fax 28960
EEG Anm/Befund	***6033/26080**/23392
Natel EEG Epta	**41303**
ENMG	23098 / Fax 23011
Orthoptik	25240
Labor Chemie	22408
Labor Hämatologie	23308
Labor Hämostase	23315
Mikrobiologie	23265

Neurologie stationär + ANZ

StrokeUnit Case-Manag	*8181 stroke@
L Sekretariat	23381 bettendispo_akutbetten@
L Süd/Mitte/Sekr	23389 / 23390 /*7324
Akutreha 1. /2. Stock	23604/23602 Kons*4479
FANI	29083
ANZ casemanagement@	**28083** / Fax 20321
ANZ direkt	**23071** (nur für intern)
SWEZ	23054
ZfB / DBS Sucher	*8948 / *5178
Neuropsychosomatik	26607