Inflammatory and immune-mediated polyneuropathies represent an important differential diagnosis of hereditary and acquired polyneuropathies. In this article, we will provide you with all the relevant facts concerning the Guillain-Barré syndrome, the Miller-Fisher syndrome, and the Elsberg syndrome. Also, we will cover the chronic-inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy with conduction blocks. Via the concise, selected preparation of the factual knowledge and through several learning tips, you will be perfectly prepared for your exams.

Definition of the Guillain-Barré Syndrome

Guillain-Barré Syndrome as Polyradiculoneuritis

The Guillain-Barré syndrome (GBS) is a polyradiculoneuritis, which can have an acute or a subacute course. It mostly occurs post-infectiously and is accompanied by a multifocal demyelination and axonal lesions of the peripheral nerves. The most frequent form in Europe is the acute inflammatory demyelinating polyneuropathy (AIDP) with
60-90%. Within days or up to 4 weeks, GBS reaches its maximum in terms of clinical manifestation.

Image: “Parts of a Neuron” by Phil Schatz. Licence: CC BY 4.0

Scarcer forms of the GBS are the Miller-Fisher syndrome (see below), the Elsberg syndrome, the acute motoric axonal neuropathy (AMAN), and the acute motoric and sensory axonal neuropathy (AMSAN). AMAN and AMSAN have highly acute courses with partially irreversible axonal damages. The chronic course of GBS is referred to as chronic-inflammatory demyelinating polyneuropathy (CIDP).

Epidemiology of the Guillain-Barré Syndrome

Incidence of the Guillain-Barré Syndrome

Note: In Europe, GBS is the most frequent form of an acute peripheral symmetrical paralysis (after poliomyelitis has almost completely disappeared).

The incidence of the Guillain-Barré syndrome amounts to 1-2 per 100,000 inhabitants. The incidence rate increases with age. Throughout all age groups, men are more frequently affected than women. The frequency of GBS increases with age, the peak of incidence is between the 20th and the 30th year of life.

Pathogenesis of the Guillain-Barré Syndrome

Molecular Mimicry Theory
People with GBS have already suffered earlier from a respiratory infection (especially with pathogen Mycoplasma pneumoniae), a gastrointestinal infection (especially with Campylobacter jejuni), or infections with the cytomegaly virus, varizella-zoster virus, or the Epstein-Barr virus.

The physiological immune reaction, which is primarily aimed at the pathogen, now also attacks the body’s own cells due to molecular mimicry. In this case, the myelin of the axonal membrane is affected. The molecular mimicry theory is best proven in the case of Campylobacter. However, the general pathogenesis of GBS has not been completely clarified yet.

**Note:** A previous infection is not necessarily present at GBS.

### Clinic of the Guillain-Barré Syndrome

#### Case Study of the Guillain-Barré Syndrome

**Case study:** A 35-year-old woman was prescribed the antibiotic roxithromycin due to a feverish infection of the paranasal sinus. Three days later, she developed quickly progressing weakness in all extremities and in the supply area of both rami of the facial nerve. She was then immediately transferred to the neurological department of a hospital. There, GBS was diagnosed. After initially unsuccessful treatment with immunoglobulins, she felt better after plasmapheresis. Still, a slight weakness of the facial rami remains. (see [Toxcenter](#))

**Note:** Clinical symptoms of GBS are a very popular topic in medical exams. **Attention:** In exam questions, the IMPP often only refers to acute polyradiculoneuritis in order to make the question more difficult.

### Classical Symptoms of Guillain-Barré Syndrome

**Cardinal symptom of GBS:** Flaccid, distally starting paresis, which rises in the course of the disease. Mostly, the paresis develops over several days. A development within hours or over weeks is not typical.

**Further symptoms**

- Loss of at least the distal muscular proprioceptive reflexes (from distal to
proximal), can be redeemable at the beginning of the disease
- Relative symmetry of the paresis
- Cranial nerve deficits (mostly facial nerve), sensatory deficits are rare
- Recovery after a **plateau phase** of 1-4 weeks
- GBS-suiting CSF findings: **cytoalbuminary dissociation**
- GBS-suiting electrophysiological findings
- No fever in the beginning of the neuropathy

Most patients die due to the participation of the vegetative nervous system. Partially, the patients need a temporary external pacemaker.

**Diagnostics of the Guillain-Barré Syndrome**

**Detecting the Gullain-Barré Syndrome**

The diagnostic algorithm consists of **anamnesis** (1-3 weeks previous respiratory infection, gastrointestinal infection), fitting **clinical findings** (quickly ascending flaccid paresis), and exclusion of differential diagnoses and **additional diagnostics**. The following diagnostic measures are important at GBS:

**CSF Puncture at GBS**
protein concentration, while the cell count is slightly increased or not increased at all. This phenomenon is referred to as **cytoalbuminary dissociation**.

**CAVE:** The change can tail the clinical symptoms, the protein concentration can, thus, be normal in the first week.

**Note:** CSF findings at GBS = protein ↑↑↑ (up to 10 g/l)

**Laboratory at GBS**

Determination of the antibodies IgG and IgM against gangliosides GM1, GD1a, GD1b and GQ1b, and campylobacter and mycoplasma serologies is performed.

**Neurography at GBS**

Typical signs of GBS in neurography are

- Elongated F-waves-latencies
- Decreased persistence of the F-waves
- Slowed distal motoric latency
- Decreased velocity of nerve conduction
- Conduction blocks (as a sign of demyelination)

**Electromyography at GBS**

Pathological spontaneous activity after 2-3 weeks as a sign of axonal participation.

**Examination of the Vegetative Nervous System at GBS**

- **Orthostatic reaction:** Sympathetic denervation is illustrated by an absent increase in heart frequency of 10-30/minute.
- **Heart frequency variability:** The patient inhales for 6 seconds and exhales for 6 seconds. Normally, a variability of the heart frequency of < 15 seconds/minute is present. If this variability cannot be observed, this suggests parasympathetic denervation.

**Differential Diagnoses of the Guillain-Barré Syndrome**

**Distinction From Spinal Diseases**

Atypical for GBS are symptom constellations like fever during the initial phase, asymmetry of the paresis, bladder disorders, severe sensory participation, and distinctly limited sensory levels, and significantly increased cell count in the CSF.

If these symptoms occur, one should consider spinal diseases like **cross section myelitis**, spinal masses, spinal ischemia, and spinal viral and bacterial inflammations.

**Therapy of the Guillain-Barré Syndrome**

The Guillain-Barré syndrome can be treated in both a symptomatic and a special causal manner. General causal therapy is not possible! It is still not clear if an antibiotic or
antiviral treatment against the generally treatable pathogens can positively influence the course of the disease via antigen elimination.

Special Causal Therapy of GBS

Since the auto-destructive antibodies are the cause of the disease, one tries to wash them out or to retain them. Therefore, one applies immunoglobulins over 5 days: 0.4 g/kg body weight/day. An alternative is plasmapharesis with daily elimination of the antibodies. This special causal therapy is performed if the walking distance and respiration of the affected is severely impaired.

Plasmapheresis: The “blood wash” is a technique which is used for the extracorporeal elimination of substances with great molecular weight. Those include: immunoglobulins, immune complexes, cryoglobulins, and endotoxins. The goal is to eliminate the pathogens and, thus, reverse the disease process. Besides the application at GBS, plasmapheresis is especially used at thrombocytopenic purpura, myasthenia gravis, and the Goodpasture-syndrome.

Symptomatic Therapy of GBS

As symptomatic therapy, the thrombosis prophylaxis and pneumonia prophylaxis (regular expectorating, vibration massage of the thorax) is used. If vital capacity drops below 25 % of the normal plasma level, one should perform mechanical ventilation. Occurring bradycardia and AV blocks II and III can be treated with a temporary pacemaker. Glucocorticoids are considered ineffective in the case of classical GBS!

For analgesic treatment of the neuropathic pain, antiphlogistics, antidepressants, antiepileptics, and weak opioids can be used.

Note: Supervision of respiration and cardiovascular functions is necessary. Mechanical ventilation should be performed prior to clinical decompensation. Paresthesia and pain also have to be treated accordingly. Furthermore, physiotherapy (position, breathing therapy, movement) is necessary during the acute phase.
Course and Prognosis of the Guillain-Barré Syndrome

Typical course of GBS:

- 2 weeks of aggravation
- 2 weeks plateau phase
- 2 weeks of symptom regression in reverse order

However, this chronological sequence only represents the most frequent course. Sometimes, patients with GBS also have to be treated in an intensive care unit for several months.

In ca. 1/3 of the patients, the symptoms do not completely regress. In very severe, therapy-resistant cases, tetraplegia and cranial nerve deficits can occur. Lethality of GBS amounts to ca. 3 %. If GBS remains progressive for some time, CIDP has to be considered (see below).

Unfavorable prognostic factors are:

- Old age
- Necessity for artificial respiration
- Presence of dominant axonal damages
- Quick progression of the symptoms

Variation of GBS: Miller-Fisher Syndrome

The Miller-Fisher syndrome represents a variation of the Guillain-Barré syndrome. The classical clinical symptom triad is:

- Ophthalmoplegia
- Ataxia
- Areflexia, associated with the detection of GQ1b-antibodies (ganglioside antibodies) in the serum

Weakness of the mimic muscles is also frequent. Sometimes, paresis of the extremities occurs.

In the CSF, an increase in protein can also be observed, anti-GQ1b-antibodies detection is positive in 90 % of the cases.

Distinction Features of GBS and the Miller-Fisher Syndrome

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<thead>
<tr>
<th></th>
<th>Guillain-Barré Syndrome</th>
<th>Miller-Fisher Syndrome</th>
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<tbody>
<tr>
<td>Paresis</td>
<td>Distally symmetrical, beginning at the feet</td>
<td>Outer eye muscles</td>
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<tr>
<td>Mainly affected nerves</td>
<td>Motoric</td>
<td>Sensory</td>
</tr>
<tr>
<td>Type of lesion</td>
<td>Demyelinating</td>
<td>Axonal</td>
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Variation of the GBS: Elsberg-Syndrome
Variation of GBS: Elsberg-Syndrome

The **Elsberg-syndrome**, the **radiculitis sacralis**, is also a variation of GBS. The Elsberg-syndrome sometimes also occurs after infections with herpes simplex, cytomegaly, and borreliosis. Characterizing symptoms are:

- Dysesthesia
- Paresthesia in the supply area of the peripheral nerves
- Voiding disorder and rectal dysfunction
- Sexual function disorders

**Note**: You should memorize the typical symptoms of the variations of GBS as they can become important for differential diagnostics exclusion.

Chronic GBS: Chronic-Inflammatory Demyelinating Polyneuropathy (CIDP)

**Chronic-inflamatory demyelinating polyneuropathy (CIPD)** describes the chronic course of GBS. However, CIPD occurs very rarely.

Pathogenesis of CIPD

Similar to GBS, pathogenesis of CIPD is not completely clear. One assumes that **humoral** and **cellular** factors of the immune response play a role. Like at GBS, the symptoms occur due to **de- and remyelination** of the greater fibers. However, axonal lesions leading to denervation are more frequent in CIPD.

Clinic of CIPD

As a definition, CIPD develops over the course of 8 weeks. Progressively, distally, and proximally, symmetric **muscle weakness** occurs and can even lead to the loss of muscular proprioceptive reflexes. Sensory disorders can also occur. The vegetative nervous system, which is severely affected at GBS, is less severely affected at CIPD.

Frequency distribution of **neurological deficits**:

- **Motoric deficits**: 94 %
- **Paresthesia**: 64 %
- **Cranial nerve participation**: 2-32 %

Diagnostic of CIPD

Slowing down of nervous conductivity and decrease in the compound action potential in electromyography show both demyelinating and axonal participation. F-waves are decreased or absent. Just like in the case of GBS and the Elsberg-syndrome, the protein concentration in the CSF is increased.

Therapy of CIPD

Concerning therapy, there is a distinct difference to the acute GBS-therapy: At CIPD, steroids are used. Steroids decrease the expression of pro-inflammatory cytokines and inhibit T-cell-production. The initial dose is 100 mg prednisone (consider osteoporosis prophylaxis!), which is gradually reduced in the course and replaced by permanent
Variant of GBS: Multifocal Motoric Neuropathy (MMN)

MMN is an asymmetric variation of CIPD. Here, only the motoric fibers are affected. Clinically, asymmetric reflex deficits and muscle weakness are typical. Since the second motor neuron is affected, the occurrence of atrophies and fasciculations is possible (often, the motoric part of the ulnar nerve is affected initially).

Diagnostic findings at MMN:

- **Electrophysiology:** isolated conduction blocks
- **Serology:** in one third of the patients, GM1-antibodies are increased
- **CSF:** protein is normal or slightly increased

Therapeutically, the short-term application of cyclophosphamides or immunoglobulins is reasonable.

**Note:** The distinction of MMN from amyotrophic lateral sclerosis (ALS) is particularly important since the latter is significantly less influenceable than MMN. Typically, the patients describe the beginning of the weakness in one hand with a slow spread of the symptoms to further muscle groups and the infestation of further extremities. These initial descriptions exhibit a particularly striking similarity to the patients with an ALS-diagnosis.

Review Questions

The correct answers can be found below the references.

1. Which life-threatening complication is especially typical for polyradiculitis (GBS-syndrome)?
   - A. Brain stem function disorders with vigilance impairments and central respiratory disorder
   - B. Electrolyte imbalance with cerebral seizures as a consequence
   - C. Systemic toxin accumulation in liver and kidneys as a consequence of sepsis and shock
   - D. Disorders of the autonomic cardiac innervation with the risk to develop dysrhythmia
   - E. Acute bleedings in the subarachnoid cavity

2. Which finding is least characteristic for Miller-Fisher syndrome?
   - A. Severely increased protein concentration in the CSF
   - B. Ophthalmoplegia
   - C. Loss of muscular proprioceptive reflexes
   - D. Ataxia
   - E. Epileptic seizures

3. What is no typical sign of Guillain-Barré syndrome in neurography?
   - A. Elongated F-wave-latencies
   - B. Increased persistence of the F-waves
C. Slowing down of the distal motoric latency
D. Decreased velocity of nerve conduction
E. Conduction block (as a sign of demyelination)

References


**Correct answers:** 2D, 2E, 3B

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Notes