Guillain-Barré Syndrome (GBS): Typical and Atypical Clinical Presentations
Classical Guillain-Barré Syndrome (GBS)

- As described by Landry in 1859¹
  - Ascending paralysis
  - Preceded by infection
  - Followed by respiratory insufficiency and death

- Gullian, Barré and Stroll in 1916²
  - Syndrome de radiculonévrite with a better prognosis
  - Increased protein without cellular reaction in the spinal fluid
  - Motor difficulties, areflexia, paresthesias

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GBS Background

GBS is an immune-mediated polyneuropathy with acute or subacute onset and progression for up to 4 weeks followed by slow recovery¹

- GBS responds to immunomodulation with IVIG or plasmapheresis
- GBS affects approximately 0.8–1.9 out of 100,000 people per year with regional differences in the distribution of GBS subtypes

Further details of the pathophysiology and the treatment of GBS are provided in other PNE presentations.

GBS: Guillain-Barré Syndrome, IVIG: intravenous immunoglobulin.
Figure reprinted from The Lancet, Volume 388, Willison HJ, Jacobs BC and van Doorn PA; Guillain-Barré syndrome, pp. 717–27, Copyright 2016, with permission from Elsevier.
Classification of GBS

Clinically based on symptoms

- **Distribution of symptoms:** polyneuropathy, paraplegia, cranial nerves, other
- **Quality of symptoms:** Sensory, motor, ataxia

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![Diagram of Classification of GBS](image)

Shaded areas indicate patterns of weakness. ‘Zzzzz’ indicates hypersomnolence

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GBS: Guillain-Barré Syndrome.


Classification of GBS

Electrophysiological

- Demyelinating
- Axonal
- Sometimes repeated studies are needed

Autoantibodies

- Disease associated or disease causing autoantibodies against gangliosides

GBS: Guillian-Barré Syndrome.

Figure reprinted from The Lancet, Volume 388, Willison HJ, Jacobs BC and van Doorn PA; Guillain-Barré syndrome, pp. 717–27, Copyright 2016, with permission from Elsevier.
Overview of GBS Subtypes

- Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP)
- Acute Motor Axonal Neuropathy (AMAN)
- Acute Motor and Sensory Neuropathy (AMSAN)
- Miller Fisher Syndrome (MFS)
- Pharyngeal cervical brachial variant
- Miscellaneous and Mimics

GBS: Guillain-Barré Syndrome.
Typical or classical GBS (sensory motor, AIDP)¹

Common features (not specific for the classical GBS)

- Acute or subacute onset with maximal disability reached within 4 weeks of onset
- Majority of patients report an antecedent event within 28 days of onset
- Reflexes are lost or reduced

Clinical symptoms and findings

- Bilateral and symmetrical loss of sensation and weakness (usually starting in the feet and spreading upward to include arms, cranial nerves (facial weakness), and in some cases the respiratory function)
- Pain and autonomic symptoms are frequent

Electrophysiological classification

- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)

Antibodies

- Non-specific and rarely diagnostic important

GBS: Guillian-Barré Syndrome, AIDP: Acute inflammatory demyelinating polyneuropathy.
Acute Motor Axonal Neuropathy (AMAN)\(^1\)

**Common Features**

- Acute or sub-acute onset with maximal disability reached within 4 weeks of onset
- Majority of patients report an antecedent event within 28 days of onset
- Reflexes are lost or reduced

**Clinical Symptoms and Findings**

- Bilateral and symmetrical pure motor symptoms
- Often very fast progression of weakness, can include cranial nerves and respiratory function
- Some reports have indicated poor prognosis in AMAN

**Electrophysiological Classification**

- Motor axonal neuropathy

**Antibodies**

- GM1a, GM1b, GD1a, GalNAC-GD1a

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AMAN: Acute Motor Axonal Neuropathy, GM/GD: Ganglioside M1a, M1b, D1a, GalNAC-GD1a: N-acetylgalactosaminyl ganglioside D1a.

Acute Motor Axonal Neuropathy (AMAN)¹

AMAN is the immunologically most well characterized subtype of GBS¹-²

- Antibody-mediated autoimmunity
- Molecular mimicry between lipopolysaccharides on Campylobacter jejuni bacteria and axons
- Pathogenic GM1 or GD1a autoantibodies induce axonal injury mainly at the nodes of Ranvier and nerve terminals by activating complement and recruiting macrophages


Figure reprinted from Microbes and Infection, Volume 4, Schwerer B. Antibodies against gangliosides: a link between preceding infection and immunopathogenesis of Guillain Barré syndrome, pp. 373–84, Copyright 2002, with permission from Elsevier. https://www.sciencedirect.com/journal/microbes-and-infection.
### Acute Motor and Sensory Neuropathy (AMSAN)¹

#### Common Features
- Acute or sub-acute onset with maximal disability reached within 4 weeks of onset
- Majority of patients report an antecedent event within 28 days of onset
- Reflexes are lost or reduced

#### Clinical Symptoms and Findings
- Bilateral and **symmetrical loss of sensation and weakness**
- Clinically it resembles AMAN, but includes sensory symptoms and loss

#### Electrophysiological Classification
- Acute motor and sensory neuropathy

#### Antibodies
- GM1, GD1a

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AMSAN: Acute Motor and Sensory Neuropathy, AMAN:Acute Motor Axonal Neuropathy, GM/ GD: Ganglioside M1, D1a..

Miller Fisher Syndrome¹

Common Features
- Acute or sub-acute onset with maximal disability reached within 4 weeks of onset
- Majority of patients report an antecedent event within 28 days of onset
- Reflexes are lost or reduced

Clinical Symptoms and Findings
- Ataxia, ophthalmoplegia, areflexia
- Other cranial nerves can be involved
- Spinal fluid often normal
- Some patients will subsequently develop generalized GBS (MFS-GBS overlap syndrome)
- There is also an overlap between MFS and Bickerstafs brain stem encephalitis where in addition patients will reveal CNS features including seizures and somnolence²

Electrophysiological Classification
- Normal or equivocal findings of abnormal sensory nerve conduction

Antibodies
- GQ1b antibodies are highly specific and sensitive

GBS: Guillian-Barré Syndrome, MFS: Miller Fisher Syndrome, CNS: central nervous system, GQ1b: Ganglioside Q1b.

Pharyngeal cervical brachial variant

**Common Features**
- Acute or sub-acute onset with maximal disability reached within 4 weeks of onset
- Majority of patients report an antecedent event within 28 days of onset

**Clinical Symptoms and Findings**
- Distinct pattern of weakness in:
  - Pharyngeal (dysphagia & dysarthria)
  - Cervical (neck)
  - Facial
  - Proximal upper limb
- Discrete sensory symptoms

**Electrophysiological Classification**
- Often normal or equivocal findings of sensory motor axonal neuropathy

**Antibodies**
- GT1a, GQ1b, GD1a

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GT/GQ/GD: Ganglioside T1a, Q1b, D1a.
Atypical presentations of these rare subtypes are very rare, but do occur

There are many examples including:

- Hyper-reflexic syndromes
- Asymmetrical syndromes
- Paraparetic syndromes
- Other incomplete syndromes; for example MFS without ataxia

### Differential diagnosis for classic GBS

<table>
<thead>
<tr>
<th>Viral (Enterovirus &amp; West Nile virus)</th>
<th>Neuromuscular junction disorders (MG &amp; botulism)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal cord (Transverse myelitis, spinal stenosis &amp; spinal artery occlusion)</td>
<td>Brain stem strokes (basilar artery occlusion)</td>
</tr>
<tr>
<td>Neuromuscular junction disorder (MG, LE myasthenic syndrome &amp; botulism)</td>
<td>Rhombencephalitis Infectious, autoimmune, or malignant causes</td>
</tr>
<tr>
<td>Muscle disorders (Acute myositis, peridoc paralysis &amp; functional infections)</td>
<td>Basal Meningitis Infectious, autoimmune (sarcoid), or malignant</td>
</tr>
<tr>
<td>Critical illness neuropathy &amp; myopathy</td>
<td></td>
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<tr>
<td>Vasculitic and toxic or metabolic neuropathies</td>
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# Overview of GBS Subtypes

## GBS Subtypes, clinical features and relevant antibodies

<table>
<thead>
<tr>
<th>GBS Subtypes</th>
<th>Main clinical features</th>
<th>NCS findings</th>
<th>Antibodies*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIPD</td>
<td>Sensorimeter GBS, often combined with cranial nerve deficits</td>
<td>Demyelinating polyneuropathy</td>
<td>Various</td>
</tr>
<tr>
<td>AMAN</td>
<td>Pure motor GBS; cranial nerves rarely affected</td>
<td>Axonal polyneuropathy, sensory action potential normal</td>
<td>GM1a, GM1b, GD1a, GalNAc-GD1a</td>
</tr>
<tr>
<td>AMSAN</td>
<td>Resembles severe AMAN, but sensory fibres are affected, leading sensory deficits</td>
<td>Axonal polyneuropathy, sensory action potential reduced or absent</td>
<td>GM1, GD1a</td>
</tr>
<tr>
<td>MFS</td>
<td>Ataxia, ophthalmoplegia, areflexia</td>
<td>Normal in most patients; discrete changes in sensory conduction or H-reflex may be present</td>
<td>GQ1b, GT1a</td>
</tr>
<tr>
<td>Pharyngeal-cervical brachial variant</td>
<td>Prominent weakness of oropharyngeal, facial, neck and shoulder muscles</td>
<td>Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern</td>
<td>GT1a&gt;GQ1b &gt;&gt;GD1a</td>
</tr>
</tbody>
</table>


Geographical variation of GBS subtypes

Data from the International GBS Outcome Study (IGOS)¹

Summary

- There is no gold standard test for GBS, but the diagnosis is based on a collection of typical symptoms, findings on examination, and supportive tests (CSF, nerve conduction, and antibody tests).
- Therefore, to make the correct diagnosis and initiate appropriate treatment in time, it is important to know the presentation of typical GBS as well as the features of atypical but clinically distinct variants and subtypes.
- The variants of GBS can be related to factors such as geographical location, preceding events, and age, etc.
- MFS has a good prognosis, whereas the axonal forms of GBS (AMAN and AMSAN) have been associated with poor prognosis.
- The understanding of the relationship between outcome and subgroups in GBS will be further explored with the IGOS study.