# Table of Contents

## Summary

### Basics

- Definition 4
- Epidemiology 4
- Aetiology 4
- Pathophysiology 5
- Classification 6

### Prevention

- Secondary prevention 7

### Diagnosis

- Case history 8
- Step-by-step diagnostic approach 8
- Risk factors 11
- History & examination factors 13
- Diagnostic tests 16
- Differential diagnosis 20
- Diagnostic criteria 21

### Treatment

- Step-by-step treatment approach 25
- Treatment details overview 27
- Treatment options 29
- Emerging 35

### Follow up

- Recommendations 36
- Complications 36
- Prognosis 38

### Guidelines

- Diagnostic guidelines 39
- Treatment guidelines 39

### References

- 40

### Disclaimer

- 51
<table>
<thead>
<tr>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>◊ Acute inflammatory polyneuropathy classified according to symptoms and divided into axonal and demyelinating forms.</td>
</tr>
<tr>
<td>◊ Two-thirds have a history of gastroenteritis or influenza-like illness weeks before onset of neurological symptoms.</td>
</tr>
<tr>
<td>◊ Neurophysiology is confirmatory and is abnormal in 85% of patients, even early in the disease.</td>
</tr>
<tr>
<td>◊ Up to 30% will develop respiratory muscle weakness requiring ventilation.</td>
</tr>
<tr>
<td>◊ LP is useful, and the classic finding is elevated protein with normal cell count (albuminocytological dissociation).</td>
</tr>
<tr>
<td>◊ Treatment combines supportive and disease-modifying therapy (plasma exchange or high-dose immunoglobulin).</td>
</tr>
</tbody>
</table>
Guillain-Barre syndrome (GBS) is a type of acute inflammatory neuropathy.[1] [2] It is a clinically defined syndrome characterised by motor difficulty, absence of deep tendon reflexes, paraesthesias without objective sensory loss, and increased CSF albumin with absence of cellular reaction (albuminocytological dissociation).[1] [3] Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most commonly encountered variant.[4]

**Epidemiology**

GBS is identified throughout the western hemisphere without geographical clustering and minor seasonal variations. Population-based studies give crude mean annual incidence rates varying from 0.6 to 1.9 per 100,000 population. Few outbreaks have been reported, including the 1976 outbreak in the US after the swine influenza programme (although the link between the influenza immunisation and incidence of GBS is unclear).[10] [11]

Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most common form in western countries and accounts for 85% to 90% of cases.[12] [13] This condition occurs at all ages, although rarely in infancy. Youngest and oldest ages reported are 2 months and 95 years old, respectively.[14] [15] The mean age of onset is approximately 40 years, possibly with a male predominance.[11] [16] There is no consistent age predominance secondary to lack of concordance between studies.[16] GBS is the most common cause of acute flaccid paralysis in children.[17] Acute motor axonal neuropathy (AMAN) is frequently diagnosed in Japan and China, particularly in young people. It occurs more frequently during summer.[18] Sporadic AMAN worldwide affects 10% to 20% of patients with GBS.[19] Miller-Fisher syndrome affects between 5% and 10% of GBS patients in western countries, but it is more common in eastern Asia, with 25% occurring in Japan and 19% in Taiwan.[20] [21]

**Aetiology**

This condition is characterised by an immune-mediated attack on myelin sheath or Schwann cells of sensory and motor nerves. This is due to cellular and humoral immune mechanisms, frequently triggered by an antecedent infection. Although genetic predisposition has not been fully established, the acute motor axonal neuropathy (AMAN) type of the disease occurs more commonly in Japan and China than in North America or Europe. Polymorphisms in macrophage mediators (MMP-9 and TNF-alpha) have been associated with severe weakness and poorer outcome in GBS patients.[22]

Two-thirds of patients have had infections within the 6 weeks before symptom onset, most commonly URTI and gastroenteritis. The acute infectious illness is usually viral (CMV, EBV, hepatitis B or C, HIV) or sometimes bacterial (Campylobacter jejuni, Mycoplasma species). The most commonly identified infectious triggers include C jejuni (in 13% to 39% of cases), CMV (5% to 22%), EBV (1% to 13%), and Mycoplasma pneumoniae (5%).[23] [24] [25] C jejuni infection precedes about 60% to 70% of AMAN and acute motor-sensory axonal neuropathy (AMSAN) cases and up to 30% of acute inflammatory demyelinating polyradiculoneuropathy (AIDP) cases.[26] [27] Immunisations have been proposed to trigger GBS, including the no longer used swine influenza vaccines (US in 1976) and the rabies vaccine containing brain material.[28] [29] However, an epidemiology study found no evidence of increased risk of GBS after seasonal influenza immunisation.[30] This study looked at 15 years of the General Practice Research
Guillain-Barre syndrome

database in the UK and found that the relative incidence of GBS within 90 days of influenza immunisation was 0.76 as opposed to 7.35 within 90 days of influenza-like illness.[30]

Since 2013, several cases of GBS have been reported following the outbreak of Zika virus,[31] [32] possibly secondary to molecular mimicry, with a proposed putative role for gangliosides.[32] Similarly, several other mosquito-borne viral infections such as dengue, chikungunya, and Japanese encephalitis have been linked to GBS.[33] [34] [35] [36] [37]

Pathophysiology

There is some evidence to suggest that this condition is an autoimmune disorder. Antibodies to gangliosides play an important role. They trigger an attack on various components of peripheral nerve myelin and sometimes even the axons.[38] [39] The mechanism for this is unclear but may be a consequence of molecular mimicry, whereby antibodies or T cells stimulated by antigenic epitopes on the infecting microbe cross-react with neural epitopes.[40] Host-generated antibodies against GM1-, GD1a-, GalNac-Gd1a-, and GD1b-related gangliosides are strongly associated with a subtype of AMAN, AMSAN, and Miller-Fisher syndrome, respectively.[15] [18] [41] [42] [43] [44] [45] AMAN is strongly associated with antibodies against GM1, GD1a, GalNac-GD1a, and GD1b.[41] [42] [46] [47]

Pure sensory GBS may be associated with antibodies to GD1b.[9] Ganglioside complexes have been found to influence the phenotype. Antibodies against GD1a/GD1b or GD1b/GT1b may cause severe GBS, and antibodies against complexes containing QG1b or GT1a are more likely to cause ophthalmoplegia in both GBS and Fisher syndrome patients.[48] However, large-scale prospective studies are required to confirm this. Antibodies against neurofascin, a protein present at the node of Ranvier, have been described in a small proportion (4%) of patients with GBS.[49]

In *C. jejuni*-related infections, carbohydrate mimicry between the bacterial capsular lipooligosaccharide and specific myelin gangliosides and glycolipids is thought to induce antibodies against myelin.[50] [51]

An immune cascade occurs in AIDP with early lymphocytic infiltrates in spinal roots and peripheral nerves. Subsequent macrophage-mediated segmental stripping of myelin occurs.[15] This leads to segmental demyelination and mononuclear cellular infiltration.[4] Segmental loss of the insulating properties causes profound defects in the propagation of electrical nerve impulses, resulting in conduction block and the functional correlate of flaccid paralysis.[52] Once the immune reaction stops, repair and remyelination promptly begin, which correlate with a quick and, in most cases, complete recovery from the flaccid paralysis.[15]

AMAN can be differentiated from AIDP by autopsy findings of axonal denervation of motor and sensory nerves with no demyelination and minimal inflammation.[53] [54] The earliest demonstrable pathological change seems to be the binding of IgG and activated complement components to axolemma at nodes of Ranvier in large motor fibres.[55] Macrophages become attracted to these nodes and track underneath the detached myelin lamellae along the periaxonal space. This dissects the axon from the overlying Schwann cell and compact myelin. Axolemmas in contact with invading macrophages are focally destroyed, while axons show progressive degenerative changes to the point of total disintegration.[54] *C. jejuni* strains associated with the AMAN pattern of GBS are known to have GM1-like epitopes in the liposaccharide membrane.[7] Pathological studies suggest severe and selective loss of terminal motor axons, whereas the distal sensory fibres are completely intact.[56] [57]
**Classification**

**Variants of Guillain-Barre**[2]

GBS is classified according to symptoms and is divided into axonal and demyelinating forms.

- Sensory and motor: AIDP (most common) or acute motor-sensory axonal neuropathy (AMSAN).
- Motor: acute motor demyelinating neuropathy (AMDN) or acute motor axonal neuropathy (AMAN)
  - Miller-Fisher syndrome: ophthalmoplegia, ataxia, and areflexia (also referred to as Fisher's syndrome).
- Bickerstaff's brainstem encephalitis (BBE): similar to Miller-Fisher syndrome but also includes altered consciousness (encephalopathy) or long tract signs (hyper-reflexia), or both.[5]
- Pharyngeal-cervical-brachial: acute arm weakness, swallowing dysfunction, and facial weakness.[6]
- Acute pandysautonomia: diarrhoea, vomiting, dizziness, abdominal pain, ileus, orthostatic hypotension and urinary retention, bilateral tonic pupils, fluctuating heart rate, decreased sweating, salivation, and lacrimation.[7] [8]
- Pure sensory: acute sensory loss, sensory ataxia, and areflexia but no motor involvement.[9]
Secondary prevention

No definite preventative action is recommended. However, immunisation is not recommended during the acute phase of GBS and is not suggested for a period of ≥1 years after the onset. After 1 year the need for immunisation should be reviewed on an individual basis.
**Case history**

**Case history #1**

A 20-year-old woman with no significant past medical history presents with lower back pain and bilateral foot and hand tingling. Her symptoms rapidly progress over 4 days to include lower extremity weakness to the point that she is unable to mobilise her lower extremities. She reports coryzal symptoms 2 weeks ago. On examination, she has 0/5 power in her lower extremity with areflexia, but despite the paraesthesias she does not have sensory deficits. Her aminotransferases are elevated, and LP reveals mildly elevated protein with no cells and normal glucose. She weighs 70 kg and her admission vital capacity is 1300 mL, maximum inspiratory pressure is -30 cmH2O, and maximum expiratory pressure is 35 cmH2O.

**Step-by-step diagnostic approach**

Diagnosis is made by pattern recognition.[76] The classic presentation is a progressive symmetrical muscle weakness affecting lower extremities before upper extremities, and proximal muscles before distal muscles, accompanied by paraesthesias in the feet and hands.[77] [78] The paralysis is typically flaccid with areflexia and progresses acutely over days, with 73% reaching a lowest point within 1 week and 98% by 4 weeks.[58] The progressive phase is followed by a plateau phase of persistent, unchanging symptoms lasting a variable duration before recovery begins. Mild dysautonomia occurs in 70% and causes sinus tachycardia, labile BP, postural hypotension, urinary retention, ileus, and very rarely life-threatening cardiac arrhythmia.

Initial tests include LP, spirometry, neurophysiological evaluation, and hepatic aminotransferases.

**History**

Two-thirds of patients have a history of influenza-like or respiratory illness or gastroenteritis within 6 weeks before onset of neurological symptoms.[11] [58] The most commonly presenting symptoms include a respiratory tract or GI tract infection that has resolved by the time neurological symptoms begin, which is around 1 to 3 weeks (mean 11 days in several large studies) after the initial illness.[11]

Other anecdotal triggers include history of trauma, surgical procedures, immunisations, malignancy, and HIV infection. GBS is more common in the older age groups and in males.

Since 2013, several cases of GBS have been reported following the outbreak of Zika virus.[31] [32] Similarly, several other mosquito-borne viral infections such as dengue, chikungunya, and Japanese encephalitis have been linked to GBS.[33] [34] [35] [36] [37]

**Symptoms and signs**

Paraesthesias in hands and feet frequently precede the onset of weakness.[10] These are usually mild and may extend proximally in the extremities. About 89% of patients experience pain, which typically begins in the back and legs. It occurs at onset and during disease course.[79] Presence of back pain and paralysis is easily misinterpreted as cord compression, precipitating unnecessary surgical intervention. In children, pain is a much more prominent symptom compared to adults.[80] Hyporeflexia or areflexia can be seen at the onset in both GBS and cord compression, but the presence of bowel or bladder dysfunction early on or the finding of a sensory level should alert one to the prospect of acute myelopathy.
Facial, oropharyngeal, and extraocular weakness may also occur. These cranial nerve deficits often occur after trunk and limb involvement but precede them in 15%.

Mild dysautonomia is common and results in sinus tachycardia, HTN, and postural hypotension. Other autonomic symptoms such as urinary retention and ileus can happen in up to one quarter of patients. Life-threatening cardiac arrhythmias are relatively rare. Up to 30% will develop respiratory muscle weakness requiring mechanical ventilation. In children, autonomic dysfunction may be an independent risk factor for mechanical ventilation. Typical complaints may include dyspnoea on exertion and SOB.

**Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)**

Typical symptoms include acute polyradiculoneuropathy, causing progressive weakness of 2 or more limbs with reduced or absent tendon reflexes. Time of onset is not more than 4 weeks, and alternative aetiologies should be absent. Symptoms are predominantly proximal but may affect distal muscles as well. There may be motor, sensory, or mixed disturbances, with or without autonomic features. These usually follow an antecedent influenza-like illness, or respiratory or GI infection.

**Acute motor axonal neuropathy (AMAN)**

AMAN presents as acute weakness or paralysis without any sensory loss and with reduced or absent reflexes. Most cases are preceded by *Campylobacter jejuni* infection. It is distinguished from AIDP by selective involvement of motor nerves, preservation of sensory fibres, and electrophysiology showing axonal features. AMAN has a more rapid progression and earlier lowest point than AIDP.

**Acute motor-sensory axonal neuropathy (AMSAN)**

This is associated with sensory and motor deficits with axonal loss. It often presents with fulminant paralysis and sensory loss with incomplete recovery.

**Bickerstaff's brainstem encephalitis (BBE)**

Clinical features are similar to Miller-Fisher syndrome but also include altered consciousness (encephalopathy) or long tract signs (hyper-reflexia), or both. BBE may be a separate clinical entity secondary to its clinical features of drowsiness, coma, hyper-reflexia, and extensor plantar responses. Alternatively, it may also be a variant of Miller-Fisher syndrome. If the Miller-Fisher syndrome triad presents with drowsiness and extensor plantar response, BBE is the likely underlying disease process.

**Pharyngeal-cervical-brachial**

This presents with acute arm weakness, swallowing dysfunction, and facial weakness.

**Miller-Fisher syndrome (MFS)**

This is characterised by impaired eye movements (ophthalmoplegia), abnormal coordination (ataxia), and loss of tendon reflexes (areflexia). Occasionally ophthalmoplegia may be absent. It does not cause limb or respiratory muscle weakness. Pupillary abnormalities, ptosis, and bulbary and facial palsies may occur. It is usually a self-limiting, benign condition. Occasionally, patients may have limb weakness with a MFS-GBS overlap syndrome, which has similar prognosis to that of GBS. Overlap syndromes such as the pharyngeal-cervical-brachial variant of GBS or BBE can occur in 50% of patients with MFS.
Within the first week of onset of MFS,[94] the median period between neurological symptom onset and the disappearance of ataxia/ophthalmoplegia is between 32 and 88 days.[93]

**Acute pandysautonomia**

Presenting symptoms and signs include diarrhoea, vomiting, dizziness, abdominal pain, ileus, orthostatic hypotension, and urinary retention. GBS may be associated with bilateral tonic pupils and may involve both parasympathetic and sympathetic postganglionic neurons.[8] Patients with Miller-Fisher syndrome may also have bilateral tonic pupils.[95] [96] Up to nearly half of patients with Miller-Fisher syndrome have sluggish pupils and mydriasis.[93] [96] Other signs of dysautonomia, including fluctuating heart rate, decreased sweating, salivation, and lacrimation, may be present.[7]

**Pure sensory**

This presents with acute sensory loss, sensory ataxia, and areflexia but no motor involvement.[9] It mostly affects the large sensory fibres, and may be associated with antibodies to GD1b.[9]

**Investigations**

If the diagnosis remains unclear despite clinical examination, anti-ganglioside antibodies, CSF analysis, and electrophysiological tests can be performed to differentiate subtypes.[83] [97] [98] In practice, GQ1B is the only antibody routinely tested to diagnose Miller-Fisher syndrome.

**Neurophysiological evaluation**

Nerve conduction studies are routinely performed and play an important role in diagnosis, subtype classification, and confirming that the disease is a peripheral neuropathy. There is no consensus on the neurophysiological criteria for classification, and neither are there any data on when it should be done; nevertheless, it should be done as soon as possible.[77] [78] [83] [99] [100] At least 3 sensory nerves and 3 motor nerves with multisite stimulation F waves and bilateral tibial H reflexes need to be evaluated.[83]

Early studies may be normal in 13% of examinations, but few remain normal with serial testing 1 to 2 weeks apart.[99] Early abnormalities typically include prolonged distal and F-wave latencies and reduced conduction velocities. H reflex is also prolonged or absent.[83] Evidence of demyelination is present in 85% of patients with early testing.[99]

Very reduced or absent evoked responses on distal supramaximal stimulation of motor and sensory nerves have been demonstrated. This progresses rapidly to total loss of electrical excitability consistent with axonal degeneration.[101] A positive test will at least help localise the disease process to the peripheral nervous system. If it is persistently normal despite severe deficits, the disease process may be in muscle, neuromuscular junction, spinal cord, or higher. A paradox of small median sensory action potentials with retained sural responses has been described in GBS.[102]

**CSF analysis**

CSF analysis is an important laboratory aid in excluding other infectious causes and should be performed early for this reason. Elevated CSF protein with normal cell count (albuminocytological dissociation) is the classic finding, which occurs in up to 90% at 1 week after symptom onset. However, CSF protein may be normal during the first week of the illness, and repeat LP is warranted if the diagnosis remains in question.[62] [103] A retrospective study has suggested a correlation between the level of CSF protein elevation and the amount of electrophysiologically demonstrable demyelination.[104]
If CSF pleocytosis is present, further evaluation for HIV, Lyme disease, sarcoidosis, meningitis, or carcinomatous meningitis should be initiated.[83][91] These tests would include HIV enzyme-linked immunosorbent assay (ELISA), Lyme serology and Western blot, CSF Lyme antibody, CSF ACE and a CXR, CSF VDRL, CSF cytology and flow cytometry, CSF Gram stain, CSF culture, and CSF West Nile PCR. Further viral studies should be considered if immunosuppression is a concern.

[VIDEO: Diagnostic lumbar puncture animated demonstration ]

**Spirometry**

Bedside spirometry should be performed every 6 hours initially. This will help triage the patient to the ICU or the regular ward. A forced vital capacity of <20mL/kg is an indication for ICU admission. Patients with bulbar dysfunction and high risk of aspiration should be intubated for airway protection and impending respiratory failure. Risk factors for progression to mechanical ventilation include rapid disease progression, bulbar dysfunction (odds ratio 17.5), bilateral facial nerve weakness, and dysautonomia.[108][109] Other risk factors include inability to lift head (odds ratio 5.0) or inability to cough (odds ratio 9.09).[110] Pulse oximetry and ABGs should not be relied on, as either hypoxia or hypercarbia are late signs and patients will decompensate very quickly.

**Serology and stool culture**

An increase in titres for infectious agents including CMV, EBV, *Mycoplasma*, *Haemophilus influenzae*, and *C jejuni* may help in establishing etiology for epidemiological purposes but is of limited clinical use. Some data suggest that positive serological markers for *C jejuni* are associated with worse prognostic outcome.[24][111] Testing for *C jejuni* may be considered if there is an antecedent history of diarrhoea or being in a region where AMAN is prevalent. Treatment with antibiotics may be indicated if there is persistent faecal excretion of the bacteria. If clinical features suggest a less common variant, particularly Miller-Fisher variant or pharyngeal-cervical-brachial variant, then testing for anti-ganglioside antibodies anti-GQ1b and anti-GT1a, respectively, may have some diagnostic utility. Anti-GQ1b IgG antibodies are found in 90% of patients with Miller-Fisher syndrome. The evidence for clinical utility of other anti-ganglioside antibodies remains less robust.[112][113]

**Hepatic aminotransferases**

Hepatic aminotransferases may be elevated during the first few days in 10% to 20% with GBS and often normalise by 1 to 2 weeks. Presence of elevated liver enzymes also correlates with increased severity of disease and should be routinely tested and monitored.[14][114] If transaminases remain persistently elevated, evaluation for viral hepatitides should be considered.

**Imaging**

Spinal MRI may be useful when the diagnosis is unclear and electrophysiological abnormalities are equivocal. It can also be performed to exclude disease process involving the spinal cord (i.e., epidural abscess, transverse myelitis, spinal stenosis, spinal cord stroke, or tumour). Brain magnetic imaging abnormalities are present in 30% of patients with BBE.[89]

**Risk factors**

**Strong**
Guillain-Barre syndrome

Diagnosis

preceding viral illness

- Two-thirds have a history of gastroenteritis or influenza-like illness within the weeks before onset of neurological symptoms.[11] [58]

preceding bacterial infection

- Studies have found that about 60% to 70% of acute motor axonal neuropathy (AMAN) and acute motor-sensory axonal neuropathy (AMSAN) cases and up to 30% of acute inflammatory demyelinating polyradiculoneuropathy (AIDP) cases are preceded by *Campylobacter jejuni* infection.[26] [27] *Campylobacter*-associated GBS appears to have a worse prognosis, manifested by slower recovery and greater residual neurological disability.[12] A study in Sweden estimated that the risk of developing GBS during the 2 months following *C jejuni* infection is approximately 100-fold higher.[59]

preceding mosquito-borne viral infection

- Since 2013, several cases of GBS have been reported following the outbreak of Zika virus.[31] [32] Similarly, several other mosquito-borne viral infections such as dengue, chikungunya, and Japanese encephalitis have been linked to GBS.[33] [34] [35] [36] [37]

Weak immunisation

- In the US an increased risk of GBS was associated with the swine influenza vaccine in 1976, although the severity of the risk has been controversial. Subsequently no increased risk was observed up to 1991.[10] Carefully conducted surveillance studies of subsequent mass influenza immunisation programmes of the US Army found no increased incidence of GBS.[60] An epidemiology study found no evidence of increased risk of GBS after seasonal influenza immunisation.[30] This study looked at 15 years of the General Practice Research database in the UK and found that the relative incidence of GBS within 90 days of influenza immunisation was 0.76, as opposed to 7.35 within 90 days of influenza-like illness.[30] However, it is thought that modern influenza vaccination produces <1 case per million recipients.[61]
- Eight cases of GBS that occurred after meningococcal conjugate vaccine A, C, Y, and W135 (MCV4) have been reported. The correlation is still doubtful because the rate of GBS within 6 weeks after immunisation is the same as by chance.[62]
- The possibility that GBS might be triggered by live, attenuated oral poliovirus vaccine was suggested in a report from Finland.[63]
- The occurrence of GBS is about 1 in 1000 cases following rabies vaccine containing murine myelin, an antibody response to human myelin basic protein and galactocerebroside.[29]
- One systematic review estimated the risk of GBS at 1.6 excess cases per million people vaccinated, but it concluded that this risk should be weighed against the protective benefits of vaccination.[64]

cancer and lymphoma

- Case reports often link GBS with Hodgkin’s disease.[65] Less commonly, other malignancies have also been associated with GBS. These include oat cell carcinoma, adenocarcinoma of the lung, small cell lung cancer, and chronic lymphocytic leukaemia.[66] [67] [68] [69]
older age (mean 40 years)

- Incidence increases with age. For people <30 years of age, the incidence is <1:100,000. For people >75 years of age, incidence is 4:100,000.[24] [58] The mean age of onset is approximately 40 years.[11] [16]

HIV infection

- Anecdotal: several cases have been reported in patients with HIV and GBS.[70] [71] [72] [73] [74]

male

- Male-to-female ratio varies from 1.0:1.0 to 1.9:1.0.[16] [75]

History & examination factors

**Key diagnostic factors**

**presence of risk factors (common)**

- Key risk factors include preceding viral or bacterial infection.

**muscle weakness (common)**

- Progressive symmetrical muscle weakness usually affecting lower extremities before upper extremities and proximal muscles before distal muscles accompanied by paraesthesias in the feet and hands.[77] [78] The paralysis is typically flaccid with areflexia and progresses acutely over days with 50% reaching a lowest point within 1 week and 98% by 4 weeks.[58] Weakness evolving for >4 to 8 weeks is more consistent with chronic inflammatory demyelinating polyradiculoneuropathy.[77] [78]

**respiratory distress (common)**

- Typical complaints may include dyspnoea on exertion and SOB, but respiratory muscle weakness can often be asymptomatic. Up to 30% will develop respiratory muscle weakness requiring mechanical ventilation.[62]

**speech problems (common)**

- Facial weakness and oropharyngeal weakness occurs in 50% of patients.[62] Typical complaints include slurred speech.

**paraesthesia (common)**

- Paraesthesias in hands and feet occur in 80% of patients and frequently precede the onset of weakness.[59] These may extend proximally in the extremities, but sensory abnormalities on examination are usually mild. If a distinct sensory level is noted on examination, this is unlikely to be GBS and more likely a spinal cord process.

**back/leg pain (common)**

- Pain occurs in approximately 89% of patients at onset and during the course of the disease, and typically begins with back and leg pain.[79] Presence of back pain and paralysis is easily misinterpreted as cord compression.

- In children, pain is a much more prominent symptom compared to adults.[80]

**areflexia/hyporeflexia (common)**
Guillain-Barre syndrome

**Diagnosis**

- Approximately 65% are entirely areflexic on admission, 90% can have absent ankle jerks, and 80% have absent knee jerk, while 10% may have absent reflexes only in the weakest limbs.[114] Plantar reflex should be downgoing or absent but never upgoing. Tone should be flaccid.

**facial weakness (common)**

- Occurs in 50% of patients.[62]

**bulbar dysfunction causing oropharyngeal weakness (common)**

- Together with bilateral facial weakness, bulbar dysfunction is associated with increased risk of progression to mechanical ventilation.[108] Oropharyngeal weakness occurs in 50% of patients.[62] Typical complaints include swallowing difficulty.

**extra-ocular muscle weakness (common)**

- Occurs in 15% of patients.[62]

**facial droop (common)**

- Often occurs after trunk and limb involvement but occurs before in about 15% of patients.[62]

**diplopia (common)**

- Often occurs after trunk and limb involvement but occurs before in about 15% of patients.[62]

**dysarthria (common)**

- Often occurs after trunk and limb involvement but occurs before in about 15% of patients.[62]

**dysphagia (common)**

- Often occurs after trunk and limb involvement but occurs before in about 15% of patients.[62]

**dysautonomia (common)**

- Mild dysautonomia is common and results in sinus tachycardia, HTN, and postural hypotension in approximately two-thirds of patients. Other autonomic symptoms such as urinary retention and ileus can happen in up to one quarter of patients.[81] Bladder disturbance is usually mild or absent early in the disease, and if severe, cord compression should be excluded. Life-threatening cardiac arrhythmias are relatively rare.[10] [82]
- Autonomic dysfunction in children may be an independent risk factor for mechanical ventilation.[80]

**anisocoria (uncommon)**

- If it occurs, tends to accompany severe ophthalmoparesis and ptosis.[115]

**non-reactive pupil (uncommon)**

- Although uncommon, light-fixed dilated pupils in GBS have been described.[116] [117] If pupils are fixed and dilated, the possibility of botulism needs to be considered as this is a typical finding.
- GBS may be associated with bilateral tonic pupils and may involve both parasympathetic and sympathetic post-ganglionic neurons.[8] Up to nearly half of patients with Miller-Fisher syndrome have sluggish pupils and mydriasis.[93] [96]

**ophthalmoplegia (uncommon)**
Ataxia, areflexia, and ophthalmoplegia are the classic triad for Miller-Fisher syndrome.\textsuperscript{[20]} \textsuperscript{[87]} \textsuperscript{[118]} Around 30% of patients with Miller-Fisher syndrome may develop extremity weakness manifesting as an overlapping syndrome with classic GBS.

**Other diagnostic factors**

**Ptosis (common)**
- May occur in Miller-Fisher syndrome.

**Altered level of consciousness (common)**
- Encephalopathy and hyper-reflexia may be the presenting features of Bickerstaff’s brainstem encephalitis (BBE), which may be a variant of Miller-Fisher syndrome.

**Ataxia (uncommon)**
- Characteristic feature of Miller-Fisher syndrome. A few patients with Miller-Fisher syndrome present with ataxia and hyporeflexia without ophthalmoplegia.\textsuperscript{[20]}
## Diagnostic tests

### 1st test to order

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>nerve conduction studies</td>
<td>slowing of nerve conduction velocities</td>
</tr>
</tbody>
</table>

- Interpretation of electrophysiology can be difficult, especially in early stages. However, clear electrophysiological evidence of demyelinating polyneuropathy is useful for outcome prediction.\[99\] Different sets of criteria have been published, including the following:

- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP): patchy demyelination, slowing of motor nerve conduction velocities, prolonged distal and F-wave latencies, and dispersed response on needle.\[15\] \[84\]

- At least 1 of the following in 2 nerves, or at least 2 of the following in 1 nerve: motor conduction velocity (MCV) <90% lower limit of normal (LLN; 85% if distal compound muscle action potential [dCMAP] <50% LLN), distal motor latency (DML) >110% upper limit of normal (ULN; >120% if dCMAP <100% LLN), pCMAP/dCMAP ratio <0.5% and dCMAP >20% LLN, F-response latency >120% ULN.

- Newer criteria have been proposed for AIDP, which increase the sensitivity of diagnosis, and include:\[119\]
  - at least 1 of the following in at least 2 nerves: MCV <70% LLN; DML >150% ULN; F-response latency >120% ULN, or >150% ULN (if distal CMAP <50% of LLN); or
  - F-wave absence in 2 nerves with dCMAP ≥20% LLN or greater, with an additional parameter, in 1 other nerve; or
  - pCMAP/dCMAP ratio <0.7 (excluding the tibial nerve) in 2 nerves, with an additional parameter in 1 other nerve.

- Acute motor-sensory axonal neuropathy (AMSAN): diminution of muscle and sensory action potentials.\[53\] None of the features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCAMP <10% LLN and sensory action potential amplitudes less than LLN.

- Acute motor axonal neuropathy (AMAN): reduction in distally evoked motor action potential amplitudes, early signs of denervation on needle, normal action potential on sensory nerves, and relatively preserved motor nerve conduction velocity.\[39\] \[56\] \[57\] None of the features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCMAP <10% LLN and sensory action potential amplitudes normal.

- Miller-Fisher syndrome: reduced or absent sensory action potential response without slowing of sensory conduction velocity.\[120\]
### Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LP</strong></td>
<td>Elevated CSF protein, normal/slightly high lymphocytes (&lt;50 cells/mm³)</td>
</tr>
</tbody>
</table>
| • Classic finding is elevated CSF protein with normal cell count (albuminocytological dissociation). Occurs in up to 90% at week 1 after symptom onset. CSF protein is usually normal within the first 2 to 3 days but then begins to rise very quickly, reaching a peak at 4 to 6 weeks and then persisting at a variably elevated level for many weeks. [121]  
• CSF protein level varies from 0.45 to 3.0 g/L (45-300 mg/dL), but levels as high as 10 g/L (1000 mg/dL) can be seen. [122] Around 59% of patients with Bickerstaff’s brainstem encephalitis (BBE) have elevated protein in CSF. [89] [90]  
• Extremely high protein levels (10 g/L [1000 mg/dL]) are associated with development of high intracranial pressure and papilloedema. Around 10% will not have a protein elevation and this includes patients with the Miller-Fisher variant. [123] [124] Cell counts are typically <5 cells/mm³. However, in 10% of patients, lymphocytosis <50 cells/mm³ may be present early on but quickly normalises over a few days. [121]  |
| **LFT** | Elevated AST and ALT as high as 500 U/L; bilirubin may be transiently elevated but rarely high enough to cause jaundice |
| • Hepatic aminotransferases may be elevated during the first few days in 10% to 20% of patients and often rapidly normalise by 1 to 2 weeks. [14] Elevation of hepatic enzymes is associated with a more severe disease. [114] The cause is unclear. EBV and CMV infection have been suggested, but serological markers are often negative. |
**Guillain-Barre syndrome**

**Diagnosis**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>spirometry</td>
<td>• Should be carried out at 6-hour intervals initially at the bedside.</td>
</tr>
<tr>
<td></td>
<td>• ICU monitoring and elective intubation should be considered if:</td>
</tr>
<tr>
<td></td>
<td>• vital capacity is &lt;20 mL/kg (odds ratio 15.0); maximal inspiratory</td>
</tr>
<tr>
<td></td>
<td>• pressure worse than -30 cmH2O; maximal expiratory pressure &lt;40 cmH2O;</td>
</tr>
<tr>
<td></td>
<td>• reduction of 30% in vital capacity, maximal inspiratory pressure,</td>
</tr>
<tr>
<td></td>
<td>• or maximal expiratory pressure. [108]</td>
</tr>
<tr>
<td>[VIDEO: Tracheal intubation animated demonstration ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[VIDEO: Bag-valve-mask ventilation animated demonstration ]</td>
</tr>
</tbody>
</table>

**antiganglioside antibody**

• Presence of subtype-specific antiganglioside antibodies can differentiate between subtypes and may be useful when the diagnosis remains unclear despite clinical examination, CSF analysis, and electrodagnostic tests.[83] [97] [98] In practice, GQ1b is the only antibody routinely tested to diagnose Miller-Fisher syndrome. Antibodies are present in 85% to 90% of patients with Miller-Fisher syndrome.[83] It has 90% sensitivity and is also present in pharyngo-cervical-brachial GBS variant, Bickerstaff's brainstem encephalitis (BBE), and overlap syndromes. The epitopes are expressed specifically in the nodal regions of oculomotor nerves, in dorsal root ganglion cells, and cerebellar neurons.[128] GQ1b IgG antibodies are present in 96% of patients.[15] [21] [87] [113]

• 66% BBE patients have anti-GQ1b antibodies.[89] [90]

• Pharyngo-cervical-brachial may be associated with IgG and GT1 antibodies.[112] [129]

<table>
<thead>
<tr>
<th>Other tests to consider</th>
</tr>
</thead>
</table>

**serology**

• An increase in titres for infectious agents including CMV, EBV, Mycoplasma, H influenzae, and C jejuni may help in establishing aetiology for epidemiological purposes but is of limited clinical use. Some data suggest that positive serological markers for C jejuni are associated with worse prognostic outcome.[24] [111]

• Bickerstaff's brainstem encephalitis (BBE) may have antecedent infection in 92%.[89] [90]

<table>
<thead>
<tr>
<th>stool culture</th>
<th>presence of Campylobacter jejuni, CMV, EBV, Mycoplasma pneumoniae, or Haemophilus influenzae</th>
</tr>
</thead>
</table>

• Testing for C jejuni may be considered if there is an antecedent history of diarrhoea or in a region where acute motor axonal neuropathy (AMAN) is prevalent.
<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV antibodies</strong></td>
<td>positive in HIV infection</td>
</tr>
<tr>
<td>• High-risk person or presence of</td>
<td></td>
</tr>
<tr>
<td>CSF lymphocytic pleocytosis (&gt;10</td>
<td></td>
</tr>
<tr>
<td>cells/mm^3).</td>
<td></td>
</tr>
<tr>
<td><strong>spinal MRI</strong></td>
<td>may show enhancement of cauda equina nerve roots with gadolinium</td>
</tr>
<tr>
<td>• Sensitive but non-specific.</td>
<td></td>
</tr>
<tr>
<td>• Enhancement of the cauda equina</td>
<td></td>
</tr>
<tr>
<td>nerve roots with gadolinium</td>
<td></td>
</tr>
<tr>
<td>has been found to be 85% sensitive</td>
<td></td>
</tr>
<tr>
<td>for acute GBS and present in</td>
<td></td>
</tr>
<tr>
<td>95% of typical cases.</td>
<td></td>
</tr>
<tr>
<td>[110] May be useful when diagnosis</td>
<td></td>
</tr>
<tr>
<td>is unclear and electrophysiological</td>
<td></td>
</tr>
<tr>
<td>abnormalities are equivocal.</td>
<td></td>
</tr>
<tr>
<td>Can exclude disease processes</td>
<td></td>
</tr>
<tr>
<td>involving the spinal cord (i.e.,</td>
<td></td>
</tr>
<tr>
<td>epidural abscess, transverse</td>
<td></td>
</tr>
<tr>
<td>myelitis, spinal stenosis, spinal</td>
<td></td>
</tr>
<tr>
<td>cord stroke, or tumour). In a</td>
<td></td>
</tr>
<tr>
<td>study of 24 patients with GBS</td>
<td></td>
</tr>
<tr>
<td>scanned on day 13, enhancement of</td>
<td></td>
</tr>
<tr>
<td>the cauda equina nerve roots with</td>
<td></td>
</tr>
<tr>
<td>gadolinium on lumbosacral MRI was</td>
<td></td>
</tr>
<tr>
<td>found to be 83% sensitive for</td>
<td></td>
</tr>
<tr>
<td>acute GBS and was present in</td>
<td></td>
</tr>
<tr>
<td>95% of typical cases.</td>
<td></td>
</tr>
<tr>
<td>[130]</td>
<td></td>
</tr>
<tr>
<td><strong>Borrelia burgdorferi serology</strong></td>
<td>positive in Lyme disease</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CSF meningococcal PCR</strong></td>
<td>positive in meningococcal meningitis</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CSF cytology</strong></td>
<td>positive in carcinomatous meningitis</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CSF ACE</strong></td>
<td>positive in sarcoidosis</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CXR</strong></td>
<td>bihilar lymphadenopathy in sarcoidosis</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CSF VDRL</strong></td>
<td>positive in neurosyphilis</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
<tr>
<td><strong>CSF West Nile PCR</strong></td>
<td>positive in West Nile virus infection</td>
</tr>
<tr>
<td>• Should be performed early to</td>
<td></td>
</tr>
<tr>
<td>aid exclusion of other causes.</td>
<td></td>
</tr>
</tbody>
</table>
### Differential diagnosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Differentiating signs / symptoms</th>
<th>Differentiating tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse myelitis</td>
<td>• Spinal cord disorders including transverse myelitis present with asymmetrical motor or sensory loss usually involving lower extremities, early bowel or bladder dysfunction with persistent incontinence, and segmental radicular pain. • Physical examination demonstrates upper motor neuron signs (hyperreflexia, positive Babinski’s response) and a sensory level.</td>
<td>• CSF analysis: pleocytosis with modest number of lymphocytes and increase in total protein. • MRI shows focal demyelination with possible enhancement at the appropriate level.</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>• Early involvement of muscle groups including extraocular, levator, pharyngeal jaw, neck, and respiratory muscles. Sometimes presents without limb weakness. • Excessive fatigability and variation of symptoms and signs through the day is common. • Reflexes are preserved, and sensory features, dysautonomia, and bladder dysfunction are absent.</td>
<td>• Electrophysiological study shows normal nerve conduction and presence of decremental response to repetitive nerve stimulation. • EMG shows abnormal jitter and blocking. • Edrophonium test is normally positive. However, many centres do not routinely perform this test because of potential side effects.</td>
</tr>
<tr>
<td>Lambert-Eaton myasthenic syndrome (LEMS)</td>
<td>• Can be difficult to differentiate because of similar clinical characteristics. However, some characteristics are more typical for LEMS. These include slower development of clinical symptoms, dry mouth, lack of objective sensory loss, rare involvement of respiratory muscle group, and potentiation of reflexes after exercise or contraction.</td>
<td>• Electrophysiological study: hallmark is a low amplitude compound muscle action potential (CMAP) after single nerve stimulus, increase in CMAP amplitude after voluntary contraction, or repetitive stimulation at high frequencies.</td>
</tr>
<tr>
<td>Condition</td>
<td>Differentiating signs / symptoms</td>
<td>Differentiating tests</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Botulism</td>
<td>• History of ingesting food tainted with botulinum toxin.</td>
<td>• Electrophysiological study: reduced amplitude of evoked muscle potentials, increase in amplitude with repetitive nerve stimulation, and increased number of myopathic units, which is atypical for GBS.[124]</td>
</tr>
<tr>
<td></td>
<td>• Descending paralysis begins in the bulbar muscles then the limbs, face, neck, and respiratory muscles.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Respiratory muscles are involved with mild limb weakness, and reflexes are usually preserved.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Ptosis, dilated non-reactive pupils are present. Dilated non-reactive pupils are uncommon in GBS, but more common in botulism.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Constipation is also a characteristic feature of botulism.[124]</td>
<td></td>
</tr>
<tr>
<td>Polymyositis</td>
<td>• Presence of pain and muscle tenderness usually in the shoulder and upper arm, involvement of flexor neck muscle disproportionate to limb weakness, absence of sensory symptoms, preservation of reflexes, absence of dysautonomia, and presence of skin lesions, which are uncommon presentation for GBS.[124]</td>
<td>• Elevated ESR and CK, normal nerve conduction study, and myopathic changes with fibrillation on EMG.</td>
</tr>
<tr>
<td></td>
<td>• May have elevated ESR. CSF does not show albuminocytological dissociation.</td>
<td>• Muscle biopsy shows muscle fibre destruction and regeneration, and lymphocyte infiltrates.[124]</td>
</tr>
<tr>
<td></td>
<td>• Usually patients complain of fever, fatigue, weakness, and arthralgia.[124]</td>
<td></td>
</tr>
<tr>
<td>Vasculitic neuropathy</td>
<td>• Common features include painful asymmetrical presentation of muscle weakness, uncommon involvement of cranial nerves, respiratory paralysis, and sphincter dysfunction.</td>
<td>• May have elevated ESR. CSF does not show albuminocytological dissociation.</td>
</tr>
<tr>
<td></td>
<td>• Usually patients complain of fever, fatigue, weakness, and arthralgia.[124]</td>
<td>• Electrophysiological study shows evidence of denervation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Nerve biopsy shows signs of inflammation and scarring.[124]</td>
</tr>
</tbody>
</table>

### Diagnostic criteria

**Assessment of current diagnostic criteria for Guillain-Barre syndrome[77]**

**Required features**

- Progressive weakness in both arms and legs
- Areflexia (or hyporeflexia).
Features supportive of diagnosis

- Progression of symptoms over days to 4 weeks
- Relative symmetry
- Mild sensory signs or symptoms
- Cranial nerve involvement, especially bilateral facial weakness
- Recovery beginning 2 to 4 weeks after progression ceases
- Autonomic dysfunction
- Absence of fever at onset
- Typical CSF and EMG/nerve conduction studies features.

Features casting doubt on the diagnosis

- Asymmetrical weakness
- Persistent bladder and bowel dysfunction
- Bladder or bowel dysfunction at onset
- >50 mononuclear leukocytes/mm³ or presence of polymorphonuclear leukocytes in CSF
- Distinct sensory level.

Features that rule out the diagnosis

- Hexacarbon abuse
- Abnormal porphyrin metabolism
- Recent diphtheria infection
- Lead intoxication
- Other similar conditions: poliomyelitis, botulism, hysterical paralysis, toxic neuropathy.

**Electrophysiological classification of Guillain-Barre syndrome[^99]**

Neurophysiological criteria for acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor-sensory axonal neuropathy (AMSAN), and acute motor axonal neuropathy (AMAN).[83][99]

At least 3 sensory nerves and 3 motor nerves with multi-site stimulation F waves, and bilateral tibial H reflexes, need to be evaluated.[83]

**AIDP**

At least 1 of the following in each of at least 2 nerves, or at least 2 of the following in 1 nerve if all others inexcitable and distal compound muscle action potential (dCMAP) >10% lower limit of normal (LLN):

- Motor conduction velocity <90% LLN (85% if dCMAP <50% LLN)
- Distal motor latency >110% upper limit of normal (ULN) (>120% if dCMAP <100% LLN)
- pCMAP/dCMAP ratio <0.5 and dCMAP >20% LLN
- F-response latency >120% ULN.

**AMSAN**

- None of the features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCMAP <10% LLN
- Sensory action potential amplitudes less than LLN.

**AMAN**
Guillain-Barre syndrome

Diagnosis

- None of the features of AIDP except 1 demyelinating feature allowed in 1 nerve if dCMAP <10% LLN
- Sensory action potential amplitudes normal.

Inexcitable

- dCMAP absent in all nerves or present in only 1 nerve with dCMAP <10%.

Electrodiagnostic criteria for acute and chronic inflammatory demyelinating polyradiculoneuropathy[100]

Different sets of criteria have been published, including the following (sensitivity 64% to 72%):

- 150% prolongation of motor distal latency above ULN
- 70% slowing of motor conduction velocity below LLN
- 125% (150% if the distal negative-peak CMAP amplitude was 80% of LLN) prolongation of F wave latency above ULN
- Abnormal temporal dispersion (peak CMAP duration increase) in ≥2 nerves.

Diagnostic and classification criteria for the Guillain-Barre syndrome[78]

Necessary criteria for clinical diagnosis:[78]

- Sub-acutely developing flaccid paralysis over <4 weeks
- Symmetrical weakness from the onset of the symptoms
- Diminished or absent reflexes
- No other aetiology for flaccid weakness identified.

Hughes Scale[131]

0 - healthy
1 - minor symptoms or signs of neuropathy but capable of manual work
2 - able to walk without support of a stick but incapable of manual work
3 - able to walk with a stick, appliance, or support
4 - confined to bed or chair-bound
5 - requiring assisted ventilation
6 - dead

Identification of patients with GBS at risk of respiratory failure using the 20/30/40 rule[108]

In patients with no bulbar dysfunction, or with mild bulbar dysfunction without aspiration risk, the 20/30/40 rule should be used.

ICU monitoring and elective intubation should be considered if:[108]
Guillain-Barre syndrome

Diagnosis

- Vital capacity <20 mL/kg (odds ratio 15.0)
- Maximal inspiratory pressure worse than -30 cmH2O
- Maximal expiratory pressure <40 cmH2O
- Reduction of 30% in vital capacity, maximal inspiratory pressure, or maximal expiratory pressure.

[VIDEO: Tracheal intubation animated demonstration ]

[VIDEO: Bag-valve-mask ventilation animated demonstration ]
Step-by-step treatment approach

A multidisciplinary approach to the acute phase combining supportive and disease-modifying therapy (with plasma exchange or high-dose immunoglobulin [IVIG]) is required. The use of plasma exchange or immunoglobulin depends on the institution or whether the patient has a contraindication to immunoglobulin such as IgA deficiency. Both have been shown to be equally efficacious. One Cochrane review suggested that IVIG given within 2 weeks of the onset was as efficacious as plasma exchange, and more likely to be completed than plasma exchange.[40] Their combination is not supported.

Supportive therapy: respiratory management

Respiratory failure is common, and up to 30% of patients need ventilatory support or airway protection. Risk factors for progression to mechanical ventilation include rapid disease progression, bulbar dysfunction, bilateral facial nerve weakness, and dysautonomia. Pulse oximetry and ABGs should not be relied on, as hypoxia or hypercarbia is a late sign and patients will decompensate very quickly. There is insufficient evidence to recommend specific methods for monitoring respiratory function, but respiratory status should be monitored in all patients.[132] Bedside spirometry should be performed every 6 hours initially. Early spirometry will also help triage the patient between the ICU and regular ward. Patients with bulbar dysfunction, high risk of aspiration (i.e., infiltrates on CXR), and new atelectasis on CXR should be intubated early for airway protection and impending respiratory failure. In patients with no bulbar dysfunction or with mild bulbar dysfunction without aspiration risk, the 20/30/40 rule should be used as detailed below.[108] The patient should be monitored in the ICU and elective intubation considered if:

- Vital capacity is <20 mL/kg
- Maximal inspiratory pressure is worse than -30 cmH2O (negative inspiratory force)
- Maximal expiratory pressure is <40 cmH2O
- Vital capacity, maximal inspiratory pressure, or maximal expiratory pressure is reduced by 30% from baseline initial measurement.[108]

The mean duration of ventilation is 15 to 43 days, and weaning should be guided by serial PFTs and assessment of strength.[132] The need for tracheostomy should be addressed from week 2 onwards, especially if PFTs do not show improvement. If there is improvement of PFTs above baseline, tracheostomy may be delayed by an additional week before reassessment.[132]

[VIDEO: Tracheal intubation animated demonstration ]

[VIDEO: Bag-valve-mask ventilation animated demonstration ]

[VIDEO: Nasopharyngeal airway animated demonstration ]

[VIDEO: Oropharyngeal airway animated demonstration ]

Supportive therapy: cardiovascular management

Haemodynamic monitoring of pulse and BP should be started on admission. Telemetry would be prudent here, especially if there is evidence of dysautonomia. If dysautonomia is present, continuous cardiac monitoring and placement of a Foley catheter should be initiated on admission. There are insufficient data for methods and setting of monitors, but all patients with severe disease should have their pulse and BP monitored until they are off ventilator support and have begun to recover.[18][132] Fluid balance should be monitored carefully, especially because the autonomic dysfunction renders clinical determination of
hydration status very difficult. Hypotensive episodes can be managed with fluid boluses. If BP is very labile, then intra-arterial BP monitoring should be initiated. Hypertensive episodes should be treated with short-acting agents (e.g., labetalol, esmolol, and nitroprusside) to prevent abrupt hypotension. Other factors that may potentiate dysautonomia include manoeuvres such as suctioning, changing position (i.e., lying to sitting), and medicines (antihypertensive drugs, succinylcholine).[135]

**Supportive therapy: DVT prophylaxis**

There are no studies evaluating efficiency of DVT prophylaxis specifically in this disorder. Immobility and hypercoagulability from treatments such as intravenous immunoglobulin (IVIG) can increase the risk of DVT in these patients.[136] Subcutaneous heparin or enoxaparin and support stockings are recommended for non-ambulatory patients until they are able to walk independently.[132]

**Supportive therapy: pain management**

Gabapentin or carbamazepine are generally recommended in the ICU in the acute phase;[132] however, further studies are required to investigate the safety and efficacy of potential interventions in patients with pain.[137] Adjunctive therapy with tricyclic antidepressants, tramadol, gabapentin, carbamazepine, or mexiletine may be helpful for long-term management of neuropathic pain.[132] Although opioids may be effective, they may aggravate autonomic gut dysmotility and bladder distension.[82] [132] [138]

**Immunotherapy**

Immunotherapy comprises IVIG or plasma exchange. Both have been shown to be equally efficacious.[139] The choice between them is often institution-dependent. IVIG is a pooled blood product and runs the risk of transmitting infection, and can precipitate anaphylaxis in an IgA-deficient person. It is, however, much easier to administer because it is a peripheral intravenous infusion. If there is a contraindication to IVIG, such as IgA deficiency or ongoing renal failure, then plasma exchange would be a better option. Plasma exchange requires central venous access and close monitoring for electrolyte abnormalities and coagulopathies. When started within 2 weeks from symptom onset, IVIG has equivalent efficacy to exchange in hastening recovery in patients who require help with walking. Plasma exchange is recommended for ambulatory patients beyond 2 weeks from onset of neurological symptoms, as trials with IVIG did not include ambulatory patients beyond 2 weeks of symptom onset.[140] [141] Complications are seen less frequently with IVIG than with plasma exchange, and hence IVIG may be favoured over plasma exchange.[142] There is no evidence concerning the relative efficacy of plasma exchange and IVIG in axonal forms of GBS. Combination treatment (plasma exchange followed by IVIG) is not recommended.[40] [140] Unlike in other immune-mediated disorders, oral corticosteroids are not beneficial and may even be harmful, possibly due to harmful effects on denervated muscle or due to inhibition of the macrophage repair process.[143] Intravenous corticosteroids do not produce any significant short- or long-term benefits.[143]

**Plasmapheresis (plasma exchange)**

Plasma exchange has been shown to be most effective if started within 7 days of symptom onset, but improvement in outcome was seen in a study despite giving initiating plasma exchange up to 30 days after symptom onset.[38] [144] Plasma exchanges should be initiated in parallel with supportive care. In mild GBS, 2 plasma exchanges are superior to 1 or none, and in moderate GBS, 4 plasma exchanges are superior to 2.[38] In severe disease, where the patient is mechanically ventilated, 6 plasma exchanges are not superior to 4.[38] The risk of relapse is higher with plasma exchange.[38] Large
randomised multicentre trials have established effectiveness in severe disease.[13] [145] [146] Evidence has suggested that plasma exchange was superior to supportive care in the following areas:

- Mean time to recover walking with aid (primary outcome)
- Shorter time to onset of recovery (primary outcome)
- Improvement by 1 disability grade by 4 weeks (secondary outcome).

Other secondary outcomes include improvement in time to recover walking without aid, percentage requiring mechanical ventilation, duration of ventilation, full muscle strength, recovery after 1 year, and severe sequelae after 1 year.[38]

The recommended dose is given by central venous catheter, 50 mL/kg bodyweight over 7 to 14 days started within 2 weeks of disease onset. Two plasma exchanges are given for mild GBS with disability grade 0 to 2, and 4 plasma exchanges for severe GBS with disability grade 3 to 6 with albumin in the continuous flow machine.[38] It is recommended that plasma exchange be performed as early as possible within 4 weeks of onset for non-ambulatory patients and within 2 weeks of onset for ambulatory patients.[140]

### Intravenous immunoglobulin

The goal of IVIG is to hasten recovery and reduce long-term morbidity. It is recommended for ambulatory patients within 2 weeks from the onset of neurological symptoms.[40] [140] IVIG is recommended for patients who require help to walk within 2 or 4 weeks from onset of neurological symptoms.[140]

Possible mechanisms for beneficial effects include blockade of Fc receptors on macrophages preventing antibody targeted attachment on Schwann cell membrane and myelin or on axolemma in axonal variants of GBS; regulation of autoantibodies or cytokines by anti-idiotypic or anti-cytokine antibodies in the pooled immunoglobulin; and interference with the complement cascade or regulatory effects on T cells.[147]

An alternative hypothesis may be that high concentrations of circulating immunoglobulin accelerate the breakdown of IgG. Circulating IgG is picked up by a specialised receptor, FcRn, on the endothelial cell surface, which endocytose the IgG and return it intact to the circulation. Excessive amounts of IgG exceed the capacity of the recycling system, which diverts the excess to lysosomes, where it is broken down.[148]

### Rehabilitation

This is recommended in the acute phase. It comprises gentle strengthening involving isometric, isotonic, isokinetic, and manual resistive and progressive resistive exercises. It should be focused on proper limb positioning, posture, orthotics, and nutrition.[132] A multi-disciplinary approach has been shown to improve disability and quality of life as well as reduce fatigue.[149]
## Acute Treatment

<table>
<thead>
<tr>
<th>Condition</th>
<th>1st</th>
<th>Plus</th>
</tr>
</thead>
<tbody>
<tr>
<td>without IgA deficiency or renal failure</td>
<td>plasma exchange</td>
<td>supportive treatment</td>
</tr>
<tr>
<td>without IgA deficiency or renal failure</td>
<td>1st</td>
<td>intravenous immunoglobulin (IVIG)</td>
</tr>
<tr>
<td>without IgA deficiency or renal failure</td>
<td>plus</td>
<td>supportive treatment</td>
</tr>
<tr>
<td>with IgA deficiency or renal failure</td>
<td>plasma exchange</td>
<td>supportive treatment</td>
</tr>
<tr>
<td>with IgA deficiency or renal failure</td>
<td>plus</td>
<td>supportive treatment</td>
</tr>
</tbody>
</table>
## Treatment options

### Acute

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>without IgA deficiency or renal failure</strong></td>
<td>1st</td>
<td>plasma exchange</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» Both plasma exchange and intravenous immunoglobulin (IVIG) have been shown to be equally efficacious. The choice between them is often institution-dependent.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» If there is a contraindication to IVIG (namely, IgA deficiency or ongoing renal failure), then plasma exchange would be a better option.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» Ambulant patients: plasma exchange is recommended within 2 weeks of onset. Two plasma exchanges are given for mild GBS (disability grade 0 to 2).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» Non-ambulatory patients: plasma exchange is recommended within 4 weeks from onset of neurological symptoms.[140]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» Plasma is separated from cells using membrane filtration or centrifugation concurrently with plasma and albumin replacement. This is labour intensive and requires teams skilled in extracorporeal circulation and exposes the patient to procedure-related morbidities.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» The dose for plasma exchange is given through a central venous catheter (Mahurkar), 50 mL/kg bodyweight every other day for 7 to 14 days.[139] During administration, patients should be closely monitored for electrolyte abnormalities and coagulopathies.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» Complications include severe infection, BP instability, cardiac arrhythmias, and pulmonary embolus.[150] [151] Compared with IVIG, plasma exchange showed more instances of pneumonia, atelectasis, thrombosis, and haemodynamic difficulties.[139] Other adverse effects include hypocalcaemia.</td>
</tr>
<tr>
<td><strong>without IgA deficiency or renal failure</strong></td>
<td>plus</td>
<td>supportive treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» All patients with severe disease should have their pulse and BP monitored until they are off ventilator support and have begun to recover.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>» DVT prophylaxis: subcutaneous heparin or enoxaparin and support stockings are...</td>
</tr>
</tbody>
</table>
### Acute

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>recommended for non-ambulatory patients until they are able to walk independently.[132]</td>
</tr>
</tbody>
</table>

- **Intubation and ventilation:** risk factors for respiratory failure include rapid disease progression, bulbar dysfunction, bilateral facial nerve weakness, and dysautonomia. Early intubation should be considered for patients with bulbar dysfunction, high risk of aspiration, and new atelectasis on CXR. Elective intubation should be considered in patients with no bulbar/mild bulbar dysfunction if vital capacity is <20 mL/kg; maximal inspiratory pressure is worse than -30 cmH2O; maximal expiratory pressure is <40 cmH2O; vital capacity, maximal inspiratory pressure, or maximal expiratory pressure is reduced by 30% from baseline initial measurement.\[108\] Once the patient is intubated, the need for tracheostomy should be addressed from week 2 onwards. If there is no improvement of PFT, percutaneous tracheostomy should be performed. If there is improvement of PFT above baseline, tracheostomy may be delayed for an additional week before reassessment.\[132\]

[VIDEO: Tracheal intubation animated demonstration ]

[VIDEO: Bag-valve-mask ventilation animated demonstration ]

- **Pain in the acute phase:** gabapentin or carbamazepine are generally recommended in the ICU;\[132\] however, further studies are required to investigate the safety and efficacy of potential interventions in patients with pain.\[137\] Tricyclic antidepressants, tramadol, gabapentin, carbamazepine, or mexiletine may be helpful for long-term management of neuropathic pain.

- **Rehabilitation:** all patients should undergo an individual programme of rehabilitation in the acute phase.\[132\] A multi-disciplinary approach has been shown to improve disability and quality of life as well as reduce fatigue.\[149\]

- **Hypotension:** can be managed with fluid boluses. Intra-arterial BP monitoring should be started if BP is very labile.

- **HTN:** should be treated with short-acting agents to prevent overshoot phenomenon. Episodes of HTN can be treated with labetalol, esmolol, or nitroprusside.
### Acute

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>without IgA deficiency or renal failure</td>
<td>1st</td>
<td>intravenous immunoglobulin (IVIG)</td>
</tr>
</tbody>
</table>

- Both plasma exchange and IVIG have been shown to be equally efficacious. The choice between them is often institution-dependent. IVIG is a pooled blood product and runs the risk of transmitting infection, and can precipitate anaphylaxis in an IgA-deficient person. It is, however, much easier to administer because it is a peripheral intravenous infusion.

- In ambulatory patients IVIG is recommended within 2 weeks of symptom onset.\[40\] In non-ambulatory patients IVIG is recommended within 2 to 4 weeks of onset.\[140\]

- Complications have been found to be significantly less frequent with IVIG than with plasma exchange.\[140\] Potential complications include transmission of infective agents (e.g., HIV, hepatitis B or C, Creutzfeldt-Jakob disease) and anaphylaxis (almost always in patients with severe immunoglobulin A deficiency).\[40\]

<table>
<thead>
<tr>
<th>Primary options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>intravenous normal immunoglobulin human:</strong> 400 mg/kg/day intravenously for 5 days</td>
</tr>
</tbody>
</table>

- All patients with severe disease should have their pulse and BP monitored until they are off ventilator support and have begun to recover.

- DVT prophylaxis: subcutaneous heparin or enoxaparin and support stockings are recommended for non-ambulatory patients until they are able to walk independently.\[132\]

- Intubation and ventilation: risk factors for respiratory failure include rapid disease progression, bulbar dysfunction, bilateral facial nerve weakness, and dysautonomia. Early intubation should be considered for patients with bulbar dysfunction, high risk of aspiration, and new atelectasis on CXR. Elective intubation should be considered in patients with no bulbar/mild bulbar dysfunction if vital capacity of <20 mL/kg; maximal inspiratory pressure is worse than -30 cmH2O; maximal expiratory pressure is <40 cmH2O; vital capacity, maximal inspiratory pressure, or maximal expiratory pressure is reduced by 30% from baseline initial measurement.\[108\] Once the patient is intubated, the need for tracheostomy should be addressed from week 2 onwards. If there
**Acute**

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>is no improvement of PFT, percutaneous tracheostomy should be performed. If there is improvement of PFT above baseline, tracheostomy may be delayed for an additional week before reassessment.[132]</td>
</tr>
</tbody>
</table>

[VIDEO: Tracheal intubation animated demonstration ]

[VIDEO: Bag-valve-mask ventilation animated demonstration ]

- Pain in the acute phase: gabapentin or carbamazepine are generally recommended in the ICU,[132] however, further studies are required to investigate the safety and efficacy of potential interventions in patients with pain.[137] Tricyclic antidepressants, tramadol, gabapentin, carbamazepine, or mexiletine may be helpful for long-term management of neuropathic pain.

- Rehabilitation: all patients should undergo an individual programme of rehabilitation in the acute phase.[132] A multi-disciplinary approach has been shown to improve disability and quality of life as well as reduce fatigue.[149]

- Hypotension: this can be managed with fluid boluses. Intra-arterial BP monitoring should be started if BP is very labile.

- HTN: should be treated with short-acting agents to prevent overshoot phenomenon. Episodes of HTN can be treated with labetalol, esmolol, or nitroprusside.

- With IgA deficiency or renal failure 1st plasma exchange

  - If there is a contraindication to intravenous immunoglobulin (namely, IgA deficiency or ongoing renal failure), then plasma exchange would be a better option.

  - Ambulant patients: plasma exchange is recommended within 2 weeks of onset. Two plasma exchanges are given for mild GBS (disability grade 0 to 2).

  - Non-ambulatory patients: plasma exchange is recommended within 4 weeks from onset of neurological symptoms.[140]

  - Plasma is separated from cells using membrane filtration or centrifugation concurrently with plasma and albumin.
### Treatment

<table>
<thead>
<tr>
<th>Acute</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient group</td>
<td>Tx line</td>
<td>Treatment</td>
</tr>
<tr>
<td>with IgA deficiency or renal failure</td>
<td>plus</td>
<td>supportive treatment</td>
</tr>
</tbody>
</table>

- **replacement.** This is labour intensive and requires teams skilled in extracorporeal circulation, and exposes the patient to procedure-related morbidities.

  - The dose for plasma exchange is given through a central venous catheter (Mahurkar), 50 mL/kg bodyweight every other day for 7-14 days.[139] During administration, patients should be closely monitored for electrolyte abnormalities and coagulopathies.

  - Complications include severe infection, BP instability, cardiac arrhythmias, and pulmonary embolus.[150] [151] Compared with IVIG, plasma exchange showed more instances of pneumonia, atelectasis, thrombosis, and haemodynamic difficulties.[139] Other adverse effects include hypocalcaemia.

- **DVT prophylaxis:** subcutaneous heparin or enoxaparin and support stockings are recommended for non-ambulatory patients until they are able to walk independently.[132]

- **Intubation and ventilation:** risk factors for respiratory failure include rapid disease progression, bulbar dysfunction, bilateral facial nerve weakness, and dysautonomia. Early intubation should be considered for patients with bulbar dysfunction, high risk of aspiration, and new atelectasis on CXR. Elective intubation should be considered in patients with no bulbar/mild bulbar dysfunction if vital capacity of <20 mL/kg; maximal inspiratory pressure is worse than -30 cmH2O; maximal expiratory pressure is <40 cmH2O; vital capacity, maximal inspiratory pressure, or maximal expiratory pressure is reduced by 30% from baseline initial measurement.[108] Once the patient is intubated, the need for tracheostomy should be addressed from week 2 onwards. If there is no improvement of PFT, percutaneous tracheostomy should be performed. If there is improvement of PFT above baseline, tracheostomy may be delayed for an additional week before reassessment.[132]
<table>
<thead>
<tr>
<th>Acute</th>
<th>Tx line</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient group</td>
<td>[VIDEO: Tracheal intubation animated demonstration]</td>
<td>Pain in the acute phase: gabapentin or carbamazepine are generally recommended in the ICU,[132] however, further studies are required to investigate the safety and efficacy of potential interventions in patients with pain.[137] Tricyclic antidepressants, tramadol, gabapentin, carbamazepine, or mexiletine may be helpful for long-term management of neuropathic pain.</td>
</tr>
<tr>
<td></td>
<td>[VIDEO: Bag-valve-mask ventilation animated demonstration]</td>
<td>Rehabilitation: all patients should undergo an individual programme of rehabilitation in the acute phase.[132] A multi-disciplinary approach has been shown to improve disability and quality of life as well as reduce fatigue.[149]</td>
</tr>
<tr>
<td></td>
<td>© BMJ Publishing Group Ltd 2018. All rights reserved.</td>
<td>Hypotension: this can be managed with fluid boluses. Intra-arterial BP monitoring should be started if BP is very labile.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HTN: should be treated with short-acting agents to prevent overshoot phenomenon. Episodes of HTN can be treated with labetalol, esmolol, or nitroprusside.</td>
</tr>
</tbody>
</table>
Emerging

Complement activation inhibition

Drugs inhibiting various stages of complement activation are being tried in several antibody-mediated neurological diseases. This is likely also to be useful in GBS, especially with positive antiganglioside antibodies.
Recommendations

Monitoring

Most patients show continued progression for up to 2 weeks followed by a plateau phase of 2 to 4 weeks and recovery of function. Patient should have follow-up within 2 weeks after the acute syndrome to evaluate for relapse, at which point repeat intravenous immunoglobulin or plasma exchange can be considered. Thereafter, follow-up is every 4 to 6 weeks for 6 months, then to 6 months for 1 year, and then yearly. Patient should continue working with physiotherapy and occupational therapy.

Patient instructions

Patients should be instructed to contact their physician with any worsening symptoms of weakness, numbness, paraesthesia, facial weakness, difficulty with swallowing or breathing, or worsening bladder function.

Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>respiratory failure</td>
<td>short term</td>
<td>medium</td>
</tr>
</tbody>
</table>

Neuromuscular respiratory function becomes compromised in 17% to 30% of patients with GBS. In some patients, bulbar dysfunction causes difficulty with clearing secretions, compromising gas exchange and increasing the risk of aspiration.

Clinical features that indicate fatigue of respiratory muscles are tachypnoea, sweating, tachycardia, asynchronous movements of the chest and abdomen, and episodic use of accessory muscles of respiration.[132]

In the case of worsening respiratory failure, patient should be started on invasive or non-invasive mechanical ventilator.

| bladder areflexia       | short term| medium |

Bladder areflexia and disturbed bladder sensation occurs secondary to dysfunction of peripheral types of parasympathetic and somatic nerve.[81]

Voiding is more frequently compromised with axonal type GBS. Micturitional disturbances on urodynamic studies have shown evacuation and storage disorders, bladder areflexia, and disturbed bladder sensation indicative of peripheral types of parasympathetic and somatic nerve dysfunction.

Maintaining an indwelling Foley catheter during the acute phase is helpful.[132]

| adynamic ileus         | short term| medium |

This PDF of the BMJ Best Practice topic is based on the web version that was last updated: Nov 20, 2017. BMJ Best Practice topics are regularly updated and the most recent version of the topics can be found on bestpractice.bmj.com. Use of this content is subject to our disclaimer. © BMJ Publishing Group Ltd 2018. All rights reserved.
Complications | Timeframe | Likelihood
--- | --- | ---
Adynamic ileus occurs secondary to dysfunction of the autonomic nervous system. Daily abdominal examination and auscultation should be performed to detect this early.[132]

Feeding should be suspended and nasogastric tube placed. Nasogastric feeds can be given at 10 mL/hour if the ileus is not severe.

Opioids should be avoided and promotility agents are contraindicated with dysautonomia.

Erythromycin or neostigmine may be helpful.[156] [157]

<table>
<thead>
<tr>
<th>Complication</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>paralysis</td>
<td>short term</td>
<td>medium</td>
</tr>
</tbody>
</table>
After 1 year approximately 15% of patients are unable to walk without help.[1]

Treatment in the acute phase should include an individual programme of gentle strengthening involving isometric, isotonic, isokinetic, and manual resistive and progressive resistive exercises.

Rehabilitation should be focused on proper limb positioning, posture, orthotics and nutrition.[132]

<table>
<thead>
<tr>
<th>Complication</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>fatigue</td>
<td>long term</td>
<td>high</td>
</tr>
</tbody>
</table>
The cause and contributing factors are not fully known, but fatigue appears in part to be a sequel of forced inactivity and general muscle deconditioning.

Supervised exercise programmes are recommended for both fatigue and functional abilities, which were measurably improved in studies.[132]

<table>
<thead>
<tr>
<th>Complication</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>immobilisation hypercalcaemia</td>
<td>long term</td>
<td>low</td>
</tr>
</tbody>
</table>
This may become evident approximately 4 months after the onset of paralysis, as in other states of immobilisation that favour resorption of the calcium.[154] Subcutaneous calcitonin combined with oral etidronate disodium has been found to be useful if sodium infusions fail.[155]

<table>
<thead>
<tr>
<th>Complication</th>
<th>Timeframe</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>variable</td>
<td>medium</td>
</tr>
</tbody>
</table>
Immobilisation is a risk factor for the development of DVT.[158] There is a lack of clinical studies that address methods of prophylaxis or monitoring of patients at risk for thrombosis. Observational studies in orthopaedic or general surgery patients suggest a benefit from subcutaneous heparin 5000 U every 12 hours in preventing DVT.

In acutely ill medical patients, prophylactic treatment with subcutaneous enoxaparin 40 mg daily reduced the incidence of DVT from 15% to 5% compared with placebo. Support stockings reduced the risk by almost 70% in patients at moderate risk for DVT post-operatively.

Subcutaneous heparin or enoxaparin and support stockings are recommended for non-ambulatory adult patients.[132]
Prognosis

The overall prognosis of GBS is good, with approximately 85% of survivors making a good functional recovery. Mortality of 20% has been shown in ventilated patients.[152]

Prognosis worsens with older age.[24] [58] Factors associated with poorer outcome include more severe weakness, rapid onset, older age, muscle wasting, electrically inexcitable nerves, and preceding diarrhoeal illness.[1] Miller-Fisher syndrome has a better prognosis than other GBS subtypes. Most severely disabled patients with acute motor axonal neuropathy have been found to walk independently within a few years.[2] Most patients with a poor outcome have been mechanically ventilated. Mortality of 20% has been demonstrated in these patients.[152] Recovery from severe disease may be prolonged, but most patients are able to walk independently.[152] Acute and long-term disability appear to be associated with axonal involvement and a Hughes score ≥2 at the lowest point.[153]
Guillain-Barre syndrome

Diagnostic guidelines

Europe

Diagnostic and classification criteria for the Guillain-Barre syndrome

Published by: GBS-consensus group of the Dutch Neuromuscular Research Support Centre

Last published: 2001

Summary: Discusses the diagnostic criteria for clinical diagnosis.

Electrophysiological classification of Guillain-Barre syndrome

Published by: Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group

Last published: 1998

Summary: Discusses neurophysiological criteria for acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor-sensory axonal neuropathy (AMSAN), and acute motor axonal neuropathy (AMAN).

Treatment guidelines

North America

Practice parameter: immunotherapy for Guillain-Barre syndrome

Published by: American Academy of Neurology

Last published: 2003

Summary: Provides an evidence-based statement to guide immunotherapy use. Plasma exchange is recommended for non-ambulatory patients within 4 weeks of onset and for ambulatory patients within 2 weeks of onset. Intravenous immunglobulin (IVIG) is recommended within 2 to 4 weeks from onset for patients requiring help to walk. Combination treatment with plasma exchange followed by IVIG is not recommended.
Key articles


References

Guillain-Barre syndrome

References


Guillain-Barre syndrome


Disclaimer

This content is meant for medical professionals situated outside of the United States and Canada. The BMJ Publishing Group Ltd ("BMJ Group") tries to ensure that the information provided is accurate and up-to-date, but we do not warrant that it is nor do our licensors who supply certain content linked to or otherwise accessible from our content. The BMJ Group does not advocate or endorse the use of any drug or therapy contained within nor does it diagnose patients. Medical professionals should use their own professional judgement in using this information and caring for their patients and the information herein should not be considered a substitute for that.

This information is not intended to cover all possible diagnosis methods, treatments, follow up, drugs and any contraindications or side effects. In addition such standards and practices in medicine change as new data become available, and you should consult a variety of sources. We strongly recommend that users independently verify specified diagnosis, treatments and follow up and ensure it is appropriate for your patient within your region. In addition, with respect to prescription medication, you are advised to check the product information sheet accompanying each drug to verify conditions of use and identify any changes in dosage schedule or contraindications, particularly if the agent to be administered is new, infrequently used, or has a narrow therapeutic range. You must always check that drugs referenced are licensed for the specified use and at the specified doses in your region. This information is provided on an "as is" basis and to the fullest extent permitted by law the BMJ Group and its licensors assume no responsibility for any aspect of healthcare administered with the aid of this information or any other use of this information.

View our full Website Terms and Conditions.
Contributors:

// Authors:

Saiju Jacob, MD, DPhil, MRCP (UK), FRCP (Lon)
Consultant Neurologist
Queen Elizabeth Neurosciences Centre, University Hospital Birmingham, Birmingham, UK
DISCLOSURES: SJ declares that he has no competing interests.

// Acknowledgements:

Dr Saiju Jacob would like to gratefully acknowledge Dr John B. Winer, Dr Michael T. Torbey, Dr Dhruvil J. Pandya, and Dr Prem A. Kandiah, previous contributors to this monograph. JBW, MTT, DJP, and PAK declare that they have no competing interests.

// Peer Reviewers:

Cigdem Akman, MD
Division of Pediatric Neurology
Columbia University College of Physicians and Surgeons, New York, NY
DISCLOSURES: CA declares that he has no competing interests.

Robert Hadden, FRCP, PhD
Consultant Neurologist
King's College Hospital, London, UK
DISCLOSURES: RH has been paid by Baxter Heathcare Ltd for membership of its neurology advisory board, and is a co-author of several studies referenced in this monograph.