PolyNeuro exchange

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

Classical Guillian-Barré Syndrome (GBS)

- As described by Landry in 1859[1]
  - Ascending paralysis
  - Preceded by infection
  - Followed by respiratory insufficiency and death
- Gullian, Barré and Stroll in 1916[2]
  - Syndrome de radiculonévrite with a better prognosis
  - Increased protein without cellular reaction in the spinal fluid
  - Motor difficulties, areflexia, paresthesias

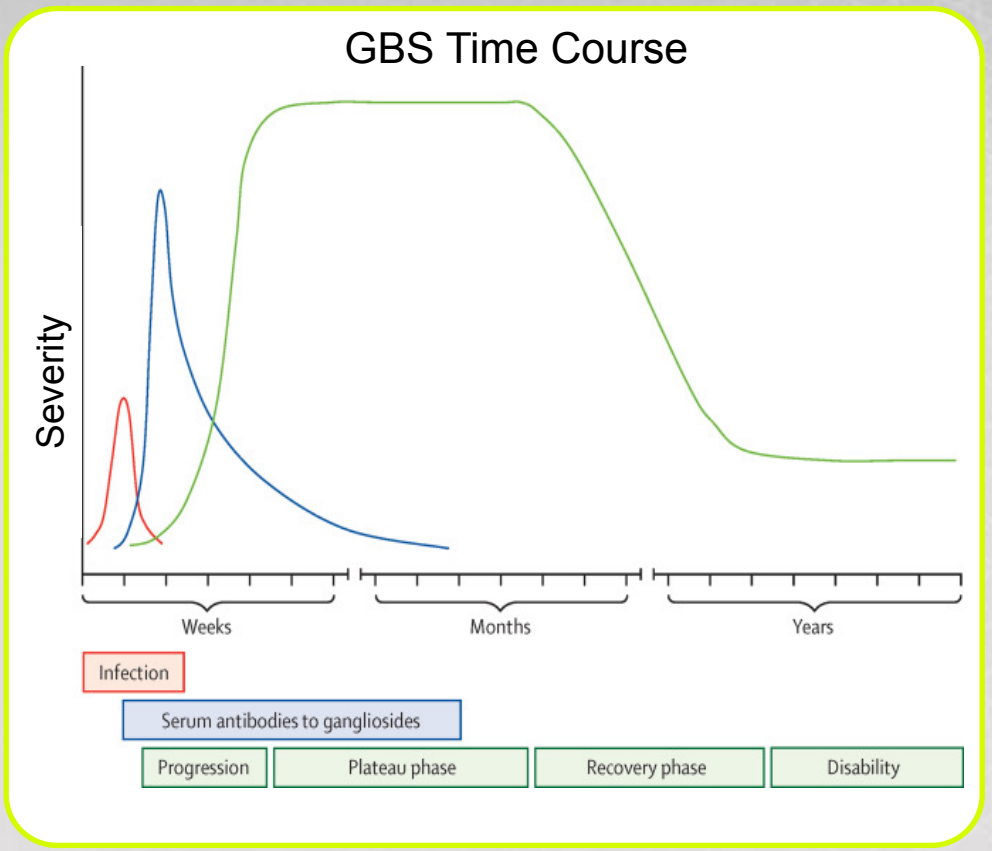
1. Landry O. Gazette Hebdomadiare de Médecine et de Chirurgie. 1859;6:472–74 et 1859;6:486–88.
2. Gullian G, Barré JA & Strohl A. Bulletin of the Society of Medicine Hospital of Paris. 1916;40:1462–70.

GBS Background

GBS is an immune-mediated polyneuropathy with acute or subacute onset and progression for up to 4 weeks followed by slow recovery[1]

- GBS responds to immuno-modulation 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



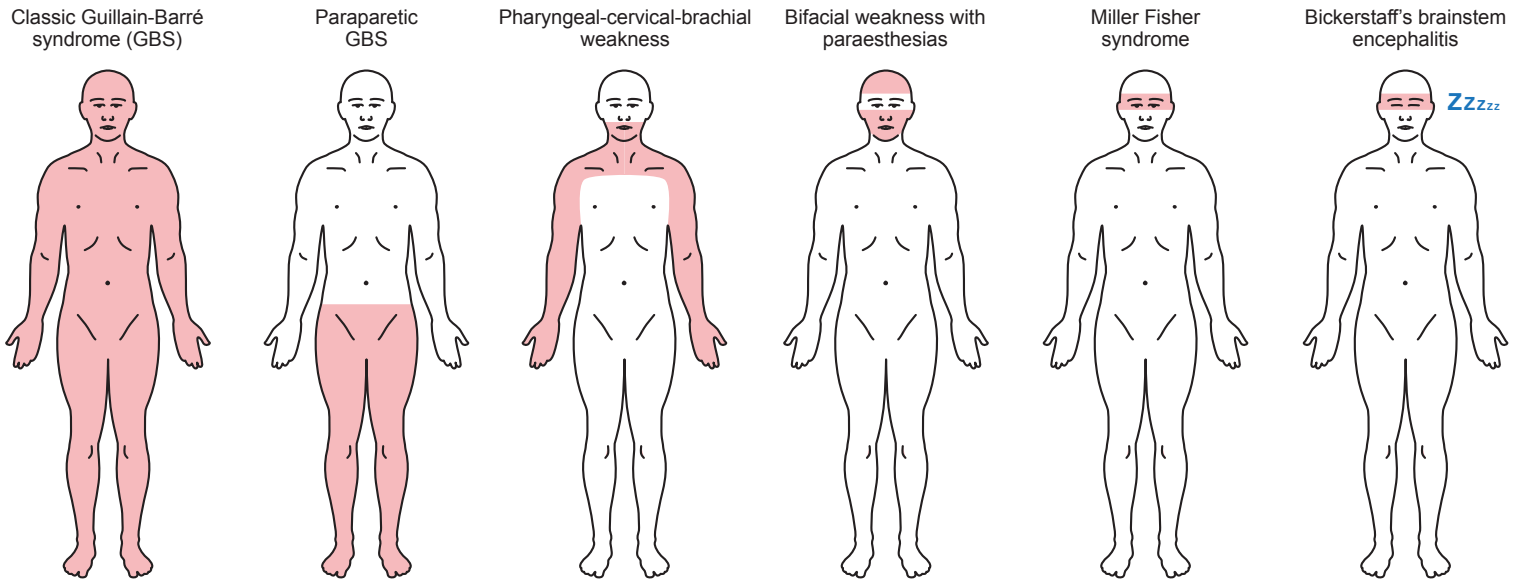
GBS: Guillian-Barré Syndrome, IVIG: intravenous immunoglobulin.

1. Willison HJ *et al*. Lancet. 2016;388;717–27.

Classification of GBS[1]

Clinically based on symptoms

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



Shaded areas indicate patterns of weakness. 'Zzzzz' indicates hypersomnolence

GBS: Guillian-Barré Syndrome.

1. Wakerley BR & Yuki N. Pract Neurol. 2015;15:90–9.

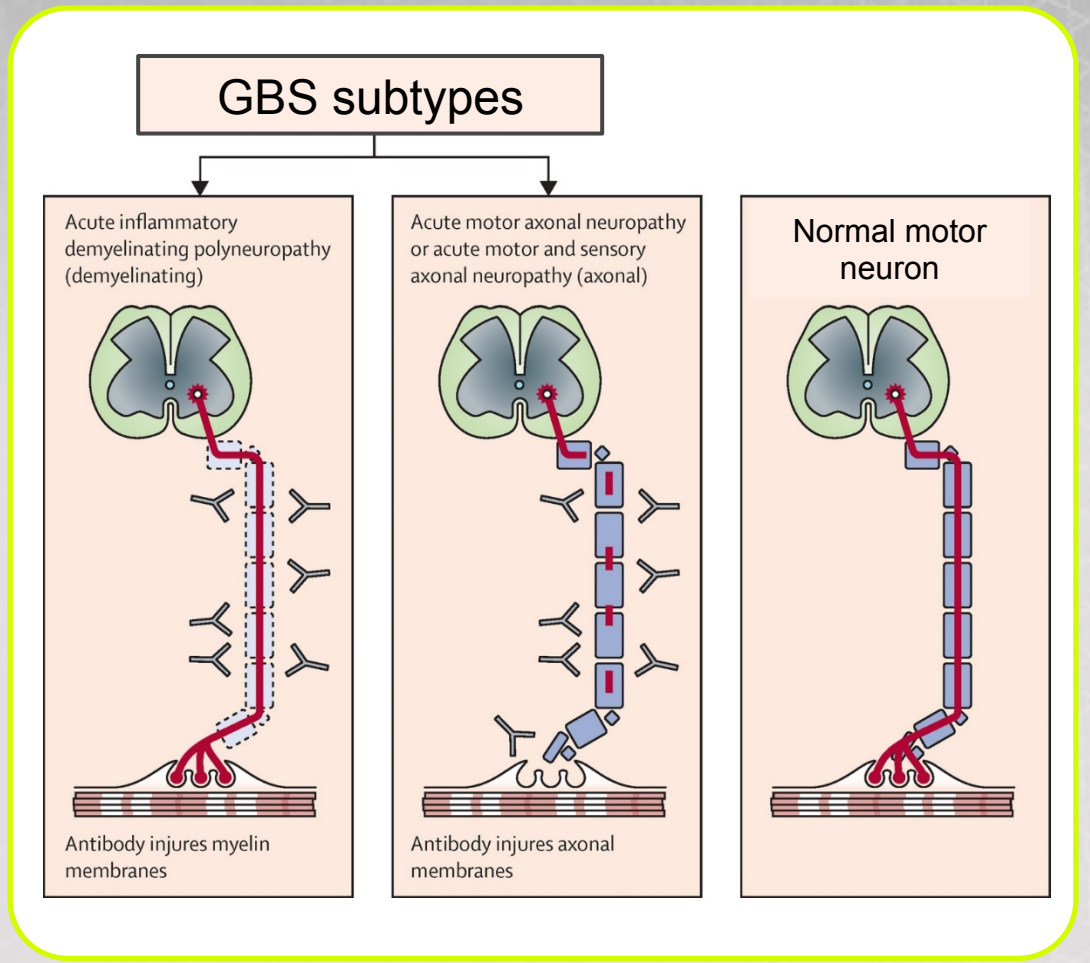
Classification of GBS[1]

Electrophysiological

- Demyelinating
- Axonal
- Sometimes repeated studies are needed

Autoantibodies

- Disease associated or disease causing autoantibodies against gangliosides



GBS: Guillian-Barré Syndrome.

1. Willison HJ *et al.* Lancet. 2016;388;717–27.

Overview of GBS Subtypes[1]

- 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: Guillian-Barré Syndrome.

1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.

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.

1. Willison HJ *et al.* Lancet. 2016;388;717–27.

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

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

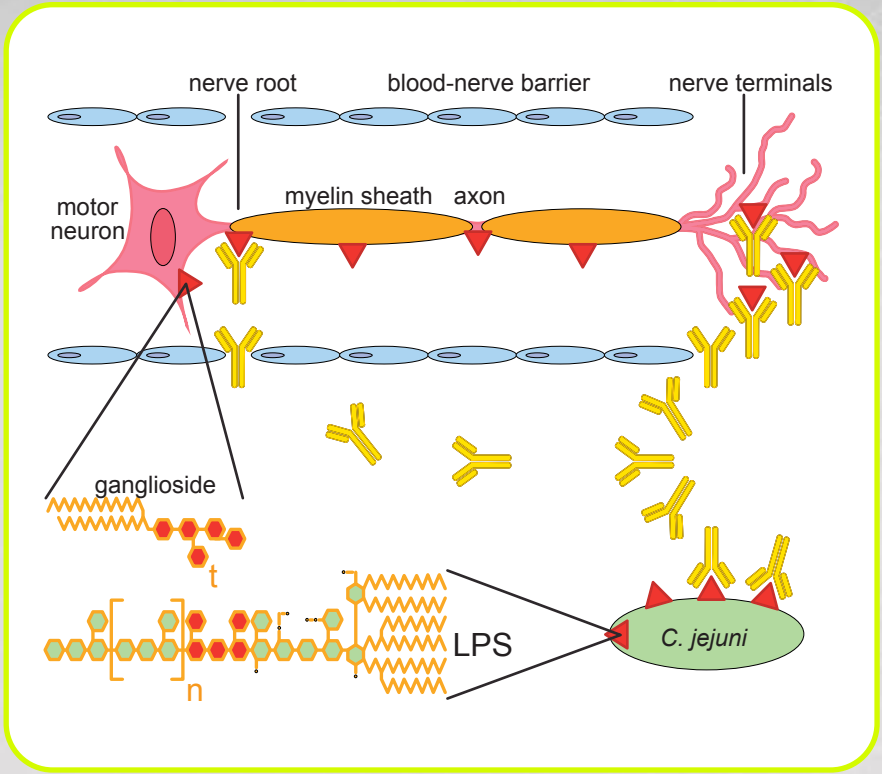
1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.

Acute Motor Axonal Neuropathy (AMAN)[1]

A model for autoimmune response in GBS

AMAN is the immunologically most well characterized subtype of GBS[1-2]

- 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



GBS: Guillian-Barré Syndrome, AMAN: Acute Motor Axonal Neuropathy, GM1: Ganglioside M1; LPS: lipopolysaccharide.

1. Schwerer B. Microbes Infect. 2002;4(3):373–84.
2. Willison HJ *et al.* Lancet Neurol. 2016;388;717–27.

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

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

1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.

Miller Fisher Syndrome[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

- **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 somnolence[2]

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.

1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.
2. Wakerley BR & Yuki N et al. Pract Neurol. 2015;15:90–9.

Pharyngeal cervical brachial variant[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

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

GT/GQ/GD: Ganglioside T1a, Q1b, D1a.

1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.

Miscellaneous and Mimics[1]

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	Differential diagnosis for MFS, Bickerstaff's brainstem encephalitis and pharyngeal-cervical-brachial GBS (brain stem)
Viral (Enterovirus & West Nile virus)	**Neuromuscular junction disorders** (MG & botulism)
Spinal cord (Transverse myelitis, spinal stenosis & spinal artery occlusion)	**Brain stem strokes** (basilar artery occlusion)
Neuromuscular junction disorder (MG, LE myasthenic syndrome & botulism)	**Rhombencephalitis** Infectious, autoimmune, or malignant causes
Muscle disorders (Acute myositis, peridoc paralysis & functional infections)	**Basal Meningitis** Infectious, autoimmune (sarcoid), or malignant
Critical illness neuropathy & myopathy	
Vasculitic and toxic or metabolic neuropathies	

MFS: Miller Fisher Syndrome, MG: Myasthenia Gravis, LE: Lambert Eaton.

1. Wakerley BR & Yuki N et al. Pract Neurol. 2015;15:90–9.

Overview of GBS Subtypes

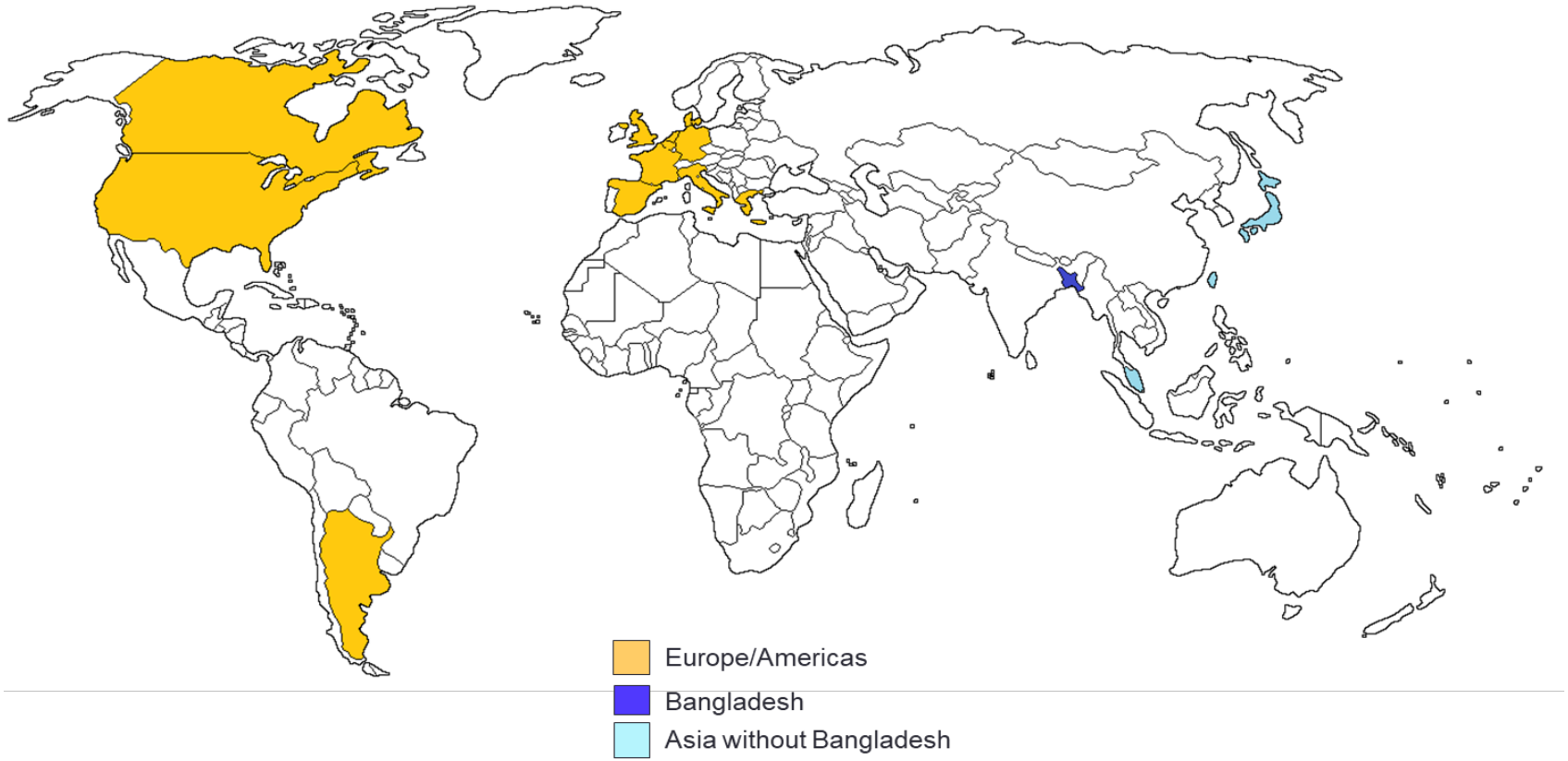
GBS Subtypes, clinical features and relevant antibodies[1]			
GBS Subtypes	**Main clinical features**	**NCS findings**	**Antibodies***
AIPD	Sensorimeter GBS, often combined with cranial nerve deficits	Demylelinating polyneuropathy	Various
AMAN	Pure motor GBS; cranial nerves rarely affected	Axonal polyneuropathy, sensory action potential normal	GM1a, GM1b, GD1a, GalNAc-GD1a
AMSAN	Resembles severe AMAN, but sensory fibres are affected, leading sensory deficits	Axonal polyneuropathy, sensory action potential reduced or absent	GM1, GD1a
MFS	Ataxia, ophthalmoplegia, areflexia	Normal in most patients; discrete changes in sensory conduction or H-reflex may be present	GQ1b, GT1a
Pharyngeal-cervical brachial variant	Prominent weakness of oropharyngeal, facial, neck and shoulder muscles	Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern	GT1a>GQ1b >>GD1a

GBS: Guillian-Barré Syndrome. AIDP: Acute inflammatory demyelinating polyneuropathy, AMAN:Acute Motor Axonal Neuropathy, AMSAN: Acute Motor and Sensory Neuropathy, MFS: Miller Fisher Syndrome.

1. Van den Berg B *et al*. Nat. Rev Neurol. 2014;10(8):469–82.

Geographical variation of GBS subtypes

Data from the International GBS Outcome Study (IGOS)[1]



1. https://gbsstudies.erasmusmc.nl/participating-centers-worldwide.

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

GBS: Guillian-Barré Syndrome, AMAN: Acute Motor Axonal Neuropathy, AMSAN: Acute Motor and Sensory Neuropathy, MFS: Miller Fisher Syndrome, IGOS: International GBS Outcome Study.