Jung S
Dietmann A, Meinel T, Bücke P, Millonig A, Prange U, Seiler A, Baud M, Seiffge D, Horvath T,
Fischer U, Bassetti C

Emergency and intensive care medicine
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- **15-17** Antibody-mediated autoimmune encephalitis
- **18** ICANS/CRES
- **19** Immune checkpoint inhibitor toxicity
- **20-23** Multiple sclerosis

### Neuro ICU

- **24** Coma
- **25** Intracranial pressure
- **26-29** Hypoxic–ischaemic encephalopathy

### Toxic and metabolic

- **30** Toxic syndromes
- **31** PRES
- **32** Electrolyte disorder
- **33** Vitamin deficiency
- **33** Thyroid associated

### Cognitive

- **34-35** Functional neurological disorder
- **36** Amnesia
- **37** Delirium

### Headache

- **38-40** Headache
- **40** Facial pain
- **41** CSF circulation disorders

### Attack-like loss of consciousness

- **04-09** Epilepsy
- **10-11** Transient loss of consciousness (TLoC)

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Imprint

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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

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Mechanism of action</th>
<th>Approved for</th>
<th>Additional indications</th>
<th>Contra-indications</th>
<th>Systemic side effects</th>
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<td>Respiratory failure</td>
<td>Na+ &lt;128 mM 5</td>
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<tr>
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<td><strong>HCO3^-</strong></td>
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<td>Respiratory failure</td>
<td>Na+ &lt;128 mM 5</td>
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<td>Respiratory failure</td>
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<td>Mood stabilizer</td>
<td>Allergy 3, cardiac arrhythmia 4</td>
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<td>Migraine</td>
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<td>Mania, RLS, neuronalgia (V,IX)</td>
<td>Allergy 3, MAOI, cardiac arrhythmia 4</td>
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<td><strong>Dox</strong></td>
<td>Oxcarbazepine</td>
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<td><strong>ESL</strong></td>
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<td>Lacosamide</td>
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<td>Neuralgia, RLS, anxiolytic</td>
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<tr>
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<td>Pregabalin</td>
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<tr>
<td><strong>PGB</strong></td>
<td>Pregabalin</td>
<td>Zusatz (3. line)</td>
<td>QT-shortening 4</td>
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<td>Cannabidiol</td>
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<td>QT-shortening 4</td>
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<td>Ethosuximide</td>
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<td>Alcohol, sleep apnea</td>
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<tr>
<td><strong>VGB</strong></td>
<td>Ethosuximide</td>
<td>Monotherapy</td>
<td>Alcohol, sleep apnea</td>
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<tr>
<td>Active Ingredient</td>
<td>Main side effects</td>
<td>Remarks</td>
<td>Trade names</td>
<td>Formulation (mg)</td>
<td>mg/ml</td>
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<td><strong>Broad Spectrum</strong></td>
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<td>CLZ Clonazepam</td>
<td>Depression/suicide</td>
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<td>Rivotril</td>
<td>Tablet 0.5 2</td>
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<td>CLB Clobazam</td>
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<tr>
<td>LTG Lamotrigine</td>
<td>Myoklonus 10, asept. meningitis</td>
<td>Lamotrigin</td>
<td>Tablet 25 50 100 200</td>
<td>25</td>
<td>25/2w 100-500</td>
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<tr>
<td>LVT Levetiracetam</td>
<td>Diarrhoea, alopecia</td>
<td>Levetiracetam</td>
<td>Tablet 250 500 1000</td>
<td>1000</td>
<td>500/3d 1000-3000</td>
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<tr>
<td>LEV Lamotrigine</td>
<td></td>
<td></td>
<td>Lamictal</td>
<td>Tablet 5 25 50 100 200</td>
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<tr>
<td>BRV Brivaracetam</td>
<td></td>
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<td>Brivact</td>
<td>Tablet 25 50 75 100</td>
<td>50</td>
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<tr>
<td>VPA Valproate</td>
<td>Alopecia, leukopenia, thrombocytopenia, T3/T4, NH3-encephalopathy</td>
<td>Valproat</td>
<td>Tablet 300 500</td>
<td>500</td>
<td>300/3d 1000-2500</td>
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<tr>
<td>TPM Topiramate</td>
<td>Dysgeusia, glaucoma, paraesthesia, anosmia</td>
<td>Topiramat</td>
<td>Tablet 25 50 100 200</td>
<td>50</td>
<td>50/3d 100-600</td>
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<tr>
<td>ZNS Zonisamide</td>
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<td>Zonegran</td>
<td>Capsule 25 50 100</td>
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<td>PER Perampanel</td>
<td>Dizziness, ataxia</td>
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<td>Fycompa</td>
<td>Tablet 2 4 6 8 10 12</td>
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<td><strong>Focal epilepsy</strong></td>
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<td>PHT (Fos)Phenytoin1</td>
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<td>Phenydan</td>
<td>Tablet 100</td>
<td>Loading</td>
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<td>Benign leukopenia T3/T4</td>
<td>Tegretol</td>
<td>Tablet 200 400</td>
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<td>200/3d 800-1600</td>
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<td>DXC Oxcarbazepine</td>
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<td>Apydan</td>
<td>Tablet 150 300 600</td>
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<td>ESL Eslicarbazepine</td>
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<td>Trileptal</td>
<td>Tablet 150 300 600</td>
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<td>LCM Lacosamide</td>
<td>Atrial fibrillation</td>
<td>Vimpat</td>
<td>Tablet 50 100 150 200</td>
<td>100-200</td>
<td>100/w 100-400</td>
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<tr>
<td>CBN Cenobamate</td>
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<td>Ontozry</td>
<td>Tablet 12.5 25 50 100 200</td>
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<td>Apixaban</td>
<td>Tablet 15 50 100</td>
<td>1-3mg/kg 100</td>
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<td>Capsule 600 800, capsule 100 300 400</td>
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<td>Capsule 25-300</td>
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<tr>
<td><strong>Lennox-Gastaut</strong></td>
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<td>FBM Felbamate</td>
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<td>Taloxa</td>
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<td>RUF Rufinamide</td>
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<td>Inovelon</td>
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<tr>
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<td>Petinimid</td>
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<td>T1/2</td>
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<td><strong>Seizure-suppressing drugs</strong></td>
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<td></td>
</tr>
<tr>
<td><strong>Active ingredient</strong></td>
<td><strong>Interval</strong></td>
<td><strong>T1/2</strong></td>
<td><strong>Women</strong></td>
<td><strong>Mainly metabolized by:</strong></td>
<td><strong>Remarks</strong></td>
</tr>
<tr>
<td>CLZ</td>
<td>Clonazepam</td>
<td>1</td>
<td>?</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>CLB</td>
<td>Clobazam</td>
<td>1-2</td>
<td>18</td>
<td>↓</td>
<td>0.9</td>
</tr>
<tr>
<td>LTG</td>
<td>Lamotrigine</td>
<td>1-2</td>
<td>25</td>
<td>↓</td>
<td>1</td>
</tr>
<tr>
<td>LTG</td>
<td>Levetiracetam</td>
<td>2</td>
<td>9</td>
<td>OK</td>
<td>1</td>
</tr>
<tr>
<td>VPA</td>
<td>Valproate</td>
<td>2</td>
<td>9-15</td>
<td>↓</td>
<td>VPA</td>
</tr>
<tr>
<td>TPM</td>
<td>Topiramate</td>
<td>2</td>
<td>21</td>
<td>↓</td>
<td>2</td>
</tr>
<tr>
<td>ZNS</td>
<td>Zonisamide</td>
<td>1</td>
<td>70</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>PER</td>
<td>Perampanel</td>
<td>1</td>
<td>100</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>PHT</td>
<td>Phenytoin</td>
<td>1-3</td>
<td>22</td>
<td>↓</td>
<td>1</td>
</tr>
<tr>
<td>CBZ</td>
<td>Carbamazepine</td>
<td>2-3</td>
<td>30-60</td>
<td>↓</td>
<td>1.5</td>
</tr>
<tr>
<td>ESL</td>
<td>Eslicarbazepine</td>
<td>1</td>
<td>15</td>
<td>↓</td>
<td>?</td>
</tr>
<tr>
<td>LCM</td>
<td>Lacosamide</td>
<td>2</td>
<td>15</td>
<td>↓</td>
<td>?</td>
</tr>
<tr>
<td>CNB</td>
<td>Cenobamate</td>
<td>1</td>
<td>30-70</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>PB</td>
<td>Phenobarbital</td>
<td>1</td>
<td>80</td>
<td>↓</td>
<td>3.0</td>
</tr>
<tr>
<td>GAB</td>
<td>Gabapentin</td>
<td>3</td>
<td>6</td>
<td>OK</td>
<td>1</td>
</tr>
<tr>
<td>PGB</td>
<td>Pregabalin</td>
<td>2-3</td>
<td>6</td>
<td>↓</td>
<td>0.1</td>
</tr>
<tr>
<td>FBM</td>
<td>Felbamate</td>
<td>2-3</td>
<td>22</td>
<td>?</td>
<td>↓</td>
</tr>
<tr>
<td>RUF</td>
<td>Rufinamide</td>
<td>2</td>
<td>10</td>
<td>↑↑</td>
<td>0.3</td>
</tr>
<tr>
<td>CBD</td>
<td>Cannabidiol</td>
<td>2</td>
<td>17</td>
<td>?</td>
<td>↑</td>
</tr>
<tr>
<td>ESM</td>
<td>Ethosuximide</td>
<td>2-3</td>
<td>60</td>
<td>?</td>
<td>0</td>
</tr>
<tr>
<td>VGB</td>
<td>Vigabatrin</td>
<td>2</td>
<td>10</td>
<td>?</td>
<td>0</td>
</tr>
</tbody>
</table>
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 NH₃ 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

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

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

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

**General**

**NORSE**: New onset refractory status epilepticus  
**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

---

**Initial treatment of status epilepticus**

- Complete the search for the cause within the first 48–72 hours

---

**Aetiology known**

**First-line immunosuppressive therapy**

- IV methylprednisolone 20–30 mg/kg (max. 1 g) for 3–5 days  
  or  
- IVIIG 2g/kg for 2–5 days  
  or  
- Plasma exchange procedure (plasmapheresis/immunoabsorption) 5–7 cycles

**Second line immunosuppressive therapy**

- Autoantibody-associated (confirmed or urgent suspicion): rituximab, if there is no effect.
- Supplementation with IL-1R antagonist (anakinra) and IL-6 antagonist (tocilizumab) in the course
- Cryptogenic: IL1r antagonist (anakinra) or IL-6 antagonist (tocilizumab)

---

**Unknown aetiology**

- Treatment according to aetiology

---

*Adapted from Wickström et al. Epilepsia 2022*
**Status epilepticus with impaired consciousness**

- **Stage 1**
  - 0-15 min
  - Clonazepam (Rivotril)
    - 1mg i.v.
    - max. 3mg
    - max. 10mg/Gabe x2
  - Midazolam (Dormicum)
    - 0.1-0.2mg/kg i.v.
    - max. 10mg/Gabe x2
  - Lorazepam (Temesta)
    - 0.1mg/kg i.v.
    - max. 4mg/Gabe x2
  - Diazepam (Valium)
    - 0.1mg/kg i.v.
    - max. 10mg/Gabe x2

- **Stage 2**
  - 15-30 min
  - Levetiracetam
    - 60mg/kg
  - Midazolam
    - 20mg/kg
  - Lorazepam
    - 40mg/kg
  - Diazepam
    - 10mg/kg

- **Stage 3**
  - Burst-Suppression
    - Duration 24 h
  - CAVE: Hypotension possible in case of fast fosphenytoin infusion, max. 150 mg/
  - Stepwise proceed until reaching burst-suppression; aim: achieve within 45min
    - Propofol bolus, then maintenance
      - Bolus 2mg/kg, then 2mg/kg/h
      - Propofol maximum dose + Midazolam Bolus
        - Bolus 0.2mg/kg, then 0.3mg/kg/h
      - Propofol maximum dose + Midazolam maximum dose
        - 1mg/kg/h
      - Midazolam 0.5-2mg/kg/h + Ketamin
        - 0.5-7.5mg/kg/h
      - Midazolam 0.5-2mg/kg/h + Ketamin
      - 0.5-7.5mg/kg/h
      - Midazolam 0.5-2mg/kg/h + Ketamin
      - 0.5-7.5mg/kg/h
    - Treatment switch depending on treatment in step 3

- **Stage 4**
  - Burst-Suppression
    - Duration 24-48 h
  - Treatment switch depending on treatment in step 3
    - Midazolam 0.5-2mg/kg/h + Ketamin
      - 0.5-7.5mg/kg/h
      - Thiopeptil 5mg/kg Bolus, then EECG-triggered
      - 0.5-7.5mg/kg/h
      - no limits

**Diagnosis**
- Lab: chemistry, HCG, drugs, medication level
- CT oder MRI
- Lumbar puncture

**Management**
- 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

**Maintenance therapies**
- Immunotherapy (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 epilepsy dept.)

**Causal therapy**
- Status epilepticus without impaired consciousness
### 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


### 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, dyspnea, 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?** Dyspnea on exertion, reduced performance, dizziness, cardiac insufficiency
- **Family history?** Sudden cardiac death SCD, PM/ICD, cardiomyopathies, thrombophilia/LE

### DD syncope, epileptic seizure, functional seizure

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

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

**Personal medical history**

<table>
<thead>
<tr>
<th>Major criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe structural or coronary cardiopathy (heart failure, low LVEF, post myocardial infarction)</td>
</tr>
</tbody>
</table>

**Examination findings**

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria (Classification as major if history is compatible with rhythmogenic syncope)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained sys. BP &lt;90 mmHg</td>
<td>longer 2nd degree AV block or 1st degree AV block</td>
</tr>
<tr>
<td>Evidence of gastrointestinal bleeding</td>
<td>Wenckebach phenomenon (Mobitz I)</td>
</tr>
<tr>
<td>Persistent bradycardia &lt;40/min while awake and no regular endurance sport</td>
<td>Inappropriate sinus bradycardia/AF 40–50/min</td>
</tr>
<tr>
<td>Newly detected systolic</td>
<td>Paroxysmal SVT or AF</td>
</tr>
<tr>
<td>Unclear increase in troponin, NTproBNP, D-dimer</td>
<td>Pre-excitation (delta wave, short PQ time)</td>
</tr>
</tbody>
</table>

**ECG**

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

**Transient loss of consciousness (TLOC)**

- **Red flags**
- **Major criteria**
  - New chest pain, shortness of breath, abdominal pain, headache
  - Syncope during exertion or lying down
  - Palpitations before TLOC
- **Minor criteria**
  - No warning symptoms or only short (<10 sec) prodromes
  - Family history for SCD at a young age
  - Syncope while sitting

- **Clinical**
- **Major criteria**
  - New chest pain, shortness of breath, abdominal pain, headache
  - Syncope during exertion or lying down
  - Palpitations before TLOC
- **Minor criteria**
  - 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)
- **Exam**
  - Unexplained systolic 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**
  - 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

- **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
<table>
<thead>
<tr>
<th>Pathogen-induced meningitis and encephalitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community-acquired bacterial meningitis</strong></td>
</tr>
<tr>
<td><strong>Viral Meningitis/Encephalitis</strong></td>
</tr>
<tr>
<td><strong>Meningo/encephalitis Borrelia/Listeria/TB/fungal</strong></td>
</tr>
<tr>
<td><strong>Begin</strong></td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td><strong>Caveat</strong></td>
</tr>
<tr>
<td><strong>Isolation</strong></td>
</tr>
<tr>
<td><strong>Lumbar puncture</strong></td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
</tr>
<tr>
<td><strong>Pathogen</strong></td>
</tr>
<tr>
<td><strong>Start treatment</strong></td>
</tr>
<tr>
<td><strong>Treatment antibiotika.insel.ch</strong></td>
</tr>
<tr>
<td><strong>Immune deficient?</strong></td>
</tr>
<tr>
<td><strong>Recording</strong></td>
</tr>
<tr>
<td><strong>Obligation to report</strong></td>
</tr>
<tr>
<td><strong>Chemo-prophylaxis post-expos.</strong></td>
</tr>
<tr>
<td><strong>Focus search</strong></td>
</tr>
</tbody>
</table>
Loss of consciousness or focal neurological deficits or epilept. seizure?

Yes

Empirical therapy (see below) → Skull CT → no evidence of increased ICP

Empirical therapy (see below)

Lumbar puncture

Blood test incl. LeucDiff + 3×2 blood culture

Loss of consciousness or focal neurological deficits or epilept. seizure?

No

Lumbar puncture

Time is brain!!!

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
Pathogen-induced meningitis and encephalitis

### Extended diagnostics

- **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)! Adapted from Boucher et al. 2017

| Acute meningitis | Common: EV (71), TBE, VZV, HSV-2>1, echoviruses, coxsackie, parechovirus, Toscana (travel history), WNV (travel history), borrelia
| Meningo-/encephalitis | Common: TICK-BORNE ENCEPHALITIS (TBE), HSV1>2, VZV, EV (70/71)
| Immunsuppression | All pathogens, more frequently: EBV, CMV, HHV6, VZV, EV, listeria, TB, nocardia, Cryptococcus neoformans, JC virus, 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. brucii 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, Angiostrongylus sp., C. gattii, melioidosis
| Asia | JEV, TBEV, Chandipura, Nipah, EV71, chikungunya, rabies, Oriecta tsutsugamushi, P. falciparum, Amylostomum brasilianum, 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, SLEV, EEEV, WEEV, VEEV, 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
<table>
<thead>
<tr>
<th>DD infectious/autoimmune meningitis/encephalitis</th>
<th>Infectious</th>
<th>Autoimmune/not infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic meningitis</strong></td>
<td>TB, Borrelia, T. pallidum, Thropheryma whippelii, Brucella, echorovirus, LCMV, VZV, HIV, fungal (cryptococci, Coccidioides, Histoplasma, Candida, Aspergillus), Acanthamoeba, Taenia solium, Toxoplasma gondii</td>
<td>IgG-4, GFAP, sarcoidosis, SLE, RA, Sjögren, Vogt-Koyanagi, Harada, Behcet's disease, carcinomatous meningosis, shunt-associated</td>
</tr>
<tr>
<td><strong>Recurrent-meningitis</strong></td>
<td>HSV-2&gt;1, EBV, bacterial (portal of entry, immune deficiency, sinusitis/mastoiditis, osteomyelitis, otitis?), fungal (Cryptococcus neoformans, Candida species, Histoplasma capsulatum, Coccidioides immitis, Blastomyces dermatitidis), Toxoplasma gondii</td>
<td>Epidermoid cysts, craniofaryngeoma, medication (NSAR, Trim-Sulf, cephalosporin, amoxi, cipro, LTG, CBZ, IVIG, MTX, AZA, TNF blocker, chemo, contrast, Behcet, SLE, Sjögren, sarcoidosis, Vogt-Koyanagi-Harada, GPA, RA)</td>
</tr>
<tr>
<td><strong>Basal meningitis</strong></td>
<td>TBC, listeria, cryptococci, dimorphic fungi</td>
<td>Sarcoïdosis, gliomatosis</td>
</tr>
<tr>
<td><strong>Limbic system/temporal lobe</strong></td>
<td>HSV-1, HSV-2, tick-borne encephalitis, syphilis, WNV, CJD, Bartonella henselae, Mycobacterium tuberculosis, (HHV-6 immunosup.)</td>
<td>Hu, CRMP5/CV2, Ma2, NMDAR, AMPAR, LGI1, CASPR2, GAD65, GABABR, DPPX, mGlur5, AK5, Neurexin-3α, lymphoma, Susac syndrome</td>
</tr>
<tr>
<td><strong>Brainstem, rhombencephalitis</strong></td>
<td>Listeria monocytogenes, Mycobacterium tuberculosis, Treponema pallidum, Brucella, Thropheryma whippleii, Blastomyces dermatitidis, HSV1/2, VZV, HIV, PML, EV71, EV (68/71), JE, TICK-BORNE encephalitis (TBE), WNV, Mycoplasma, EBV, HHV6, CMV, EEE, Borrelia, adenovirus, influenza A, polio, rabies, legionella, salmonella, melioidosis, arboviruses, aspergillosis, COVID-19</td>
<td>MS, ADEM, ANNA-1, ANNA-2, PCA-1, Ma1-2, KLHL11, IgLON5, DPPX, AQP4, MOG, Behcet, sarcoidosis, Gq11/Bickerstaff, CLIPPERS, Susac, SLE, Sjögren, Vogt-Koyanagi-Harada, lymphoma, osmotic demyelination</td>
</tr>
<tr>
<td><strong>Thalamus/basal ganglia</strong></td>
<td>Respiratory viruses (influenza, parainfluenza, adenovirus, RSV), arboviruses, WNV, JE, rabies, CID, Mycobacterium tuberculosis, toxoplasmosis, Cryptococcus, tick-borne encephalitis</td>
<td>NMDA, CRMP5, ANNA-1, Neurexin 3α, LGI-1, GAD65, anti-phospholipid Ak syndrome, Sjögren</td>
</tr>
<tr>
<td><strong>Cerebellum</strong></td>
<td>Tick-borne encephalitis, VZV, WNV, EBV, PML, influenza, rabies, HSV, HIV, CMV, JC, Coxackievirus, echorovirus Post-infection: EBV, influenza A/B, mumps, VZV, rotavirus, echorovirus, M. pneumoniae</td>
<td>NMO, ADEM, MOG, MS, ANNA-1/2, PCA-1, Tr, CASPR2, KLHL11, NIF, mGlur1, GAD65, VGCC, amphiphysin, SLE, Sjögren, lymphoma</td>
</tr>
<tr>
<td><strong>Substances</strong></td>
<td>Benzol, cisplatin, cytarabin, gemcitabin, heroin, ICI, TNF-A inhibitors, sulfasalazine</td>
<td></td>
</tr>
<tr>
<td><strong>Neoplastic</strong></td>
<td>Metastases, primarily intramedullary tumors</td>
<td>Neoplastic</td>
</tr>
<tr>
<td><strong>Chronic myelitis</strong></td>
<td>Borrelia, brucellosis, HIV, HTLV-1, TB, T. pallidium, schistosomiasis</td>
<td>Syrinx, tumor, compression, copper (also due to excess zinc), vitamin B12/E, superficial siderosis, CADASIL, ALS, HSP, SCA, Friedreich, adrenomyeloneuropathy</td>
</tr>
<tr>
<td><strong>Conus medullaris/cauda equina</strong></td>
<td>HSV-2, HSV-1, CMV, Treponema pallidum, Mycobacterium tuberculosis, schistosomiasis, mycosis</td>
<td>Neurosarcoidosis</td>
</tr>
<tr>
<td><strong>Radiculo-neuropathy</strong></td>
<td>VZV, Borrelia, HSV 2&gt;1, Hep C, Hep E, HIV, HTLV, CMV, EBV, tick-borne encephalitis, WNV, TB, brucellosis, Bartonella henselae leprosy, leptospirosis, Chagas, rabies, Zika</td>
<td>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</td>
</tr>
</tbody>
</table>
### Antibody cell membrane associated + synaptic antigens

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

### Antibodies to intracellular antigens

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

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 cerebel-
    lum)
  - 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, le-
thargy, personality change, psychiatric symptoms
2) One criterion from:
   - New focal CNS findings
   - Epileptic seizures not explained by known epilepsy
   - CSF pleocytosis > 5 cells/mm³
   - 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/mm³
   - 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

<table>
<thead>
<tr>
<th>CRES Grade 1</th>
<th>MRI</th>
<th>Anticonvulsive: Levetiracetam 2 × 750 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTOX-10: 7-9</td>
<td>Possibly LP</td>
<td>Restlessness: lorazepam/haloperidol</td>
</tr>
<tr>
<td>Slowing down</td>
<td>EEG if suspected</td>
<td>Steroids: none</td>
</tr>
<tr>
<td>Impaired handwriting</td>
<td>Anti-Il6 therapy: Tocilizumab only for CRS</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRES Grade 2</th>
<th>MRI</th>
<th>Anticonvulsive: Levetiracetam 2 × 750 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTOX-10: 3-6</td>
<td>Possibly LP</td>
<td>Restlessness: Lorazepam/Haloperidol</td>
</tr>
<tr>
<td>Delirium</td>
<td>EEG every 1–2 days</td>
<td>Steroids: Dexamethasone 10 mg 4 × /d</td>
</tr>
<tr>
<td>Somnolence</td>
<td>Anti-Il6 therapy: Tocilizumab only for CRS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRES Grade 3</th>
<th>MRI</th>
<th>Anticonvulsive: adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTOX-10: 0-2</td>
<td>Possibly LP</td>
<td>Cerebral oedema: normocapnia, hyperosmolar</td>
</tr>
<tr>
<td>Epileptic seizures</td>
<td>EEG daily</td>
<td>Steroids: Dexamethasone 20 mg 4 × /d, if necessary ↑</td>
</tr>
<tr>
<td>Focal cerebral oedema max soporous</td>
<td>Anti-Il6 therapy: Tocilizumab/Siltuximab</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRES Grade 4</th>
<th>MRI</th>
<th>Anticonvulsive: adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARTOX-10: unarousable</td>
<td>Possibly LP</td>
<td>Cerebral edema: possibly EVD, hypercapnia</td>
</tr>
<tr>
<td>Status epilepticus</td>
<td>EEG daily</td>
<td>Steroids: Methylprednisolone 1-2 g burst</td>
</tr>
<tr>
<td>Generaliz. cerebral oedema</td>
<td>Anti-Il6 therapy: Siltuximab</td>
<td></td>
</tr>
<tr>
<td>Coma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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!

**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 methylprednisolone 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, methylprednisolone 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 methylprednisolone 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
### 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)
  - Evidence of at least one contrast-enhancing and at least one non-contrast-enhancing lesion in an MR examination
  - 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 erythrocyte
    - 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

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
Multiple sclerosis

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

<table>
<thead>
<tr>
<th>Highly active* form</th>
<th>RRMS</th>
<th>RMS</th>
<th>SPMS</th>
<th>PPMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line therapy</td>
<td>Cladribine</td>
<td>Natalizumab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Active* form</th>
<th>First-line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natalizumab**</td>
<td>Ocrelizumab Ofatumumab Ponesimod Rituximab***</td>
</tr>
<tr>
<td>Interferon-beta 1b Ocrelizumab Ofatumumab</td>
<td>Interferon-beta 1b*** Ocrelizumab Rituximab*** Siponimod</td>
</tr>
</tbody>
</table>

| Designation without specifying the activity | First-line therapy | Beta-interferon Dimethylfumarate Diroximelfumarate Fingolimod Glatirameracetate Ozanimod |
|------------------------------------------|--------------------|
| Ocrelizumab | |

alphabetic 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)
### Mesencephalic syndrome

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>narrow sluggish</td>
</tr>
<tr>
<td>Pain stimulus</td>
<td>flexion-extension syn.</td>
</tr>
<tr>
<td>VOR</td>
<td>+/-</td>
</tr>
<tr>
<td>Tone</td>
<td>increased</td>
</tr>
</tbody>
</table>

### Bulbar brain syndrome

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>medium to wide, not very reactive</td>
</tr>
<tr>
<td>Pain stimulus</td>
<td>stretch synergisms</td>
</tr>
<tr>
<td>VOR</td>
<td>weak/-</td>
</tr>
<tr>
<td>Tone</td>
<td>greatly increased</td>
</tr>
</tbody>
</table>

### 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

### 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**
  - normoxæmia (paO2 60–80 mmHg)
  - normocapnia (paCO2 35–45 mmHg)
  - short-term moderate hyperventilation (paCO2 up to 30 mmHg as rescue therapy)
  - PEEP < 15 cmH₂O 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)
## 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

<table>
<thead>
<tr>
<th>MRI</th>
<th>CT as an alternative only if MRI is absolutely contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG if indicated</td>
<td>Indication: detection of steeply configured periodic discharges (spiky or sharp periodic discharges) &lt; 2.5Hz or rhythmic spike waves in the first EEG</td>
</tr>
<tr>
<td>NSE</td>
<td>After &gt; 48 hours</td>
</tr>
</tbody>
</table>

### > 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 |

---

**Hypoxic ischaemic encephalopathy (HIE)**
<table>
<thead>
<tr>
<th>Therapy regimen for epileptic activity</th>
<th></th>
</tr>
</thead>
</table>
| **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 mitochondrialopathy  
→ 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) |  |

<table>
<thead>
<tr>
<th>Barbella score (only for patients with epileptiform EEG within &lt;72h)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EEG 24–36 hours</strong></td>
<td>No epileptiform discharges 1 point</td>
</tr>
<tr>
<td>Continuous background ≥ 50% 1 point</td>
<td></td>
</tr>
<tr>
<td>Reactivity 1 point</td>
<td></td>
</tr>
<tr>
<td><strong>EEG 72 hours</strong></td>
<td>Normal background amplitude 1 point</td>
</tr>
<tr>
<td>Stimulus-induced rhythmic periodic or ictal discharges 1 point</td>
<td></td>
</tr>
<tr>
<td>Reactivity 1 point</td>
<td></td>
</tr>
</tbody>
</table>

**Evaluation:** > 4 points are associated with a good prognosis
### Hypoxic ischaemic encephalopathy (HIE)

#### Indicative of a good prognosis

<table>
<thead>
<tr>
<th>Course</th>
<th>Indicative of a poor prognosis</th>
</tr>
</thead>
</table>
| 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) |

#### 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

#### 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)
- > 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
Hypoxic ischaemic encephalopathy (HIE)

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

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Trigger</th>
<th>Vital signs</th>
<th>Pupils</th>
<th>Other symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroleptic malignant syndrome (NMS)</td>
<td>Start/dose change of neuroleptics, MCP, lithium, carbamazepine, dehydration, condition after MNS, age etc.</td>
<td>Hyperthermia, tachypnoea, tachycardia, hypertension</td>
<td>Normal</td>
<td>Rigor, dystonia, hyporeflexia, disturbance of consciousness up to coma, mutism</td>
<td>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)</td>
</tr>
<tr>
<td>Malignant hyperthermia (MH)</td>
<td>Complications of anaesthesia, predisposition: myopathies, trigger: succinylcholine, inhalation anaesthesia (including isoflurane, desflurane)</td>
<td>Up to 24 hours after anaesthesia: hyperthermia, tachycardia, hypotension, initially: increase in endexp. $\text{paCO}_2 &gt; 45$ mmHg</td>
<td>Normal</td>
<td>Generalized increase in tone (despite relaxation)</td>
<td>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; Cl: verapamil, digitalis, alpha/beta mimetics</td>
</tr>
<tr>
<td>Serotonin syndrome</td>
<td>Serotonergic medication (combinations!), e.g. MAOI, SSRI, SNRI, triptans, tricyclics, tramadol, lithium, grapefruit juice, etc.</td>
<td>Hyperthermia, tachypnoea, tachycardia, hypertension</td>
<td>Mydriasis</td>
<td>Tremor, hyperreflexia, clonus/myoclonus, hallucinations, diarrhoea, sweating</td>
<td>Discontinuation of the triggering agent, volume administration, if necessary benzodiazepines</td>
</tr>
<tr>
<td>Anticholinergic syndrome</td>
<td>Antihistamines, tricyclics, scopolamine, atropine</td>
<td>Hyperthermia, tachypnoea, tachycardia, hypertension</td>
<td>Mydriasis</td>
<td>Agitation, hypervigilance, possible coma, delirium, flushing, anhidrosis, urinary retention</td>
<td>Symptomatic, possibly phsysostigmine (if peripheral and central symptoms), benzodiazepines</td>
</tr>
<tr>
<td>Sympathomimetic toxidrome</td>
<td>Cocaine, amphetamines, pseudoephedrine, adrenaline, dobutamine, dopamine</td>
<td>Hyperthermia, tachypnoea, tachycardia, hypertension</td>
<td>Mydriasis</td>
<td>Agitation, psychosis, tremor, epileptic seizures, sweating</td>
<td>Symptomatic</td>
</tr>
</tbody>
</table>
(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

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

**Hyponatraemia**
>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⁺ hypocalcaemia**
<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

**Hypercalcaemia**
>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, paraesthesia, confusion, coma, hearing and taste disorders

**Ca²⁺ 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

**normovolaemia**
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
### Vitamin deficiency and thyroid

#### Vitamin 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

#### Vitamin 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 N!), DD copper deficiency/zinc overdose), hyperhomocystinaemia

**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

[Images of organic paresis with pronation, functional paresis without pronation, and Hoover sign]
### Functional neurological disorders

#### Positive signs

**adjusted according to Espay JAMA Neurol 2019**

**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).
  - Sterno-cleidomastoid 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
**Amnesia DD**
- transient global amnesia
- encephalitis
- transient epileptic amnesia
- Ischemia/haemorrhage/inflammation thalamic/hippocampal
- Wernicke encephalopathy
- venous thrombosis
- post traumatic
- functional

**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**

<table>
<thead>
<tr>
<th>Normal neurostatus +</th>
<th>Calculation incl. Serial 7</th>
<th>visuospatial testing</th>
<th>language testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>• orientation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• digit span</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• backward spelling</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**8 word list**

<table>
<thead>
<tr>
<th>8 word list</th>
<th>Pass 1</th>
<th>Pass 2</th>
<th>Pass 3</th>
<th>Recall after 10 min</th>
<th>Cue</th>
<th>Recognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flower</td>
<td>Carnation, tulip, rose</td>
</tr>
<tr>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Number</td>
<td>13, 17, 19</td>
</tr>
<tr>
<td>Belt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Garment</td>
<td>Trousers, belt, shoe</td>
</tr>
<tr>
<td>Toyota</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Car make</td>
<td>Mercedes, Honda, Toyota</td>
</tr>
<tr>
<td>Hall</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Weather</td>
<td>Lightning, hail, cloud</td>
</tr>
<tr>
<td>Back</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Body part</td>
<td>Back, neck, nose</td>
</tr>
<tr>
<td>Pigeon</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Bird species</td>
<td>Duck, tit, pigeon</td>
</tr>
<tr>
<td>Spruce</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tree species</td>
<td>Spruce, maple, fir</td>
</tr>
</tbody>
</table>
**General**

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

<table>
<thead>
<tr>
<th>+4 combative</th>
<th>+3 very agitated</th>
<th>+2 agitated</th>
<th>+1 restless</th>
<th>0 alert and calm</th>
</tr>
</thead>
<tbody>
<tr>
<td>−5 unarousable</td>
<td>−4 deep sedation</td>
<td>−3 moderate sedation</td>
<td>−2 light sedation</td>
<td>−1 drowsy</td>
</tr>
</tbody>
</table>

**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 10 mg 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

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

### Red flags for secondary headache

- Thunderclap headache
- First headache
- Changes of known headache
- Positional headache
- Aggravated by sneezing, coughing, exertion
- First-time or altered aura Increasing headache
- New permanent headache
- Severe unilateral headache
- Strictly circumscribed headache

## 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 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 ≥5 min, two or more aura symptoms occur one after the other, duration of the aura 5–60 min, 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

- Acetylsalicylate 1000 mg i.v. or metamizol (Novalgin®) 1000 mg i.v.
- Sumatriptan (Imigran®) 6 mg s.c. or 10–20 mg 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 40–240 mg/d), topiramate 2×50 mg/d, flunarizine 5–10 mg/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
Headache and facial pain  www.ichd-3.org/de

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% O₂ 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 cmH₂O
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 30–80 mg/d); alternatively topiramate (25–100 mg/d)

**Step 2**: repeated LP until CSF pressure <20 cm H₂O

**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 H₂O), 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*

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

**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
**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](http://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 cauteration 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 Abbie +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.: calculate 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

- 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**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Einzeldosen (mg/100 mg L-Dopa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-dopa</td>
<td>100</td>
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<tr>
<td>retard L-dopa</td>
<td>133</td>
</tr>
<tr>
<td>Duodopa</td>
<td>90</td>
</tr>
<tr>
<td>Entacapone</td>
<td>LD x 0.33</td>
</tr>
<tr>
<td>Tolcapone</td>
<td>LD x 0.5</td>
</tr>
<tr>
<td>Pramipexole</td>
<td>1 mg Salz</td>
</tr>
<tr>
<td>Ropinirole</td>
<td>5</td>
</tr>
<tr>
<td>Rotigotine</td>
<td>3.3</td>
</tr>
<tr>
<td>Piribedil</td>
<td>100</td>
</tr>
<tr>
<td>Lisuride</td>
<td>1</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>10</td>
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<tr>
<td>Pergolide</td>
<td>1</td>
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<tr>
<td>Cabergoline</td>
<td>1.5</td>
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<tr>
<td>DHEC</td>
<td>20</td>
</tr>
<tr>
<td>Selegiline 10 mg (oral)</td>
<td>10</td>
</tr>
<tr>
<td>Selegiline 1.25 mg (sublingual)</td>
<td>1.25</td>
</tr>
<tr>
<td>Rasagline</td>
<td>1</td>
</tr>
<tr>
<td>Amantadine</td>
<td>100</td>
</tr>
<tr>
<td>Apomorphine (Infusion or injection)</td>
<td>10</td>
</tr>
</tbody>
</table>

*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

Anisocoria more evident in the dark (narrower pupil is abnormal)
- Horner syndrome
- Hypohidrosis ipsilateral redness only half of the face, ipsilat. conjunctiva

Anisocoria the same in the light and the dark
- Sudden LR <1mm
- Physiological

Anisocoria more evident in the light (dilated pupil is abnormal)
- Consensual LR reduced
- Convergence miosis preserved
- Internal oculomotor paresis
- DD Ciliary ganglionitis

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


Consensual LR reduced
- Convergence miosis absent
- Pupillotonia (Adie)
- Argyll-Robertson
- Parinaud
- Pharmacological – Differentiation is only possible pharmacologically
Causes of acute (transient) visual disturbances

<table>
<thead>
<tr>
<th>Monocular</th>
<th>Binocular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinal stroke (e.g. occlusion of the ophthalmic artery)</td>
<td>Retrochiasmal lesions</td>
</tr>
<tr>
<td>Retinal TIA*</td>
<td>Lesions of the chiasma</td>
</tr>
<tr>
<td>Ischemic optic neuropathy</td>
<td>Intracranial pressure with congestion papillae and the associated impairment of vision</td>
</tr>
<tr>
<td>Vitreous haemorrhage</td>
<td>and field of vision</td>
</tr>
<tr>
<td>Symptomatic posterior vitreous detachment (flashes, soot rain) trauma</td>
<td>Epileptic hypoglycaemia</td>
</tr>
<tr>
<td>Refractive disorder (e.g. dry eye, slipped lens, keratoconus)</td>
<td>PRES CO intoxication</td>
</tr>
<tr>
<td>Glaucoma attack</td>
<td>Stroke, SAB, reversible cerebral vasoconstriction syndrome (RCVS)</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>migraine</td>
</tr>
<tr>
<td>Obscurations (blackouts lasting only seconds and greyout with papilloedema)</td>
<td>*2 forms:</td>
</tr>
<tr>
<td></td>
<td>1. amaurosis fugax: sudden onset uninfluenced by external factors</td>
</tr>
<tr>
<td></td>
<td>2. retinal insufficiency (e.g. in haemodynamically caused ischaemia with e.g. high-grade</td>
</tr>
<tr>
<td></td>
<td>ICA stenosis/ICA occlusion): usually recurrent and only transient dark vision/blindness</td>
</tr>
<tr>
<td></td>
<td>when looking at bright light, recovery in dark surroundings</td>
</tr>
</tbody>
</table>

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, hypeaesthesia
- **Lesion of intrapontine nerve segment** possibly contra-lesional paresis, hypeaesthesia, 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*
**Cranial nerves**

**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 + dexamethasone 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® (famiciclovir) 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

<table>
<thead>
<tr>
<th></th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
<th>VIII</th>
<th>IX</th>
<th>X</th>
<th>XI</th>
<th>XII</th>
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</thead>
<tbody>
<tr>
<td>Orbital apex</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>V1</td>
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<tr>
<td>Cavernosus sinus</td>
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<td>Petrous apicitis (Gradenigo’s syndrome)</td>
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<td>Cerebellopontine angle syndrome</td>
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<td>internal auditory canal</td>
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<tr>
<td>Jugular foramen</td>
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<tr>
<td>Jugulare foramen/intercondylar space (Collet Sicard)</td>
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<tr>
<td>Retropharyngeal space</td>
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<tr>
<td>Brainstem</td>
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<tr>
<td>Meningitis/meningeosis carcinomatosa</td>
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Mimics

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

Depending on the location

Variable
### 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

<table>
<thead>
<tr>
<th>Examination</th>
<th>Ask about/pointing to</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body and head position</strong></td>
<td>Head tilt (nose in direction of pull of paretic muscle)</td>
</tr>
<tr>
<td><strong>Vertical head movements</strong></td>
<td>Compensatory head movements in vertical supranuclear saccades/gaze palsy (focal midbrain lesions, M. Niemann-Pick type C (NPC), GM2 gangliosidosis)</td>
</tr>
<tr>
<td><strong>Horizontal head movements</strong></td>
<td>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)</td>
</tr>
<tr>
<td><strong>Increased blinking</strong></td>
<td>Saccadic palsy, hypometric and slowed saccades (NPC, lid apraxia, but not in PSP and other atypical parkinsonian syndromes)</td>
</tr>
<tr>
<td><strong>Horizontal forehead wrinkle</strong></td>
<td>Vertical upward supranuclear gaze palsy</td>
</tr>
</tbody>
</table>
| **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**                         | Range of motion? (eye motility disorder?), terminal position nystagmus?                 |
| **Gaze holding function**                       | 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**                                    | 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 predictable, 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)

**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

- 45° head rotation to the opposite side of the vestibular organ to be tested
- Alternative to head hanging position: lower body position 30° (entirely supine)
Diagnosis lateral semicircular canal on both sides (supine roll)

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

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**
- Benign paroxysmal positional vertigo (BPLS) (<1 min)
- Vestibular paroxysmia (<1 min)
- Anterior semicircular canal dehiscence
- TIA

**Acute vestibular syndrome: days – weeks**
- 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**
- Vestibular migraine (5 min – 72 hrs)
- Meniere's disease (20 min – 12 hrs)
- Episodic ataxia type 2 (minutes – days)
- TIA

**Chronic vestibular syndrome: months – years**
- Bilateral vestibulopathy
- Persistent postural perceptual dizziness (including phobic postural dizziness)
- Cerebellar or extrapyramidal problems

### Episodic position-dependent vestibular syndromes

<table>
<thead>
<tr>
<th>BLS</th>
<th>Posterior semicircular canal</th>
<th>Therapie</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>diagnosis: lateral position or Dix-Hallpike</td>
<td>Epley oder Sémont (Plus) Manöver</td>
</tr>
<tr>
<td></td>
<td>• Nystagmus vertical to the forehead and rotationally geotropic with a crescendo-decrescendo character and a duration of less than one minute</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Horizontal semicircular canal</th>
<th>diagnostic: supine roll manoeuvre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canalolithiasis</td>
<td>Gufoni Manöver</td>
</tr>
<tr>
<td>• Nystagmus geotropic (towards the lower ear) in both lateral positions of the head with crescendo-decrescendo character</td>
<td></td>
</tr>
<tr>
<td>• The side with the higher intensity of the nystagmus is affected</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cupulolithiasis</th>
<th>Gufoni plus Manöver</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Apogeotropic nystagmus (towards the overlying ear), can last for a very long time</td>
<td></td>
</tr>
<tr>
<td>• The side with the less intense nystagmus is affected</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Central postural or positional nystagmus</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 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)</td>
</tr>
</tbody>
</table>

### 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+)

<table>
<thead>
<tr>
<th></th>
<th>Peripheral</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H I</strong></td>
<td><strong>Head-impulse test</strong></td>
<td>normal (but pathologically possible if the vestibular core is affected)</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td><strong>Nystagmus</strong> &lt;br&gt;(when looking straight ahead and turning left/right)</td>
<td>- dominantly vertical and/or torsional</td>
</tr>
<tr>
<td></td>
<td>dominantly horizontally directional, beating away from failed vestibular organ</td>
<td>- dominant horizontally changing direction when looking left/right</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- lack of suppression by fixation</td>
</tr>
<tr>
<td><strong>T S</strong></td>
<td><strong>Test of skew</strong> &lt;br&gt;(alternating cover test)</td>
<td>Skew deviation (vertical corrective movement when covering, in 30% of all central origin)</td>
</tr>
<tr>
<td><strong>+</strong></td>
<td><strong>Hearing loss</strong></td>
<td>ipsilaterial pathological (e.g. AICA infarction)</td>
</tr>
<tr>
<td><strong>++</strong></td>
<td><strong>Neurostatus</strong></td>
<td>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)</td>
</tr>
<tr>
<td><strong>++</strong></td>
<td><strong>Gait and core stability</strong></td>
<td>Cannot stand/walk freely, possible trunk ataxia &quot;can't walk&quot;</td>
</tr>
<tr>
<td></td>
<td>can walk freely but doesn't want to &quot;won't walk&quot;</td>
<td></td>
</tr>
</tbody>
</table>

### 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

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**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®) 3x24 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)

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**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
Liberatory manoeuvre

Therapy for right posterior semicircular canal (Sémont Plus)

For positions 2 and 3: 20° head reclination or inclination (=Sémont Plus): do not use a pillow for this.
Liberatory manoeuvre

Therapy geotropic horizontal semicircular canal on the right (Gufoni)

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

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

## Eye movement disorders

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

- **Motor deficit/atrophy abductor pollicis brevis** (push thumb 90° from palm level)
- **Sensory disturbance** hypeaesthesia 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** hypeaesthesia 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)
**Radicular syndrome**

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

<table>
<thead>
<tr>
<th>Pain</th>
<th>Hypoesthesia</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C 5</strong></td>
<td></td>
<td>Paresis deltoideus arm abduction 30–90° &gt; biceps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BTR weakened</td>
</tr>
<tr>
<td><strong>C 6</strong></td>
<td></td>
<td>Paresis biceps and brachioradialis (palpate when tense)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BTR &gt; RPR absent/weakened</td>
</tr>
<tr>
<td><strong>C 7</strong></td>
<td></td>
<td>Paresis triceps&gt; finger flexors (and pectoralis major/pronator teres syndrome)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TTR weakened</td>
</tr>
<tr>
<td><strong>C 8</strong></td>
<td></td>
<td>Paresis of hypothenar muscles, e.g. abductor digiti minimi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possibly weakened TTR and Trömner reflex (Horner syndrome?)</td>
</tr>
<tr>
<td><strong>L 3</strong></td>
<td></td>
<td>Paresis knee extension &gt; leg adduction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PTR &gt; adductor reflex weakened</td>
</tr>
<tr>
<td><strong>L 4</strong></td>
<td></td>
<td>Paresis knee extension (climbing on chair)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PRR weakened</td>
</tr>
<tr>
<td><strong>L 5</strong></td>
<td></td>
<td>Paresis M. tibialis anterior &lt; 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 Rfx ↓)</td>
</tr>
<tr>
<td><strong>S 1</strong></td>
<td></td>
<td>Paresis triceps surae (toe stand/walk/jump) + paresis hip extension (for DD tibial paresis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ARR weakened (if necessary, test while kneeling with feet over the edge of the bed)</td>
</tr>
</tbody>
</table>

**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!
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 CO₂ anaesthesia with respiratory involvement → O₂ 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
- **IVlg 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 (upwards gaze 1 min), ice pack test, myasthenia score
- Tension 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

#### 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:
- aBGA, nasogastric tube, NIV, or intubation
- 1st 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. = 1 mg neostigmine i.v.)
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 $-0.026A-4.34 \pm 1.00$
- Set point for females 4.43 body weight $-0.026A-2.89 \pm 0.71$

- 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 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 $\rightarrow$ 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

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**Medications causing myasthenia gravis** List not comprehensive

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

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**DD myasthenic crisis/cholinergic crisis**

<table>
<thead>
<tr>
<th></th>
<th><strong>Myasthenic crisis</strong></th>
<th><strong>Cholinergic crisis</strong> (rare, above all with pyridostigmine &gt;120 mg every 3 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>Normal/Mydriasis</td>
<td>Miosis</td>
</tr>
<tr>
<td>Pulse</td>
<td>Tachycardia</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Musculature</td>
<td>Paresis</td>
<td>Paresis + fasciculations</td>
</tr>
<tr>
<td>Respiration</td>
<td>Insufficiency</td>
<td>Less in the foreground</td>
</tr>
<tr>
<td>GI tract</td>
<td>Normal</td>
<td>Diarrhoea, cramps</td>
</tr>
<tr>
<td>Amelioration by:</td>
<td>Cholinergics</td>
<td>Atropine</td>
</tr>
</tbody>
</table>

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**Respiratory failure**
# 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
- 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 x/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 usually 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

- **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](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 thiopental, 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](#))
  - [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* Körpermitflüssigkeiten > Liquor > steriles Gefäß > Bakterien > Bakt Mikr/Kult
- **Mycobacteria** *xserv* Körpermitflüssigkeiten > 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 neoforms/gattii, HV 1 and 2, VZV, enterovirus, cytomegalovirus, HHV 6, parechoviruses
- **Cytopathology** Mo–Fr until 16 Uhr: an extra tube ad pathol; *xserv* Patholgie > 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 Laboromed > Flowzietometrie: 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**

<table>
<thead>
<tr>
<th>INR &gt; 1.4</th>
<th>LP possible</th>
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<td>Plasma level*</td>
<td>LP möglich, aber leicht erhöhtes Blutungsrisiko wahrscheinlich</td>
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**DOAC intake**

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**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

**Plasma level**

- Plasma level* <30 ng/ml or last intake before >48h+ normal kidney function
- Plasma level* 30–100 ng/ml
- Plasma level* >100 ng/ml

**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

---

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### 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

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

#### 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 |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelopathy</td>
<td>Cu, holotranscobalamin, NMO-AK, MOG-AK, vasculitis block, SS-A, SS-B, possibly paraneoplastic AK, ACE, siLL2-R, infection see Neuropocket (including mycoplasma, tick-borne encephalitis, enteroviruses, herpes viruses)</td>
</tr>
<tr>
<td>Muscle</td>
<td>CK, CK-MB, hs troponin T, (in exceptional cases troponin I; external), LDH, Ca2+, anorg. phosphate, 25-hydroxy-vit D</td>
</tr>
<tr>
<td>Myositis</td>
<td>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)</td>
</tr>
<tr>
<td>Polymyositis overlap</td>
<td>(PM-Scl 100 und 75, U1-RNP (A,C,70kDa), Ku)</td>
</tr>
</tbody>
</table>
| 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 |
**Rule of 4** (adapted from P. Gates)

1. **4 Medial structures**
   - Motor pathway
   - Medial lemniscus
   - Medial longitudinal fasciculus
   - Motor cranial nerves

2. **4 lateral structures beginning with s**
   - Spinocerebellar pathways
   - Sensory nucleus of trigeminal nerve
   - Sympathetic pathway
   - Spinothalamic 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))**

---

**Paramedian syndrome**
- Ipsilateral Horner syndrome + Sz/Temp
- Ipsilateral cerebellar ataxia

**Lateral syndrome**
- + IX, X, XI: lateral medulla
- + V motor, VII, VIII: lateral pons
- + Contralateral VII: upper pons/ mesencephalon + III: mesencephalon
- + VI pons
- + XII: medulla
<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serratus anterior N. thoracicus longus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Arm/shoulder elevation, winged scapula with increase in anteverision and wall support (auxiliary respiratory muscle)</td>
</tr>
<tr>
<td>Pectoralis maj. Clavic Anteil C5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anteverision, adduction, internal rotation (auxiliary respiratory muscle)</td>
</tr>
<tr>
<td>Supraspinatus N.suprascapularis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Arm abduction 0-15°</td>
</tr>
<tr>
<td>Infraspinatus N. suprascapularis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Main external rotator</td>
</tr>
<tr>
<td>Latissimus dorsi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Adduction, internal rotation (retroversion, cough muscle)</td>
</tr>
<tr>
<td>Teres major N. thoracodorsalis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Internal rotation, adduction, retroversion (apron grip)</td>
</tr>
<tr>
<td>Deltoideus N. axillaris</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abduction (ante/retro version)</td>
</tr>
</tbody>
</table>

**N. musculocutaneus**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biceps</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Elbow flexion in supination, strongest supinator</td>
</tr>
<tr>
<td>Brachialis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>strongest flexor in the elbow (pronation and supination)</td>
</tr>
</tbody>
</table>

**N. radialis**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triceps</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extension elbow</td>
</tr>
<tr>
<td>Brachioradialis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion elbow in pronation/neutral position</td>
</tr>
</tbody>
</table>

**Nervus interosseus posterior**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supinator</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Supination</td>
</tr>
<tr>
<td>Ext. carpi radialis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extension wrist, radial abduction</td>
</tr>
<tr>
<td>Ext. carpi ulnaris</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extension wrist, ulnar abduction</td>
</tr>
<tr>
<td>Ext. dig. comm.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extension wrist and fingers II-V</td>
</tr>
<tr>
<td>Ext. poll. longus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spread thumbs by hand (tendon palpate radial back of hand), radial abduction</td>
</tr>
<tr>
<td>Ext. indicis propr.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Extension index finger</td>
</tr>
<tr>
<td>Abd. poll. longus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spread thumbs by hand, radial abduction, supination</td>
</tr>
</tbody>
</table>

**N. mediusan**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pronator teres</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pronation, less flexion elbows</td>
</tr>
<tr>
<td>Flex. carpi radialis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wrist flexion, radial abduction</td>
</tr>
<tr>
<td>Flex. dig. superficialis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion to the middle phalanx dig. II-V</td>
</tr>
<tr>
<td>Abd. poll. brevis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Push the thumb out from the palm of the hand towards the palmar side. Typical atrophy in CTS at the proximal-lateral thenar</td>
</tr>
<tr>
<td>Opponens pollicis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Opposition of the thumb</td>
</tr>
</tbody>
</table>

**Nervus interosseus anterior**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flex. poll. longus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion and opposition of the thumb</td>
</tr>
<tr>
<td>Flex dig prof, dig II III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion to the end joint</td>
</tr>
<tr>
<td>Pronator quadratus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pronation forearm</td>
</tr>
<tr>
<td>Flex pollicis brevis (C. Superf.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion thumb metatarsophalangeal joint opposition + flexion in saddle joint</td>
</tr>
</tbody>
</table>

**N. ulnaris**

<table>
<thead>
<tr>
<th>Muscle/Nerve</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>Th1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flex. carpi ulnaris</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion + ulnar abduction wrist</td>
</tr>
<tr>
<td>Flex dig. prof, dig. IV V</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion to the end joint</td>
</tr>
<tr>
<td>Abd. dig. minimi</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Abduction little finger</td>
</tr>
<tr>
<td>Adductor pollicis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Adduction + opposition movement thumb</td>
</tr>
<tr>
<td>Flex pollicis brevis (C. prof.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flexion in the metatarsophalangeal joint</td>
</tr>
<tr>
<td>Interossei palmar/dorsal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Palmar: finger adduction, dorsal: finger spreading</td>
</tr>
</tbody>
</table>
## Key muscles

<table>
<thead>
<tr>
<th>Movement</th>
<th>Root</th>
<th>Nerve</th>
<th>Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder abduction</td>
<td>C5</td>
<td>Axillaris</td>
<td>Deltoides</td>
</tr>
<tr>
<td>Elbow flexion</td>
<td>C5/C6</td>
<td>Musculocutaneous</td>
<td>Biceps brachialis</td>
</tr>
<tr>
<td>Elbow extensions</td>
<td>C7</td>
<td>Radialis</td>
<td>Triceps</td>
</tr>
<tr>
<td>Wrist dorsal ext</td>
<td>C6</td>
<td>Radialis</td>
<td>Ext. Carpi radialis longus</td>
</tr>
<tr>
<td>Finger stretching</td>
<td>C7</td>
<td>Interosseous posterior</td>
<td>Ext. dig. comm.</td>
</tr>
<tr>
<td>Finger flexion</td>
<td>C8</td>
<td>Interosseous anterior</td>
<td>Flexor dig. longus + flexor dig. prof.</td>
</tr>
<tr>
<td>Finger abduction</td>
<td>Th1</td>
<td>Ulnaris</td>
<td>Interosseous dors I</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Movement</th>
<th>Root</th>
<th>Nerve</th>
<th>Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip flexion</td>
<td>L1/2</td>
<td>Femoralis + Plessus</td>
<td>Iliopsoas</td>
</tr>
<tr>
<td>Hip adduction</td>
<td>L2/3</td>
<td>Obturator</td>
<td>Adductoren</td>
</tr>
<tr>
<td>Hip abduction</td>
<td>L4/5</td>
<td>Gluteus superior</td>
<td>Gluteus medius</td>
</tr>
<tr>
<td>Hip extension</td>
<td>L5/S1</td>
<td>Gluteus inferior</td>
<td>Gluteus maximus</td>
</tr>
<tr>
<td>Knee flexion</td>
<td>S1</td>
<td>Ischiadicus</td>
<td>Kniebeuger</td>
</tr>
<tr>
<td>Knee extensor</td>
<td>L3/4</td>
<td>Femoralis</td>
<td>Quadriceps femoris</td>
</tr>
<tr>
<td>Knee flexor</td>
<td>L5/S2</td>
<td>Ischiadicus</td>
<td>Biceps femoris</td>
</tr>
<tr>
<td>Foot dorsal extension</td>
<td>L4</td>
<td>Peroneus prof.</td>
<td>Tibialis anterior</td>
</tr>
<tr>
<td>Foot eversion</td>
<td>L5/S1</td>
<td>Peroneus sup.</td>
<td>Peroneii</td>
</tr>
<tr>
<td>Foot inversion</td>
<td>L5</td>
<td>Tibialis</td>
<td>Tibialis posterior</td>
</tr>
<tr>
<td>Foot plantar flexion</td>
<td>S1/2</td>
<td>Tibialis</td>
<td>Gastrocnemius/soleus</td>
</tr>
<tr>
<td>Big toe extension</td>
<td>L5</td>
<td>Peroneus prof.</td>
<td>Extensor hallucis longus</td>
</tr>
</tbody>
</table>
### UKN Neurologie Care: shift management

<table>
<thead>
<tr>
<th>Service</th>
<th>Phone/Fax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care base A / B</td>
<td>23725 / 22441</td>
</tr>
<tr>
<td>FTN FastTrack care</td>
<td>8213 / 23414</td>
</tr>
<tr>
<td>NCH TA / OA</td>
<td>6310 / 7310</td>
</tr>
<tr>
<td>Cardiology TA / OA NF</td>
<td>6248 / 22005</td>
</tr>
<tr>
<td>KAIM TA</td>
<td>6360</td>
</tr>
<tr>
<td>Infectiologie TA / Hygi.</td>
<td>6666 / 6699</td>
</tr>
<tr>
<td>HNO TA</td>
<td>6230</td>
</tr>
<tr>
<td>Haematologie</td>
<td>6220</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>27367</td>
</tr>
</tbody>
</table>

### MRI Regist./result

- 21377 / 23460

### CT Neuro Regist./Fax/ result

- 28272 / 28283 / 5563

### CT Notfall MTRA/result

- 46201 / 6201 + NRAD *5563

### NeuroAngio

- 22448 / 23484

---

### 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_akutetten@
- L Süd/Mitte/Sekr 23389 / 23390 / 7324
- Akutreha 1. / 2. Stock 23604 / 23602 Kons *4479
- FANI 29083
- ANZ casemanagement@ 28083 / Fax 20321
- ANZ direkkt 23071 (nur für intern)
- SWEZ 23054
- ZfB / DBS Sucher *8948 / 5178
- Neuropsychosomatik 26607

---

### Siemens MR Regist./result

- 21377 / 23460

### CT Neuro Regist./Fax/ result

- 28272 / 28283 / 5563

### CT Notfall MTRA/result

- 46201 / 6201 + NRAD *5563

### NeuroAngio

- 22448 / 23484

---

### 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

---

### Register & triage

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