Lec 12

Status Epilepticus

Seizures are classified by:

- The extent of brain involvement (generalized vs. focal seizures),
- The presence or absence of abnormal movements (convulsive vs. nonconvulsive seizures), and
- The type of movement abnormality (e.g., tonic, clonic, etc.).

The movements caused by seizures can be:

- tonic (sustained muscle contraction),
- clonic (rhythmic movements with a regular amplitude and frequency), or
- myoclonic (irregular, twitchy movements).

Some movements are familiar (e.g., chewing) and repetitive; these are called automatisms.

Generalized Seizures arise from synchronous, rhythmic electrical discharges that involve most of the cerebral cortex, and they are always associated with loss of consciousness. These seizures typically produce tonic-clonic movements of the extremities, but they can also occur without abnormal movements (generalized nonconvulsive seizures).

Partial Seizures can arise from diffuse or localized rhythmic discharges, and the clinical manifestations can vary widely, as demonstrated by the following two examples:

- Partial complex seizures are nonconvulsive seizures that produce behavioral changes and can be accompanied by repetitive chewing motions or lip smacking (automatisms). These seizures are a common cause of nonconvulsive status epilepticus, but they do not appear de novo in critically ill patients.
- Epilepsia partialis continua is a convulsive seizure that is characterized by persistent tonic-clonic movements of the facial and limb muscles on one side of the body.

Myoclonus

Myoclonus (irregular, jerking movements of the extremities) can occur spontaneously, or in response to painful stimuli or loud noises (startle myoclonus). These movements can be seen in any type of encephalopathy (metabolic, ischemic).

Myoclonus is not universally regarded as a seizure because it is not associated with rhythmic discharges on the EEG.

Status Epilepticus

Can be defined as 5 minutes of continuous seizure activity, or two seizures without an intervening period of consciousness). This can involve any type of seizure, and can be "convulsive" (i.e., associated with abnormal movements) or "nonconvulsive" (i.e., not associated with abnormal movements.

Nonconvulsive Status Epilepticus:

Most cases of nonconvulsive status epilepticus (NSE) involve partial complex seizures (which are not common in ICU patients), but as many as 25% of generalized seizures can be nonconvulsive. Generalized NSE is accompanied by loss of consciousness and can be an occult source of coma in ICU patients).

Predisposing Conditions

A variety of conditions can promote new-onset seizures in critically ill patients. In one survey, the most common predisposing conditions were:

1) drug intoxication.
2) drug withdrawal,
3) hypoglycemia.
4) Other predisposing conditions include metabolic encephalopathies (e.g., liver failure, uremia), ischemic and traumatic brain injuries, intracranial mass lesions, and meningoencephalitis.

MANAGEMENT OF STATUS EPILEPTICUS

Aims of management of Status Epilepticus are as follows:

- Termination of Status Epilepticus
- Prevention of Seizure Recurrence
- Management of Precipitating cause
- Management of complications

Approach: Diagnostic workup All patients

- Obtain IV access.
- Monitor vital signs (ABC).
- Head CT (appropriate for most cases)
- Labs: blood glucose, CBC, renal function tests, Calcium, Magnesium, electrolytes, AED levels.
- EEG monitoring (preferably) Consider based on clinical presentation
- Brain MRI
- Lumbar puncture
- Toxicology panel (i.e., isoniazid, TCAs, theophylline, cocaine, sympathomimetics, organophosphates, cyclosporine)

The following recommendations (unless otherwise cited) are from the most recent guidelines on convulsive status epilepticus (CSE) from the American Epilepsy Society

1) Fingerstick Blood Glucose: The initial encounter should include a fingerstick blood glucose level. If the blood glucose is <60mg/dl administer IV boluses of D50 (50 mL) and thiamine (100 mg).

2) Stage 1 Drugs: The most effective drugs for rapid termination of CSE are the benzodiazepines, which are effective in 60–80% of cases.
    a. LORAZEPAM: Intravenous lorazepam (4 mg IV over 2 minutes) is the drug of choice for terminating CSE. The onset of action is<2 min. and the full dose can be repeated after 5–10 minutes, if necessary.

b. MIDAZOLAM: The benefit of midazolam is rapid up-take when given by intramuscular (IM) injection. When IV access is not available, midazolam can be given IM in a dose of 10 mg. The efficacy in terminating CSE is equivalent to IV lorazepam, and the onset of action is only slightly longer than with IV lorazepam (e.g., one study showed a median onset of 3.3 minutes with IM midazolam vs. 1.6 minutes with IV lorazepam)

3) Stage 2 Drugs: are used for seizures that are refractory to benzodiazepines or are likely to recur within 24 hours. These drugs include phenytoin, fosphenytoin, valproic acid, and levetiracetam.
   a. PHENYTOIN: The IV dose of phenytoin is 20 mg/kg, or a maximum dose of 1,500 mg. Phenytoin cannot be infused faster than 50 mg/min because of the risk of cardiac depression and hypotension.
   b. FOSPHENYTOIN: Fosphenytoin is a water-soluble phenytoin analogue that produces less cardiac depression and can be infused three times faster than phenytoin (150 mg/min) (12). It is as effective as phenytoin and is preferred because of the reduced risk of hypotension.
   c. VALPROIC ACID: The IV dose of valproic acid is 40 mg/kg, or a maximum IV dose of 3,000 mg. Although considered equivalent to phenytoin in efficacy. valproic acid is superior to phenytoin for terminating benzo-diazepine-resistant.
   d. LEVETIRACETAM: The newest anticonvulsant for CSE is levetiracetam which is given in a single dose of 60 mg/kg IV, or a maximum IV dose of 4,500 mg. This drug is also considered equivalent to phenytoin in efficacy.

Table 41.1	Drug Regimens for Status Epilepticus
Drug	**Dosing Regimens and Comments**
Stage 1 Drugs	
Lorazepam	Dosing: 4 mg IV over 2 min. Repeat in 5–10 min, if necessary. Comment: Initial treatment of choice. Onset of action typically < 2 min.
Midazolam	Dosing: 10 mg by intramuscular (IM) injection. Comment: As effective as IV lorazepam, and preferred when IV access is not available.
Stage 2 Drugs	
Phenytoin	Dosing: 20 mg/kg IV or maximum single IV dose of 1,500 mg. Comment: Promotes cardiac depression and hypotension.
Fosphenytoin	Dosing: Same dose as phenytoin. Comment: Equal in efficacy to phenytoin, but has a more favorable safety profile.
Valproic Acid	Dosing: 40 mg/kg IV, or maximum single IV dose of 3,000 mg. Comment: Considered equivalent to phenytoin in efficacy.
Levetiracetam	Dosing: 60 mg/kg IV, or maximum single IV dose of 4,500 mg. Comment: Considered equivalent to phenytoin in efficacy.

Refractory Status Epilepticus

Ten percent of patients with CSE are refractory to stage 1 and 2 drugs. The recommended treatment at this point is anesthetic doses of one of the drugs in Table 41.2. Guidance from a neurologist (along with continuous electroencephalographic monitoring) is the best option at this stage.

Table 41.2 Drug Regimens for Refractory Status Epilepticus

Drug	Dosing Regimens
Pentobarbital	Load with 5–15 mg/kg IV over one hr, then infuse at 0.5–1 mg/kg/hr. If necessary, increase infusion rate up to 3 mg/kg/hr (maximum rate).
Thiopental	Start with an IV bolus of 3–5 mg/kg, and follow with 1–2 mg/kg every 2–3 min until seizures subside. Then infuse 3–7 mg/kg/hr for the next 24 hrs.
Midazolam	Load with 0.2 mg/kg IV, then infuse at 4–10 mg/kg/hr.
Propofol	Start with IV bolus of 2–3 mg/kg, and use further boluses of 1–2 mg/kg, if needed, until seizure activity subsides. Then infuse at 4–10 mg/kg/hr for 24 hrs.

MCQ TEST

1) STATUS EPILEPICUS defined as continuous seizure activity, or two seizures without an intervening period of consciousness for
    a. 5 minutes
    b. 15 minutes'
    c. 20 minutes
    d. 1 hour
    e. 3 hours
2) Stage 2 antiepileptic drugs (all true except one)
    a. Phenytoin
    b. Fosphenytoin
    c. valproic acid
    d. levetiracetam.
    e. Lorazepam
3) Diagnostic workup for all patient with epilepsy
    a. blood glucose
    b. renal function tests
    c. Calcium, Magnesium, electrolytes,
    d. Antiepileptic drugs level
    e. All the above

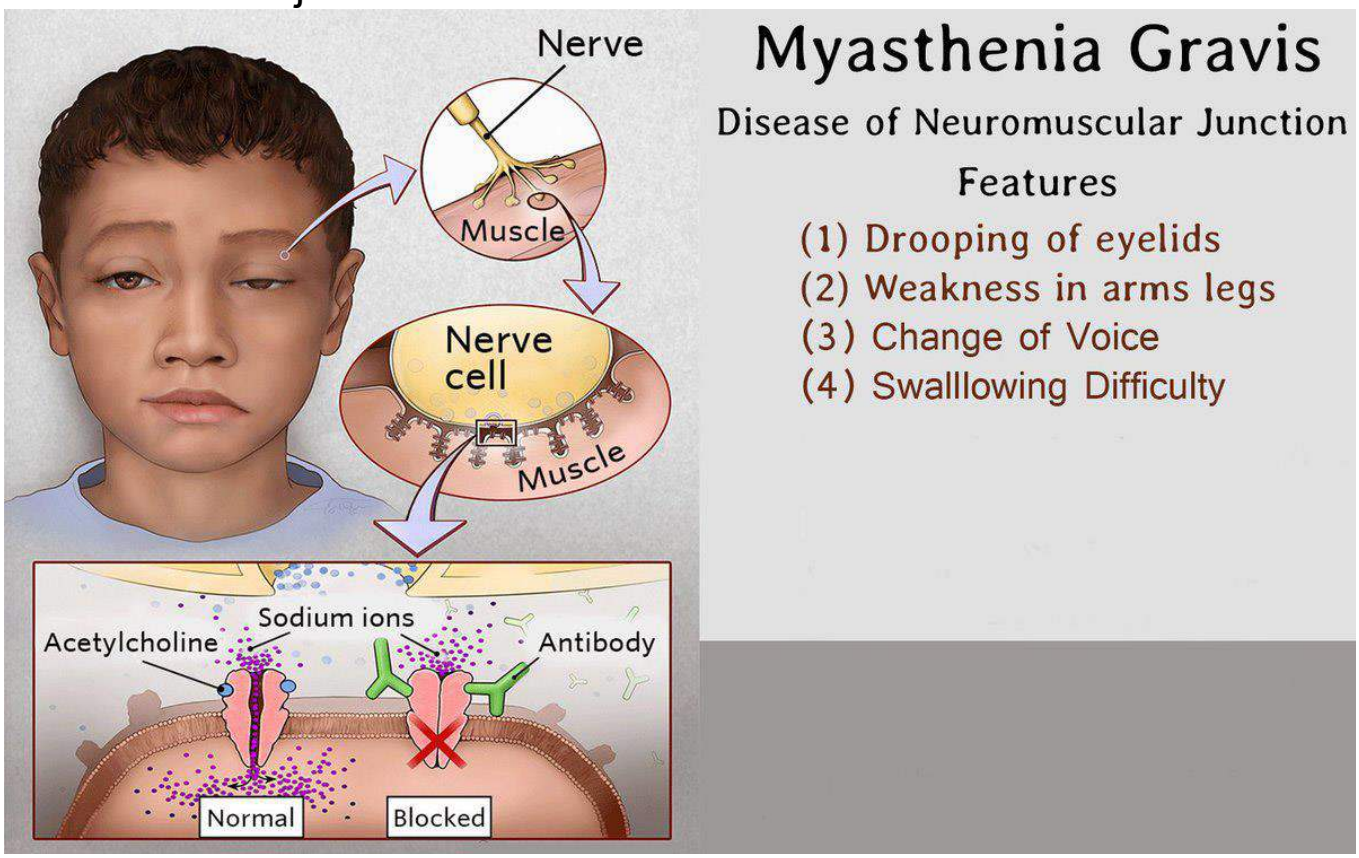
Lec 13

NEUROMUSCULAR WEAKNESS SYNDROMES

The neuromuscular weakness syndromes that deserve attention include myasthenia gravis and Guillain-Barré syndrome

Myasthenia Gravis (MG)

Is an autoimmune disease produced by antibody-mediated destruction of acetylcholine receptors on the postsynaptic side of neuromuscular junctions.



Predisposing Conditions

MG can be triggered by major surgery or a concurrent illness. Thymic tumors are responsible for up to 20% of cases. Several drugs can precipitate or aggravate MG; the principal offenders are antibiotics (e.g., aminoglycosides, ciprofloxacin) and cardiac drugs (e.g., beta-adrenergic blockers, lidocaine, procainamide, and quinidine).

Clinical Feature

The muscle weakness in MG has the following features:

- The weakness worsens with activity and improves with rest.

- Weakness is first apparent in the eyelids and extraocular muscles, and limb weakness follows in 85% of cases.
- Progressive weakness often involves the chest wall and diaphragm, and rapid progression to respiratory failure, called myasthenic crisis, occurs in 15–20% of patients.
- The deficit is purely motor, and deep tendon reflexes are preserved.

Diagnosis

The diagnosis of MG is suggested by weakness in the eyelids or extraocular muscles that worsens with repeated use. The diagnosis is confirmed by:

- Increased muscle strength after the administration of edrophonium (Tensilon), an acetylcholinesterase inhibitor.
- A positive assay for acetylcholine receptor antibodies in the blood, which are present in 85% of patients of MG.

Treatment

1) The first line of therapy is an acetylcholinesterase inhibitor like pyridostigmine (Mestinon), which is started at an oral dose of 60 mg every 6 hours, and can be increased to 120 mg every 6 hours if necessary. Pyridostigmine can be given intravenously to treat myasthenic crisis: the IV dose is 1/30th of the oral dose.
2) Immunotherapy is added, if needed, using either prednisone (1–1.5 mg/kg/day), azathioprine (1–3 mg/kg/day), or cyclosporine (2.5 mg/kg twice daily).
3) To reduce the need for long-term immunosuppressive therapy, surgical thymectomy is often advised in patients under 60 years of age.

Advanced Cases

In advanced cases requiring mechanical ventilation, there are two treatment options:

1) Plasmapheresis to clear pathological antibodies from the bloodstream.
2) IV immunoglobulin G (0.4 to 2 gm/kg/day for 2 to 5 days) to neutralize the pathologic antibodies.

Both approaches are equally effective, but plasmapheresis produces a more rapid response.

Emergency Department Care

- Patients with myasthenia gravis who are in respiratory distress may be experiencing a myasthenic crisis or a cholinergic crisis. Before these possibilities can be differentiated, ensuring adequate ventilation and oxygenation is important.
- Patients with myasthenic crisis can develop apnea very suddenly, and they must be observed closely.
- Evidence of respiratory failure may be noted through ABG determination, pulmonary function tests, or pulse oximetry.

Airway maneuvers

- Open the airway by suctioning secretions after positioning the jaw and tongue.
- Administer high-flow oxygen, and measure oxygen saturation by pulse oximetry. If respirations remain inadequate, ventilate by bag-valve mask while preparing to intubate.
- In the patient without an intact gag reflex, an oral airway may be placed.

Endotracheal intubation

- Rapid sequence intubation should be modified, because depolarizing paralytic agents (eg, succinylcholine) have less predictable results in patients with myasthenia gravis.
- The relative lack of ACh receptors makes these patients relatively resistant to succinylcholine; therefore, higher doses must be used to induce paralysis. Once paralysis is achieved, it may be prolonged.
- A rapid-onset, nondepolarizing agent (ie, rocuronium, vecuronium) is the preferred paralytic agent for these patients.
- Although nondepolarizing agents delay the onset of paralysis, compared with succinylcholine, these medications do not result in unwanted prolonged paralysis.
- Following paralysis, intubation is accomplished as usual.
- ABG sampling guides ventilator settings.

- Preliminary studies suggest that bilevel positive airway pressure (BiPAP) can prevent intubation in patients with myasthenic crisis without overt hypercapnia and should be considered in the patient who can be closely monitored. [9, 14]
- Hypercapnia present at the time of BiPAP initiation can predict failure and the need to proceed to endotracheal intubation.

Investigation and treatment

Once the airway is secured, investigation into the cause of the exacerbation of myasthenia gravis may proceed, with the most common reason for an exacerbation being infection, followed by inadequate treatment with cholinesterase inhibitors. However, up to 30% of patients will not have an identified cause of their exacerbation.

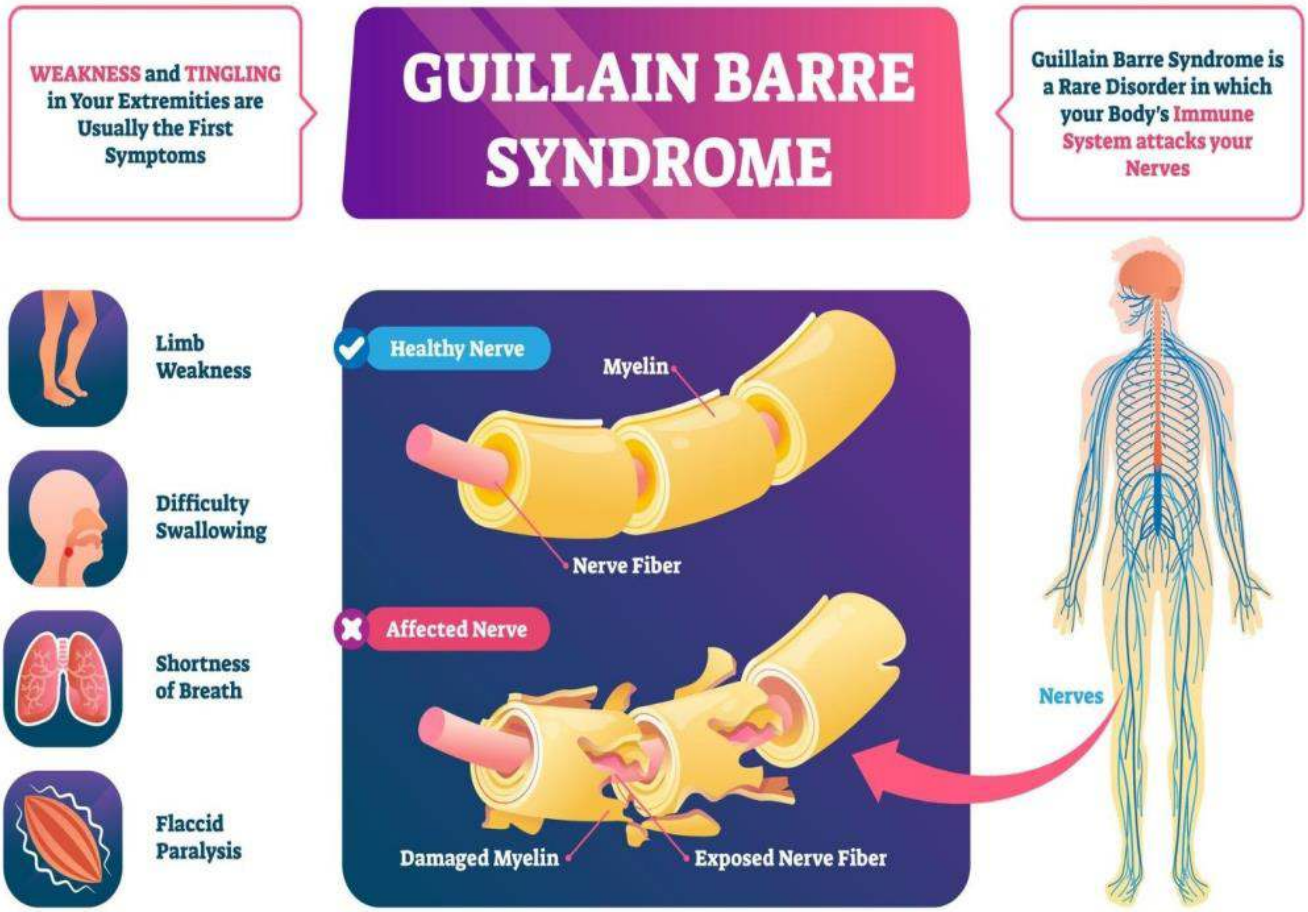
Difference between Myasthenic Crisis and Cholinergic Crisis

Myasthenic Crisis	Cholinergic Crisis
Under medication	Overmedication
Temporary improvement of symptoms with administration of Edrophonium	Symptoms improve with administration of anticholinergics (Atropine)
Heart rate increased	Heart rate decrease
Respiratory distress	Abdominal cramps
Pupil : Mydriasis	Pupil: Miosis
Increased Blood pressure	Decreased blood pressure
Normal secretion	Increased secretion

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Guillain-Barré Syndrome

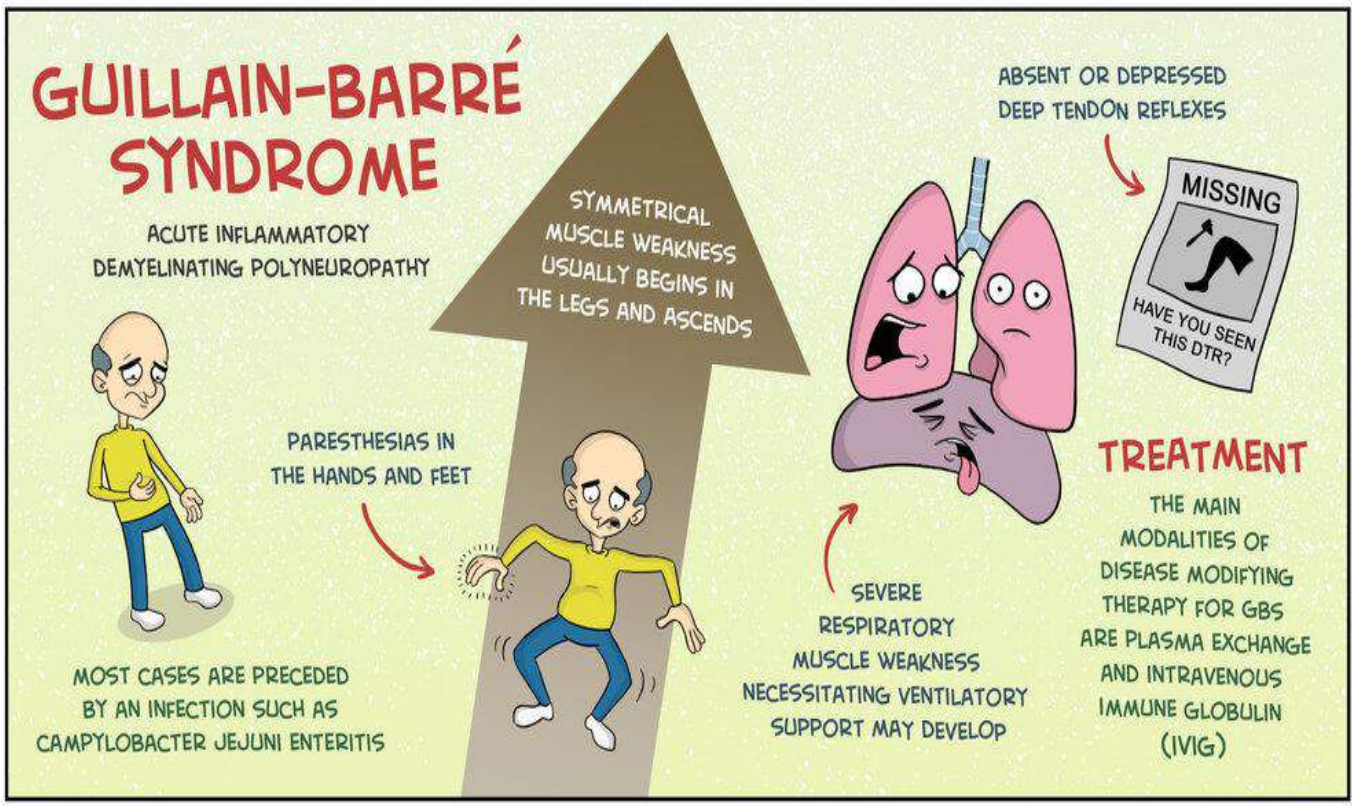
The Guillain-Barré syndrome (GBS) is a subacute inflammatory demyelinating polyneuropathy that often follows an acute infectious illness (by 1 to 3 weeks). An immune etiology is suspected.



Clinical Features

GBS presents with distal paresthesias and symmetric limb weakness that evolves over a period of a few days to a few weeks. Progression to respiratory failure occurs in 25% of cases , and autonomic instability can be a feature in advanced cases

The condition resolves spontaneously in about 80% of cases, but residual neurological deficits are common.



Diagnosis

The diagnosis of GBS is based on the clinical presentation (paresthesias and symmetric limb weakness), nerve conduction studies (slowed conduction) and cerebro-spinal fluid analysis (elevated protein in 80% of cases). The features that distinguish GBS from myasthenia gravis are shown in Table below.

Treatment

Treatment is mostly supportive, but in advanced cases with respiratory failure, plasmapheresis or IV immunoglobulin G (0.4 g/kg/day for 5 days) are equally effective in producing short-term improvement. Immunoglobulin is often preferred because it is easier to implement.

Table 41.3 Comparative Features of Myasthenia Gravis and Guillain-Barré Syndrome

Features	Myasthenia Gravis	Guillain-Barré Syndrome
Ocular weakness	Yes	No
Fluctuating weakness	Yes	No
Bulbar weakness	Yes	No
Deep tendon reflexes	Intact	Depressed
Autonomic instability	No	Yes
Nerve conduction	Normal	Slowed

MCQ TEST

1) All the following are clinical features of MG except one
   a. Ocular weakness
   b. Automatic instability
   c. Bulbar weakness
   d. Swallowing difficulty
   e. Change of voice

2) Cholinergic crisis(all true except one)
    a. Hypotension
    b. Bradycardia
    c. Increase secretion
    d. Medyriasis
    e. Abdominal crump
3) All the following are management of MG38
    a. Plasmapharesis
    b. Immunoglobulin
    c. A and B
    d. Non of the above
    e. Edrophonium
4) Clinical features og Gullian Bare Syndrome (all true except one)
    a. Normal deep tendon reflexes
    b. Ascending muscle weakness.
    c. Hypotension
    d. distal paresthesia's
    e. seizures
5) patient with MG is resistant to
    a. neostigmine
    b. succinylcholine
    c. rocuronium
    d. atracuriuom
    e. epinephrine