Introduction:
- Myasthenia Gravis (MG) is a type of weakness disease or junctionopathy
- There are 2 main types recognised in humans and animals; congenital and acquired disease
- It has a bimodal age distribution in dogs (2-4YO vs 9-12YO) and humans with the acquired form of disease
- Any breed of dog can be affected however more commonly affected breeds include German Shepherd Dogs, Akitas, German Short haired pointers, Chihuahuas, Terriers, Labradors
- New research suggests the acquired form of disease is of growing relevance in our veterinary patients and as a consequence the understanding of the clinical presentations and diagnostic test can be imperative to clinicians in private practice and academia

Pathophysiology:
- The condition in both forms (congenital and acquired) leads to a function loss of acetylcholine receptors at the post synaptic membrane of the neuromuscular junction
- In the acquired form (most common) an immune mediated disease is suspected (IgG predominantly) leading to decreased function of the Acetylcholine receptors (Ach)
- This loss of receptor function is believed to occur through a combination of the following:
  - Complement destruction of the post synaptic membrane
  - Cross linked surface antigens on receptors resulting in internalisation of the receptors (reduction in receptor half-life)
  - Direct inhibition of receptor function by antibodies
- The congenital form is believed to derive from mutations in the post synaptic Ach receptors
- Clinically both forms result in the loss of muscle contraction, weakness and exhaustion

Classification of MG:
- There are 3 (+1) categories of classification of MG in dogs
  - Focal (36-43%): affecting one muscle group only; typically, of the oesophageal, pharyngeal, laryngeal muscle groups. These dogs usually lack clinical appreciation of generalised weakness in pelvic and thoracic limbs.
  - Generalised (57-64%): generalised weakness exacerbated by exercise and improves with rest. 90% of these patients have a megaoesophagus concurrently.
  - Fulminant (<5%) acute rapid development of severe generalised weakness often accompanied with respiratory distress
  - Paraneoplastic disorder: in association with a neoplasia; most commonly thymoma (30-50% of cases), also previously reported in association with cholangiocellular carcinoma, osteogenic sarcoma, anal sac adenocarcinoma, cutaneous lymphoma. Cats with thymomas are more likely to be Myasthenic than dogs
Diagnosis:
- The gold standard for diagnosis of MG is MG titre serum levels (radioimmunoassay)
- This test can only be run in the USA or Europe and thus turnaround times can be long 2-6 weeks
- In the Southern Hemisphere when we are faced with a rapidly progressive and debilitating disease this turn around time can be frustrating to clinically deal with for owners, patients and clinicians
- 98% of patients with MG will be seropositive at time of diagnosis
- New evidence from the USA suggests to re-run serum levels for patients suspected of having MG 2 weeks after a seronegative result if the patient still fits with a diagnosis of MG. This is suspected due to a lag of serum positivity behind the clinical disease.
- Tensilon test (Endrophonium chloride = short acting anticholinesterase agent) IV (which can be difficult to source) can be utilised as a initial diagnostic tests in patients with generalised and fulminant disease (however patients with fulminant disease are unlikely to respond)
- The dose for tension is 0.1-0.2mg/kg IV once in dogs 0.25-0.5mg per cat
- 60% of patients with MG will respond to the tensilon test
- False positives are also possible with the test as other lower motor neuron diseases may respond to this test also
- Clinicians should be aware of the risk of a cholinergic crisis with administration of this drug (SLUDGE signs)
- Atropine is the antidote to reverse these clinical signs if seen; 0.2-0.4mg/kg IV once

Treatment:
- Long term treatment involves the administration of Mestinon (pyridostigmine) PO TID 0.5-3mg/kg (0.25mg/kg every 8 hours for cats) for 6-12 months until titres levels are negative and weaning of the drug can occur
- Average spontaneous remission is 6.4 months in dogs reported in 86%.
- Spontaneous remission is less common in cats and there is stronger evidence of immunosuppressive use
- Immunosuppressive or immuno-modulatory medications may be indicated in severe disease in dogs. Routine use is not supported in the literature.
- Supportive care and nutritional mega-oesophagus management may be needed on a case to case basis

Is this disease becoming increasingly more common?
It is likely that we have been under testing for this disease condition and growing evidence exists for the increased frequency of this junctionopathy

MG can exist with other lower motor neuron diseases and failure of normal recovery expected should prompt investigation for concurrent disease such as MG especially those with polyridiculoneuritis (Stanciu et al, BMC Vet Res 2016)

- In a recent article (Gomes et al, JAAHA 2019) from the United Kingdom; dogs presenting with non-structural megaesophagus (n=89) all had performed MG titres
- 40% classed as idiopathic, 40% classed as MG and 20% other
- This contrasts with previous literature where idiopathic disease (70-80% of cases) was considered far more common than any other cause of megaoesophagus including MG
From this study we can learn that every patient presenting with megaoesophagus should have a MG titre performed to rule out the disease condition before euthanasia is considered.

Patients with MG over idiopathic disease have a more favourable outcome.

**New therapies in management for a megaoesophagus:**

- Quiuntavalla et al, Vet Record 2017 investigated the use of sildenafil (PDEV inhibitor) in increasing the tone of the lower oesophageal sphincter to reduce gastric regurgitation.
  - 1mg/kg every 12 hours for 14 days lead to decreased number of regurgitation episodes, increased weight gain and lead to radiographic improvement.
  - In patients with idiopathic or undiagnosed MG with a megaoesophagus this medication is clinically applicable.

**The trouble with managing megaoesophagus dogs.**

- Haines et al, JAAHA 2018 demonstrated the lack of reliability of Baily chairs/upright feedings in dogs through fluoroscopy (n=12 dogs).
  - Whilst some dogs in the study cleared the contents of liquid and solid food in <10 minutes some took longer (up to 30 minutes).
  - Recommendations of clearance times and upright feeding should be made on a case by case basis for each individual patient to reduce risk of gastric reflux and aspiration pneumonia.

**What about cats?**

- Cats with MG are more likely to have a thymoma than dogs (Hague et al, JVIM 2015)
  - A recent study (MIGNAN et al, JVIM 2019) investigated cats with MG (n=8) without evidence of a cranial mediastinal mass.
  - These cats presented with very vague neurological signs (fatigability was the most common signs using the Wheelbarrowing technique).
  - This disease should be considered a rule out if a neurological cat presents to your clinic with very vague weakness signs.
  - All cats had an excellent outcome; half resolved without any treatment at all.
References:


