Myasthenia Gravis

- Most common autoimmune disease affecting the neuromuscular junction.
- Characterised by painless fatigable muscle weakness.
- Caused by autoantibodies against neuromuscular junction proteins, either the nicotinic acetylcholine receptor (AChR) or the muscle specific tyrosine kinase (MuSK).

**EPIDEMIOLOGY**

- Affects approximately 100 patients per million population.
- It has a bimodal age of onset—early and late onset myasthenia gravis.
- Early onset myasthenia gravis typically affects women less than 40 years of age whereas the later onset form is more common in older men.

**CLINICAL FEATURES OF MYASTHENIA GRAVIS**

- Extraocular muscle weakness (ptosis or diplopia) and later develop limb, and bulbar muscle weakness.
- Worsening of weakness after prolonged and sustained muscle contraction (fatigability) is the hallmark of myasthenia.

**Exacerbating factors**

- Infections
- Stress—trauma, postoperative
- Withdrawal of cholinesterase inhibitors
- Rapid introduction or increase of steroids
- Electrolyte
- Anaemia
- Medications

**Myasthenic crisis**

- A medical emergency that may progress to respiratory failure requiring ventilation.
- Affects approximately 10–15% of patients, usually within 2–3 years of diagnosis.
• Quieter breath sounds, reduced chest expansion, tachycardia and rise in blood pressure indicate imminent deterioration
• Measurement of forced vital capacity is a useful predictor for impending respiratory failure

**DIAGNOSIS**
• In generalised myasthenia, this is positive in 80–85% of patients. If the AChR antibodies are negative.
• MuSK antibodies should be tested as these are present in 5–8% of patients.
• (Tensilon test).
• Neurophysiology with repetitive nerve stimulation shows decremental response.
• Single fibre electromyography.
• CT scan of the chest

**TREATMENT**
• Pyridostigmine improves neuromuscular transmission by inhibiting acetylcholinesterase and so increasing the availability of acetylcholine at the motor endplate.
• Diarrhoea, abdominal cramps, nausea, increased salivation, bladder or bowel urgency are the side effects.

**Immunosuppression**
• Corticosteroids are the definitive therapy.
• immunosuppressants may be considered; as steroid sparing methotrexate, ciclosporin and mycophenolate mofetil
• In generalised myasthenia gravis, a second line immunosuppressant (“steroid sparing agent”) is started at the same time as prednisolone.

**Treatment of exacerbations of myasthenic weakness**
• Intravenous immunoglobulin (IVIg) is the most commonly used therapy for acute worsening of myasthenia.
• Plasma exchange is alternative option.
• Respiratory crisis requires ventilatory support.

**Thymectomy in myasthenic syndromes**
• 10–15% of myasthenia gravis patients have an associated thymoma.
• The characteristic pathological change in majority of patient are hyperlasia

Thymectomy is indicated in patients with
• Age less than 55 years
patients with AChR antibodies
- generalised myasthenia gravis

**LAMBERT–EATON MYASTHENIC SYNDROME**
- This rare autoimmune disorder affects synaptic transmission at both the neuromuscular junction and autonomic ganglia.
- It is caused by antibodies against P/Q type voltage gated calcium channels.
- It is about 20 times less common than myasthenia gravis
- 50–60% of patients have an underlying neoplasm, usually small cell lung cancer.

**Clinical features**
- Typically presents with proximal muscle weakness, predominantly affecting the lower limb.
- In contrast with myasthenia gravis, strength may improve after sustained exercise.
- almost all patients have some autonomic involvement; dry mouth, postural light headedness, sphincter disturbance or impotence.
- ocular, facial and bulbar muscle involvement is less common
- The tendon reflexes are commonly reduced or absent.
- but after excercising the relevant against resistance often allows the reflex to be elicited;this potentiation of absent or hypoactive tendon reflexes is virtually diagnostic.

**Diagnosis**
- VGCC antibodies are detected in approximately 90% of case and almost always positive in patients with an underlying small cell lung cancer.
- Neurophysiological assessment increamental respose on repetitive nerve stimulation.
- A comprehensive work-up for an underlying neoplasm should be undertaken

**Treatment**
- Symptomatic treatment with 3,4-diaminopyridine,
- This drug blocks potassium channels in the nerve terminal, prolonging the nerve action potential and enhancing calcium ion entry at the presynaptic nerve terminal, and release of acetylcholine
- Pyridostigmine.
- Immunosuppression with corticosteroids is used in both forms of the Lambert–Eaton myasthenic syndrome.
- Additional treatment with azathioprine, ciclosporin and mycophenolate mofetil are used in nonparaneoplastic disease.
- In severe disease, plasma exchange and IVIg are probably equally effective
• In paraneoplastic cases, treatment of the small cell lung cancer improves both the prognosis and the neurological.