Epilepsy — Symptoms and Diagnosis

Epileptic seizures can develop from the synchronous and paroxysmal activation of a group of neurons. There is high prevalence of a heterogeneous variety of epileptic syndromes in the population. A great number of people suffer from an epileptic seizure at least once in their lives, are worried, go to the emergency room, and seek for medical advice. It is therefore important for every physician to be familiar with the disorder and to know about treatment opportunities.

History of Epilepsy

In all clinical departments, there is a recurrent group of disease etiologies, e.g., infectious, autoimmune, inflammatory, neoplastic, traumatic, metabolic or genetic causes for diseases. As the only department, neurology reserves a very special etiological group for itself: epilepsy.

Early in history, people were impressed by this spectacular clinical picture and interpreted it in a context of the divine. This is the reason why there is the old term of morbus sacer since in ancient Greece epilepsy was considered a ‘holy disease.’

Later, in medieval times, the divine character faded and epileptics were more and more considered to be possessed by demons. During the reign of the National Socialism in Germany, epileptics were seen as ‘unworthy.’
**Definition of Epilepsy**

During an **epileptic seizure**, a short synchronous discharge of neurons occurs. This results in sudden symptoms which vanish just as quickly and can affect all neuronal qualities (e.g., motor function, sensory, vegetative, consciousness).

An **epileptic seizure** is no evidence for epilepsy. Roughly 5% of all people have an epileptic seizure at some point in their lives.

Epilepsy itself is a **chronic disease of the brain** which results in recurrent and unprovoked seizures.

If technical examinations result in the diagnosis of changes that are typical for epilepsy (see below), the diagnosis of epilepsy can be made after only one seizure. In this sense, it is important to remember the following vocabulary:

- **Occasional seizure**: Epileptic seizure due to a clear trigger; no seizures if the trigger is avoided.
- **Epileptic seizure**: Sudden, short, synchronous unloading of a group of neurons; can occur in every human being if the stimulus is strong enough.
- **Status epilepticus**: Longer lasting seizures (> 5 minutes) or repeated seizures between which consciousness is not regained.

**Causes of Epilepsy**

We distinguish between **idiopathic**, **symptomatic** and **cryptogenic** forms of epilepsy:

**Symptomatic** means that a structural cerebral alteration can be diagnosed, which seems to be responsible for the epileptic discharge. The cause is **cryptogenic** if such a structural alteration can seriously be suspected, yet it is not verifiable.

Pathophysiological etiologies are very heterogeneous: malformations, metabolic diseases, acquired brain lesions, radiation, early childhood hypoxia, encephalitis, etc.

Likewise, different **provocation factors** lead to increased readiness for seizure: fever, electrolyte derangement, uremia, hypoglycemia, hypoxia, alcohol (withdrawal), medicaments (withdrawal). Often, spontaneous epileptic seizures develop from a combination of (exogenous) stimuli, genetic predisposition and metabolic processes.

**General Symptoms and Clinical Relevance of Epileptic Seizures**

The clinic of epileptic seizures is very complex and extensive. It is best illustrated as a **paroxysmal excitation** of many neurons causing overshooting excitation in a certain brain region. Thus, focal frontal excitation results in cloni – occipital excitation to visual symptoms.

**Generalized seizures** can present as both a **tonic** (= stiff extension of the extremities) or **clonic** (= rhythmic convulsion), and also as **absence** (= empty, contactless gaze) or as individual generalized muscle twitches (= **myoclonic seizure**).
The ‘classical’ generalized grand mal seizure is often accompanied by an epileptic cry. Objectifying, one finds a lateral tongue bite, postictal muscle ache, and enuresis or encoressis in examination. After an epileptic discharge, intermittent palsies can occur (Todd’s palsy).

Concerning laboratory, monitoring keratin kinase is important. The massive and generalized muscle contraction in combination with hypoxia results in diffuse muscle damages with respective liberation of keratin kinase. If this parameter is significantly increased, the kidney can be damaged. Therefore, hemodilution should be sought at too high levels.

You should remember the following for the description of the clinic:

<table>
<thead>
<tr>
<th>Term</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>Positive symptoms</td>
<td>Increased function</td>
</tr>
<tr>
<td>Negative symptoms</td>
<td>Decreased function</td>
</tr>
<tr>
<td>Ictal</td>
<td>During the seizure</td>
</tr>
<tr>
<td>Postical</td>
<td>After the seizure, normal neuronal function is not yet regained. In this period, the patients are very sleepy and are cognitively impaired.</td>
</tr>
<tr>
<td>Interictal</td>
<td>Between the seizures</td>
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</tbody>
</table>

**Differential diagnosis tips for clinical practice**

Especially in emergency admission, it is important to differentiate: particularly in sleepy patients (with complicated anamnesis) with palsies, an acute ischemic event has to be excluded.

Besides imaging, the clinical examination is also helpful: Visual angle deviates to the damaged side at ischemia, to the opposite side of the epileptic event at epilepsy. So, if there is left-sided hemiparesis and visual angle deviation to the right, ischemia is more likely.

In case of doubt, diagnostic should be performed in the sense of a stroke. Other considerations of differential diagnoses should include migraine attacks with aura, a (convulsive) syncope or a psychogenic seizure.

The psychogenic seizure is characterized by a very variable duration and can often last for several minutes. The type of seizure changes, and often there are very long presentsiments - much longer than an epileptic aura. At a psychogenic seizure, the eyes are often tightly closed, especially if the examiner tries to open them. At an epileptic seizure, the eyes are mostly wide open. After a slow re-orientation, the patients often
Syndrome Classes of Epilepsy

As it became apparent, the group of epileptic disease is large and polymorphic. A classification in different syndrome classes serves the orientation and determines different approaches for therapy. The different diagnostic specificities, especially the respective EEG-leads, are described later.

Focal epilepsies

A common feature is the epileptogenic origin in a certain brain region with the specific symptoms.

**Note:** Every focal epilepsy can generalize secondarily and expand over the whole brain. Etiologically, all regional, structural alterations can be the cause (scars due to ischemia, cavernomas, vessel malformations, etc.). If impairments of consciousness occur during a focal seizure, it is referred to as complex-focal. The epileptic aura (= perceptions a few seconds before the seizure) defines focal epilepsies. These are typical characteristics of focal epileptic areas:

<table>
<thead>
<tr>
<th>Area</th>
<th>Characteristic</th>
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<tbody>
<tr>
<td>Temporal lobe epilepsy</td>
<td>The most frequent group of focal epilepsies; epigastric aura with following automotor externalizations: often hippocampus sclerosis, pharmacologically hard to adjust, often neurosurgical therapy is needed. The following process is typical: 1. Aura: visceral, also déjá-vu or jamais-vu. 2. Motor symptoms: automatisms, e.g.. smacking; stereotype symptoms, vegetative symptoms, paresthesia in smell and taste; changes in consciousness, motor disturbances (scuttling, wandering around). 3. State: re-orientation with amnesia concerning the seizure.</td>
</tr>
<tr>
<td>Frontal lobe epilepsy</td>
<td>Psychic aura, tonic/clonic seizures, Jackson-seizure (= march of convulsion): the cloni march over different body areas, versive seizures, aphasis seizures.</td>
</tr>
<tr>
<td>Parietal lobe epilepsy</td>
<td>Sensory aura, sensory (also marching) seizures, negative symptoms: apraxia, vertigo, aphasis.</td>
</tr>
<tr>
<td>Occipital lobe epilepsy</td>
<td>Visual aura, complex visual impressions or visual memories during the seizure; long lasting.</td>
</tr>
<tr>
<td>Benign focal epilepsy</td>
<td>Rolandic epilepsy, one-sided cloni with strong salivation (especially at night), halting of the seizure before adolescence (thus benign). Therapy: Sultiame, this form of epilepsy is idiopathic.</td>
</tr>
</tbody>
</table>

Generalized epilepsies

In cases of generalized epilepsies, a generalized pathology has to be assumed. Accordingly, the epileptic externalizations quickly affect the whole brain.

**Idiopathic-generalized forms of epilepsy**

The groups represent the greatest number of epilepsy occurrence. We distinguish between a series of individual diseases, of which the following are especially relevant for practice:
Childhood absence epilepsy (pyknolepsia)  
From the 3rd to 8th year of life forward, short absences, up to 100 seizures per day, good prognosis, therapy: **Ethosuximide.**

Juvenile absence epilepsy  
Similar to childhood absence epilepsy, but later onset and worse prognosis (roughly 40% are not permanently free of seizures); tonic-clonic grand mal seizures at waking up and especially later in the adult age.

Juvenile myoclonic epilepsy 'Janz syndrome,' 'impulsive petit mal'  
From the 12th to 20th year of life forward, myoclonic in the morning (especially at ungentle waking up), also bilateral myoclonic of the extremities (things are suddenly and jerkily thrown away), **astatic** and **tonic-clonic seizures.**

Grand mal epilepsy  
Generalized tonic-clonic seizures with great irregularity.

**Symptomatic or cryptogenic generalized forms of epilepsy**

Especially early-childhood brain damages like hypoxia or metabolic diseases are the main reason for the symptomatic generalized epilepsies. Often, the patients have decreased intelligence and are severely affected. The following are two important forms:

- **West syndrome:** Occurs in the first year of life. The seizure picture consists of infantile spasm (= short tonic cramp of the arms and legs in front of the body, former term: 'Blitz-Neck-Salaam'); bad prognosis, frequently progress into the Lennox-Gastaut syndrome; therapy: ACTH, steroids or benzodiazepines.

- **Lennox-Gastaut syndrome:** An epileptic encephalopathy; develops out of West syndrome or due to late generalized brain damage; seizure picture: astatic (falling) seizures, absences, generalized tonic-clonic externalizations.

**Diagnostic of Epilepsy**

An extensive anamnesis, and especially third-party anamnesis, is important for detection and assessment. Concerning instrument-based examination, EEGs, CAT and MRIs are used.

With an EEG, decelerations or changes and patterns typical for epilepsy can be identified. Respectively, whole generalized epilepsies often show changes in the whole brain area, focal epilepsies only show them in some leads. The amplitude and frequency of the leads are assessed in order to detect **spikes, spike-wave complexes** or **seizure patterns.**
It takes a lot of training and experience to correctly interpret EEGs. Beside a rest EEG, **provocation factors** (flickering light, hyperventilation, sleep deprivation) can be used to show epileptogenic potentials. Several important EEG findings with the respective epilepsy syndromes are:

- **Childhood absence epilepsy**: 3 Hz spike-wave complexes;
- **Juvenile absence epilepsy**: 3 Hz spike-wave complexes and polyspike waves;
- **Juvenile myoclonic epilepsy**: generalized polyspike waves;
- **West syndrome**: hypsarrhythmia (= irregular, high-amplitude activity, interictal, ictal flattening);
- **Lennox-Gastaut syndrome**: slow spike-wave complexes, slower than 2.5 Hz;
- **Creutzfeldt-Jakob disease**: tri-phasic waves.
Especially for the evaluation of the first seizure, with according considerations of differential diagnoses, imaging should be sought. In an emergency situation, the CT is quickly available. For better imaging of epileptogenic lesions, an MRI-examination can help.

### Therapy of Epilepsy Forms

The therapy is based on different approaches. An important aspect is lifestyle. On one hand, a decrease in seizure potential can be reached with good sleep hygiene or by quitting alcohol consumption. On the other hand, every epileptic has to be informed about possible restructuring of everyday measures: Can I perform my job as a window cleaner? Can I use my car or bike? What about swimming, cutting the hedge or working with the drilling machine?

Besides this, there are pharmacological, surgical and interventional therapy possibilities. The indication for therapy is individual.

While some patients experience very little impairing epileptic externalization and face continuous medicament intake rather with refusal, others can be very scared after a grand mal seizure and urgently need therapy. The indication for therapy is available...

- ...when diagnosing epilepsy.
- ...in cases of a higher risk for seizure after a first seizure.
- ...after a first seizure with quick necessary seizure protection.
- ...after a second seizure with intermediate seizure protection.
- ...in cases of problematic seizures (e.g., status epilepticus).
- ...with consent of the patient.

(according to Bauer & Neumann, 2008)
Medicamentous anticonvulsant therapy

The selection of the necessary anticonvulsant medication has to be deliberate and should follow the form of epilepsy, acuteness, possible comorbidity or pregnancy. Also, individual anticonvulsant medication options are differently tolerated. The following table gives a rough overview of the application areas of some frequently used anticonvulsants for seizure prophylaxis:

<table>
<thead>
<tr>
<th>Anticonvulsant</th>
<th>Daily dose</th>
<th>Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focal epilepsies</strong></td>
<td></td>
<td></td>
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<tr>
<td>Carbamazepine</td>
<td>400 – 1600 mg</td>
<td>Relatively secure in pregnancy; many side effects: enzyme induction, agranulocytosis, liver toxicity, hyponatremia, HRST, SIADH</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>200 – 600 mg</td>
<td>As intravenous emergency medication; difficult dosage due to auto-induction; high risk for withdrawal seizures; prophylaxis with vitamin D and calcium is recommended.</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>600 – 2400 mg</td>
<td>Hyponatremia</td>
</tr>
<tr>
<td><strong>Focal and generalized epilepsies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproate</td>
<td>600 – 2000 mg</td>
<td>Broad spectrum efficacy; CYP inhibition reinforces the effect of, e.g., Lamotrigin; side effects: liver toxicity, teratogenicity (neural tube defects); important for exams!!</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>1000 – 3000 mg</td>
<td>As intravenous emergency medication; quick effect; little interaction with other medicaments; side effects: fear, depressions, aggression.</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>100 – 400 mg</td>
<td>Folate inhibitor, mood elevating, can be prescribed during pregnancy; skin reactions (up to Stevens-Johnson syndrome) at too fast dosage increase.</td>
</tr>
<tr>
<td>Topiramate</td>
<td>100 – 400 mg</td>
<td>Carbonic anhydrase inhibitor (kidney stones), weight loss, cognitive impairments.</td>
</tr>
</tbody>
</table>

During therapy, routine blood level controls at **Phenytoin** and **Valproate** are recommended. Also, you should remember the following medication for clinical routine: **Ethosuximide** at absence epilepsies; Sulthiame at rolandic epilepsies or as additional medication at severe epileptic syndromes.

First aid concerning epileptic seizures

An acute epileptic seizure mostly terminates quickly and spontaneously. There is no special therapy needed. It is especially important to make sure that no collateral injuries develop due to surrounding objects or an uncontrolled fall.

**Note:** Renowned measures like the bite wedge or holding arms, legs or the head are obsolete nowadays.

If the seizure should not terminate spontaneously, the following level scheme is recommended:

1. **Benzodiazepines intravenously:** The first resort medication is Lorazepam, the second one is Diazepam. If intravenous medication is not possible, Diazepam can be given rectally or Lorazepam intranasally. Also, intramuscular application is very effective (according to some studies even equally effective) and can be routinely useful, especially if intravenous injection fails.
2. **Phenytoin intravenously as an alternative:** Phenobarbital or Valproate.
3. Narcotics with intensive care monitoring (Thiopental, Propofol).

Possibilities of epilepsy surgery

Surgical measures seek to eliminate the epileptogenic neuronal area. Of course, this can only work at focal epilepsies. Surgery is indicated if...

- ...pharmacological resistance is present (= more seizures after two appropriate anticonvulsive therapy approaches).
- ...the seizures are conceived as impairing and an increase in life quality is expected after the intervention.
- ...an appropriate motivation is present in the patient.
- ...the epileptogenic focus is well operable.
- ...no progressive neuronal disease is present.

Beside the respective procedure, there are non-resective ones like callosotomy (sectioning of the corpus callosum). At first, a partial (usually the anterior two thirds) sectioning is attempted. At seizure persistence, the complete sectioning of the corpus callosum can be performed as well. The goal is to section the interhemispheric pathways in order to prevent a generalizing spread of the seizure. This can be accompanied with severe cognitive deficits.

Interventional stimulus therapy of epilepsy

Via a pacemaker system, amygdalo-hippocampal or anterior-thalamic stimulation can occur. This can achieve a seizure reduction of up to 50 % (Vonck et al., 2002).

Even if an absolute therapy is not possible, many patients feel better if they are relieved from the pharmacological side effects, and the collateral psychiatric (e.g., depressive) impairments can be improved.

Therapy of status epilepticus

The status epilepticus is a neurological emergency. It is defined as an epileptic externalization which lasts longer than five minutes or presents as a series of seizures, between which consciousness is not regained.

Thus, status epilepticus can occur at every epileptic condition. There is the non-convulsive status epilepticus or the absence-status. The grand mal status is considered life threatening.

The therapy of the status epilepticus generally follows the coherent level scheme, which was mentioned above, concerning termination of an epileptic seizure. Only in cases of absences or myoclonic, phenytoin should not be given since it can worsen the situation.

Epilepsy while Driving

The greatest fear of affected people is the continuation of their usual life. Many fear the uncertainty of new seizures and the resulting impairments. Particularly, driving cars (of course also riding bikes, motorcycles or driving ships) is a relevant subject.

It is the duty of the treating physician to inform the patient about the respective impairments in traffic. Likewise, it is the medical duty to be familiar with the respective
legal guidelines: When owners of a driver’s license are affected, usually a preliminary withdrawal of the **driver’s license occurs**.

However, the driving ban is not absolute and definitive, but can be reversed depending on the further progression of the condition:

- If the first seizure occurred unprovoked, the driver’s license is returned after three to six months without seizures.
- If the first seizure occurred symptomatically or provoked, the driver’s license is returned after three months without seizures.
- If there is a second seizure, or if epilepsy has been diagnosed, the driver’s license is returned after a year without seizures (independently of the therapy course or the therapy type).
- If persisting epileptic seizures occur, the driver’s license is not returned as long as a significant risk for further seizures is present.

Commercial drivers with a truck driver’s license and/or for person transportation usually undergo a definite withdrawal of their driver’s license. If necessary, the person affected must change his/her job. If it can be proven that there was no seizure within five years without anti-epileptic treatment, the driver’s license can be returned.

If there is reason to believe that a driving ban is being violated, we have to consider reporting it to the police.

**Review Questions**

The correct answers can be found below the references.

1. **Which is the first-resort medication of the grand mal status in an emergency situation?**

   A. Intravenous injection of Lorazepam
   B. Intramuscular injection of Phenytoin
   C. Intravenous injection of Valproate
   D. Intramuscular injection of Levetiracetam
   E. Intramuscular injection of Diazepam

2. **In therapy with anticonvulsants, routine laboratory controls should be performed. Which of the following parameters is most likely an indicator for a relevant side effect of Carbamazepine?**

   A. Albumin
   B. CKMB
   C. Hb
   D. Sodium
   E. Amylase

3. **During a seizure, Mr. Smith had a visual angle deviation to the left. What does this say about the localization of the focus of the epilepsy?**

   A. Primarily, this is indicative of a localization of the epileptic focus in the left-sided basal ganglia.
   B. Primarily, this is indicative of a localization of the epileptic focus in the right cerebellar hemisphere.
   C. Primarily, this is indicative of a localization of the epileptic focus in the right-sided oculomotor nuclei.
D. Primarily, this is indicative of a localization of the epileptic focus in the left frontal lobe.

E. Primarily, this is indicative of a localization of the epileptic focus in the right frontal lobe.

References


**Correct Answers:** 1A, 2D, 3E

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