Guillain Barre Syndrome (GBS)

July 27, 2020 by Josh Farkas

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Guillain Barre Syndrome (GBS) refers to a group of acute, autoimmune polyneuropathies.

**Acute Inflammatory Demyelinating Polyneuropathy (AIDP)**
- This is the most common cause of GBS (85-90% of patients).
- The pathophysiology involves demyelination. Patients often can recover relatively rapidly (over several weeks to months).

**Axonal Variants**
- Acute motor axonal neuropathy (AMAN)
  - Sensory nerves aren’t affected, so patients can have preserved reflexes. However, overall the disease still clinically presents similarly acute inflammatory demyelinating polyneuropathy (AIDP, above).
  - This often progresses more rapidly than AIDP, but overall its prognosis is similar to that of AIDP.
- Acute motor and sensory axonal neuropathy (AMSAN)
  - Both sensory and motor nerves are involved, with *axon degeneration*.
  - This form carries the worst prognosis, with the potential for delayed and incomplete recovery.

**Miller Fisher Variant**
- This is the second most common variant in United States (~10%).
- Its classic clinical triad involves areflexia, external ophthalmoplegia, and cerebellar ataxia.
- Extremity weakness can occur. However, patients usually don’t develop critical illness or respiratory failure.

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**epidemiology**

**general**
- GBS is the most common cause of generalized neuromuscular paralysis.
- Genders are affected roughly equally. The risk may increase somewhat with increased age.
- Specific risk factors include lymphoma, lupus, and HIV.

**upstream triggers**
- Infection is involved in up to 75% of cases, especially:
  - Campylobacter jejuni
  - Mycoplasma pneumoniae
  - Various herpesviruses (CMV, EBV, VZV)
  - Hepatitis E virus
  - HIV
  - Zika virus
  - COVID-19
- Immunizations (*extremely rare*)
- Checkpoint inhibitors (more on this [here](https://emcrit.org/ibcc/checkpoint/#neurologic); may require different treatment).

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**symptoms & signs**

**usual presentation**
- Sensory disturbance is often the first symptom.
  - Paresthesias are common.
  - Sensory loss can occur, but this is mild compared to motor dysfunction.
  - *Pain* can result from nerve root inflammation (e.g., in back or extremities).
- Ascending flaccid paralysis
  - Relatively symmetric.
  - Speed of progression correlates with disease severity.

- Dysautonomia
  - Rapid fluctuations may occur over minutes.
  - Sympathetic activation can occur (with hypertension, agitation, diaphoresis, tachycardia, vasoconstriction).
    - i) Posterior reversible leucoencephalopathy syndrome (PRES).
    - ii) Takotsubo cardiomyopathy can occur.
  - Parasympathetic activation can occur (with bradycardia, facial flushing, vasodilation).
  - Other features may include constipation, diarrhea, and urinary retention.

**signs**

- Objective muscle weakness.
- Loss of deep tendon reflexes is a hallmark (~90% sensitive).

**disease course**

- Usually worsens over ~2 weeks (80% will nadir by 2 weeks; 90% of patients will reach nadir by 4 weeks).
- Ongoing disease progression for longer periods suggests an alternative, related disorder: chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

**differential diagnosis**

**CNS or spinal cord**

- Brainstem infection or inflammation (e.g., sarcoidosis, Sjogren's Syndrome, neuromyelitis optica)
- Inflammation or infection of the spinal cord (e.g., sarcoidosis, acute transverse myelitis)
- Structural lesion compressing the brainstem or spinal cord
- Brainstem stroke
- Vitamin deficiency (thiamine or B12)
- Acute flaccid myelitis (e.g., due to enterovirus, rabies, West Nile virus, or Japanese encephalitis virus)

**nerve roots**

- Lyme disease
- CMV, HIV, EBV, VZV
- Leptomeningeal malignancy

**peripheral nerves**

- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
- Hypothyroidism
- Vitamin deficiency (thiamine or B12)
- Vasculitis (e.g., rheumatoid arthritis, polyarteritis nodosa)
- Critical illness polyneuropathy
- Toxins (e.g., alcohol, heavy metals, ethylene glycol, methanol, or n-hexane)

**neuromuscular junction**

- Myasthenia gravis
- Lambert-Eaton myasthenic syndrome (LEMS)
- Neurotoxins (botulism, tetanus, tick paralysis)

**muscles**

https://emcrit.org/ibcc/gbs/
- Metabolic (hypokalemia, hypomagnesemia, hypophosphatemia)
- Rhabdomyolysis
- Inflammatory myositis
- Drug-induced toxic myopathy (e.g., colchicine, chloroquine)
- Mitochondrial disease
- Critical illness myopathy

### CSF examination

- The classic finding is *albuminocytologic dissociation* (elevated protein, despite normal cell count). Protein is usually elevated, up to very high levels (100-1,000 mg/dL)
  - Elevated protein has a sensitivity of ~50% during the first week, but this increases over time (to ~80% by 3-4 weeks).
  - *Normal CSF analysis doesn’t exclude GBS.*
- Cell count is generally normal in GBS (<5 cells/µL), or at the most mildly elevated (<50 cells/µL).
  - Elevated cell count >50 or increased neutrophils in CSF suggest an alternative diagnosis (e.g., HIV, Lyme, leptomeningeal carcinomatosis, or sarcoidosis).

### Electromyography

- This is the most sensitive and specific finding. Electromyography may initially be normal, but a normal study >1-2 weeks after onset suggests an alternative diagnosis.
  - Findings vary depending on the type of disorder.
    - Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) – demyelination is predominant feature.
    - Acute motor axonal neuropathy (AMAN) – axonal loss involving only motor signals.
    - Acute motor and sensory axonal neuropathy (AMSAN) – axonal loss involving afferent and efferent signals.

### MRI

- In cases without cranial nerve involvement, the differential includes spinal cord lesions. MRI may be useful to exclude these.
- *Contrast enhancement of spinal nerve roots* may suggest a diagnosis of GBS, if seen (although this can also be seen in acute flaccid myelitis).

### Diagnostic criteria

*Ultimately, the diagnosis of GBS involves a combination of excluding alternative possibilities as well as matching the patient’s findings to the diagnosis of GBS. The following criteria may provide a helpful scaffolding to approaching the diagnosis, but aren't necessarily intended for rigid application.*

#### Required and supportive features

- “Required” features – Cornerstone findings
  - Progressive weakness of extremities (initially only legs may be involved).
  - Diminished reflexes in weak limbs (although this may be absent in the acute motor axonal neuropathy variant).
- “Supportive” features:
These are cornerstone therapies for GBS.

- The exact indications are unclear, but any critically ill or hospitalized patient with new-onset GBS merits treatment.
- Both appear to be equally effective. Furthermore, the combination of treatments hasn’t been proven to be superior to one treatment alone.
- IVIG is generally used, since this is safer and easier to perform.
  - The usual dose is 0.4 grams/kg/day for 5-day course.
  - If there is no improvement after 1-2 weeks, a second repeated course of therapy may be considered (although this is controversial).
  - Patients experiencing a smaller increase in IgG levels following IVIG administration might theoretically be better candidates for repeat therapy (19938102).

**hemodynamic fluctuations**

- Why this is important:
  - (a) Bradycardia with asystole is a potential cause of death.
  - (b) Hypertension can cause target organ damage, such as Takotsubo cardiomyopathy or posterior reversible encephalopathy syndrome (PRES).
- Blood pressure swings are often short-lived, so avoid treatment when possible. Aggressive treatment of hemodynamic fluctuations may merely worsen the hemodynamic roller-coaster (e.g., initiation of a vasopressor during a hypotensive episode exacerbates a subsequent episode of hypertension).
  - However, a small fraction of patients may develop sustained hypertension. Sympathetic nerves have less myelin, so persistent sympathetic overdrive can occur.
- For prolonged or critical hypotenion:
  - Administer fluid if there is evidence of true hypovolemia (e.g., negative fluid balance, poor PO intake for days).
  - May use vasopressor, at the lowest dose possible.
- For prolonged or critical hypertension:
  - Avoid treatment unless there is target-organ damage or ongoing severe hypertension (e.g., MAP > ~120 mm).
  - Avoid beta-blockers (these may aggravate subsequent bradycardia).
  - 1st line treatment. Remove the stimulus for hypertension if possible (e.g., ensure that pain and agitation are adequately treated).
  - 2nd line treatment. For prolonged and severe hypertension, consider a short-acting vasodilator (e.g., nicardipine infusion).
- For bradycardic episodes:
  - Avoid triggers of bradycardia if possible (e.g., endotracheal suctioning).
  - Discontinue negative chronotropes (e.g., beta-blockers).
In severe cases, electrical pacing may be needed.

**other autonomic problems**

- Urinary retention and incontinence can occur (requiring Foley catheter placement).
- Gastroparesis can occur, potentially requiring treatment with pro-motility agents or a post-pyloric feeding tube.
- Small intestinal ileus and colonic pseudo-obstruction can occur. This may become a major problem, leading to bowel perforation.
  - For patients receiving opioids, therapies such as oral naloxone or peripheral IV methylnaltrexone may be helpful (along with limitation of the opioid dose as much as possible).
  - A rectal tube may be helpful.
- Extreme caution and close monitoring is needed if neostigmine is utilized for treatment of colonic pseudo-obstruction, given its potential for causing autonomic swings (e.g., bradycardia and asystole). Pre-treatment with 0.4 mg glycopyrrolate prior to administration of neostigmine (2 mg over 5 minutes) may reduce the risk of bradycardia. ([28893807](https://pubmed.ncbi.nlm.nih.gov/28893807/), [18338263](https://pubmed.ncbi.nlm.nih.gov/18338263/))

**analgesia**

- Painful neuropathy is common. For neuropathic-type pain, gabapentin may be useful.
- Scheduled acetaminophen is often beneficial, especially among intubated patients.
- Opioid may be used, but exercise caution as patients are prone to develop ileus.

**monitoring pulmonary function tests**

*Obsessive, repetitive, and uninformed measurement of respiratory mechanics is a common pitfall in the management of GBS. Like many data points in medicine (e.g., troponin), respiratory mechanics can be useful if utilized appropriately.*

**forced vital capacity (FVC)**

- Basics of the FVC:
  - FVC is the largest volume of gas that a patient can exhale. Patients are asked to take a full breath in and then exhale maximally, with measurement of the exhaled volume. FVC reflects a *global* measurement of the patient’s ventilatory ability, which takes into account inspiratory and expiratory muscle strength as well as pulmonary compliance.
  - FVC is the most reproducible and clinically useful measurement of pulmonary function.
  - A normal forced vital capacity is ~60 ml/kg. Values below roughly 30 ml/kg suggest a risk of atelectasis or hypoventilation.
- Limitations:
  - Excessive performance may cause diaphragmatic fatigue.
  - The maneuver is effort dependent.
  - Measuring FVC may be impossible in a patient with bulbar weakness.
  - There is no high-quality evidence that any particular value has any specific meaning (traditionally utilized cutoff values are not evidence-based).

**negative inspiratory force (NIF)**

- This is the greatest negative pressure the patient can generate (also known as the minimum inspiratory pressure or MIP). A pressure gauge is used to measure the negative pressure generated by the patient when asked to inhale as hard as they can. This is a measurement of the strength of the inspiratory muscles, primarily the diaphragm.
- Reasons that the NIF should not be used to monitor non-intubated patients with GBS:
  - (1) The NIF doesn’t add statistically independent or useful information beyond measurement of the forced vital capacity alone. ([11405803](https://pubmed.ncbi.nlm.nih.gov/11405803/), [21748507](https://pubmed.ncbi.nlm.nih.gov/21748507/)) What this means is that it introduces a source of *noise*, without adding meaningful information.
  - (2) The NIF is more fatiguing and uncomfortable than the forced vital capacity.
**use #1 of respiratory mechanics: triage**

- Determining which patients require observation in an ICU versus a ward is primarily dependent on history and overall gestalt impression.
- However, pulmonary function testing could play a role in risk-stratification and triage. For example, an FVC under roughly 30 ml/kg might suggest a higher risk of deterioration and the need for closer monitoring.

**use #2 of respiratory mechanics: tracking trajectory**

- Serial measurement of forced vital capacity (FVC) is often used to determine disease trajectory (e.g., 2-3 times daily during waking hours).
- Serial FVC is only one piece of information to help assess the patient, in addition to numerous others (e.g., subjective impression and strength of other muscle groups).

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**noninvasive respiratory support**

- No high-quality evidence exists here. Theoretically, respiratory support could prevent exhaustion and the requirement for intubation. However, noninvasive support requires close monitoring for early detection of patients who are frankly failing and require intubation.
  - The key is probably early initiation, before respiratory exhaustion occurs.
  - If a patient is completely dependent on BiPAP and entirely unable to breathe without it, then they should simply be intubated. However, nocturnal BiPAP might be useful to off-load respiratory muscles at night, facilitating rest.
  - BiPAP or high-flow nasal cannula (HFNC) may be used to support patients with some evidence of respiratory weakness, and who aren't requiring intubation.
    - Titration and selection depends largely on patient tolerance.
    - BiPAP may be ideally restricted to nocturnal use, possibly with use of high-flow nasal cannula support during the day.

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**global evaluation & decision to intubate**

**pulmonary function (forced vital capacity)**

- As discussed above, this provides only one piece of information.
- The decision to intubate should never be based on respiratory mechanics alone.
  - For example, poor patient effort can cause aberrantly low values.
  - Several “rules” exist suggesting that specific cutoff values indicate when to intubate (e.g., below 15-20 ml/kg). These rules are not evidence based and should not be blindly followed (more on this [here](https://emcrit.org/pulmcrit/ve-pearls-for-the-dyspneic-patient-with-guillain-barre-syndrome-or-myasthenia-gravis/)).

**weakness of other muscle groups**

- Respiratory weakness tends to track with other types of weakness, especially:
  - i) The patient's ability to lift their head off the pillow.
  - ii) Facial or bulbar weakness.
- Progressive weakness of multiple muscle groups is concerning.

**clinical evaluation of respiratory status and the decision to intubate**

- Many criteria for intubation exist, but none are based on high-quality evidence. Ultimately the decision to intubate is a clinical one which should generally be based on the integration of multiple sources of information. Important parameters to track include the following:
  - (1) Evidence of increased work of breathing (e.g., accessory muscle use, subjective dyspnea)
  - (2) Difficulty controlling secretions
  - (3) Cough strength
  - (4) Overall course of muscle weakness
  - (5) Trends in forced vital capacity

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https://emcrit.org/ibcc/gbs/
### intubation procedure
- Intubation procedure carries risk of inducing a *vagal episode* (prepare push-dose epinephrine ahead of time, but avoid its use if possible). Evaluate for volume status prior to intubation and consider some fluid resuscitation if the patient is grossly volume depleted (as may occur due to bulbar weakness and poor oral intake).
- ![Warning](https://i.imgur.com/123456.png) Succinylcholine is contraindicated (denervation of muscles may lead to excessive potassium release).

### mode of ventilation and weaning
- Patients can be ventilated using *standard ICU protocols*.
- There is no evidence that patients with Guillain Barre syndrome are better managed with SIMV or other modes of ventilation. (Indeed, SIMV is poorly supported by evidence overall and should arguably be avoided.)

### weaning from ventilation
- Overall, this may be pursued in the same manner as liberating other patients from the ventilator. Ideally, strength will improve over several days, leading to the ability to extubate.
- One test which may be useful to trend is the patient’s voluntary *forced vital capacity* on the ventilator. This can be assessed during a spontaneous breathing trial by asking the patient to blow out as possible and then to take in a full breath.
  - Diaphragm strength may improve before extremity muscle strength, so it may be possible to extubate patients with persistent extremity weakness.

### post-extubation support
- Extubating to BiPAP or high-flow nasal cannula may reduce the work of breathing, reducing the reintubation risk.

### GBS in COVID-19
- Data regarding COVID-19 and GBS is only beginning to emerge, with the following based on several case reports. ![External link](https://pubmed.ncbi.nlm.nih.gov/32302082/), ![External link](https://pubmed.ncbi.nlm.nih.gov/32533876/), ![External link](https://pubmed.ncbi.nlm.nih.gov/32490966/)
- GBS often begins ~5-10 days after the initiation of other COVID-19 symptoms (coincident with development of adaptive immunity).
- Some patients may lack respiratory symptoms, presenting instead with *weakness* as a primary complaint.
- Both axonal and demyelinating variants can occur, as well as the Miller Fisher variant.
- Weakness is the predominant clinical finding (most often ascending paralysis). Dysautonomia doesn’t seem to be a prominent issue.
- Guillain Barre Syndrome may tend to blend in with critical illness neuropathy and critical illness myopathy, which may be more frequent (especially among intubated patients).
- Intravenous immune globulin (IVIG) is generally the front-line therapy for Guillain Barre Syndrome (with equal efficacy compared to plasmapheresis and superior tolerability).

### podcast
- ![External link](https://i1.wp.com/emcrit.org/wp-content/uploads/2016/11/apps.40518.14127333176902609.7be7b901-15fe-4c27-863c-7c0dbfc26c5c.5c278f58-912b-4af9-88f8-a65ff2da477.jpg)
- Follow us on ![iTunes](https://itunes.apple.com/ca/podcast/the-internet-book-of-critical-care-podcast/id1435679111)

### questions & discussion
- ![External link](https://emcrit.org/pulmcrit/gbs/)

To keep this page small and fast, questions & discussion about this post can be found on another page. ![External link](https://emcrit.org/pulmcrit/gbs/).
Over-aggressive treatment of autonomic swings.
Excessive focus on forced vital capacity and excessive measurement of the forced vital capacity.
Use of the negative inspiratory force.
Failure to consider GBS in a patient admitted to ICU with viral illness who develops weakness.
Assuming that a patient with GBS and respiratory failure has neuromuscular respiratory failure (as opposed to other possible causes of respiratory failure which may occur, such as heart failure).

**Going further:**

- [Five pearls for the dyspneic patient with GBS](https://emcrit.org/pulmcrit/five-pearls-for-the-dyspneic-patient-with-guillain-barre-syndrome-or-myasthenia-gravis/) (PulmCrit)
- [WikEM: Guillain-Barre Syndrome](https://wikem.org/wiki/Guillain-Barre_syndrome)

**References**
