What should you know about your MG?

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What you need to know about your MG

- The basis that led to your MG diagnosis
- The onset age (hopefully) and the duration of symptoms
- Symptoms of your MG
- Ocular versus generalized subtypes
- The antibody involved (AChR, MuSK, others (?), seronegative)
- Your thymus gland status (hyperplasia, tumor, normal)
- The treatment response (non-refractory versus refractory)
- Every medication you have tried for MG and the outcome
- Every medication you felt that has worsened your MG.
- Factors that make your MG worse.
- Your major coexisting health condition
- The physician who treat your MG and your PCP.

How is myasthenia gravis diagnosed?

- Careful neurological and ophthalmological examination to look for MG specific symptoms.
- Most patients end up with MRI of brain to rule out other disorders.
- In suspected patients:
  - Blood tests for antibodies (everybody, most common method)
  - Chest CT scan to evaluate thymus status (everybody)
  - Tensilon (edrophonium) test (mostly unnecessary)
  - Repetitive nerve stimulation (necessary in the minority)
  - Single fiber EMG test (necessary in the minority)
  - Supported by treatment response in patients with characteristic symptoms (everybody)

Imperfect Tests

- Blood tests for antibodies (everybody, most common method)
  - Rarely, positive antibody does not indicate MG.
- Chest CT scan to evaluate thymus status (everybody)
  - Patients may have thymus abnormalities but do not have MG.
- Tensilon (edrophonium) test (mostly unnecessary)
  - Tensilon test can be positive in patients without MG.
- Repetitive nerve stimulation (necessary in the minority)
  - Can be positive in patients without MG.
- Single fiber EMG test (necessary in the minority)
  - Can be positive in patients without MG. Very examiner dependent.
- Treatment response in patients with characteristic symptoms (everybody)
  - Patients without MG may respond to MG treatment (pyridostigmine, steroids)

How is myasthenia gravis diagnosed?

- Diagnosis of MG relies on a combination (all necessary):
  - Characteristic symptoms and signs
  - Test results
  - Positive treatment response
- You need to know the evidences to support your MG diagnosis.
- If unsure about the diagnosis, seeking a second opinion from a physician who specializes in MG evaluation/treatment.

Onset Age and Duration of Symptoms

- MG symptoms and disease severity tend to be the worst and tend to fluctuate more frequently within the first three years, in the majority of patients.

- After the first three years, the course of the disease is usually a gradual improvement or steady state, with fluctuation/exacerbation seen in the minority.

- The medication requirement after the first three years is less. Therefore there is a chance to minimize medication usage.

Symptoms of myasthenia gravis

- Double vision and drooping eyelid (seen in 90% of MG patients)
- Lack of facial expression or forced smiling
- Difficulty in chewing, jaw drop after chewing
- Soft voice with nasal speech
- Choking, more often with liquid
- Shortness of breath, difficult to lie down
- Difficulty holding arms up (shaving, hair-dressing, working overhead)
- Difficulty getting up from sitting/squatting position
- Head drop or head lag
- Fatigue and lack of energy

- You need to be familiar with your symptoms so that you can recognize early an exacerbation and impending crisis.

Grading the severity of myasthenia gravis: MGFA classification

- 0 - remission
- 1 - ocular (15% of all patients)
- 2 - mild generalized
  - 2A – with predominantly limb weakness
  - 2B – with predominantly bulbar weakness
- 3 - moderate generalized
  - 3A- with predominantly limb weakness
  - 3B - with predominantly bulbar weakness
- 4 - severe generalized
  - 4A - with predominantly limb weakness
  - 4B - with predominantly bulbar weakness
- 5 - crisis (intubated for MG)

Subtypes of myasthenia gravis based on symptoms

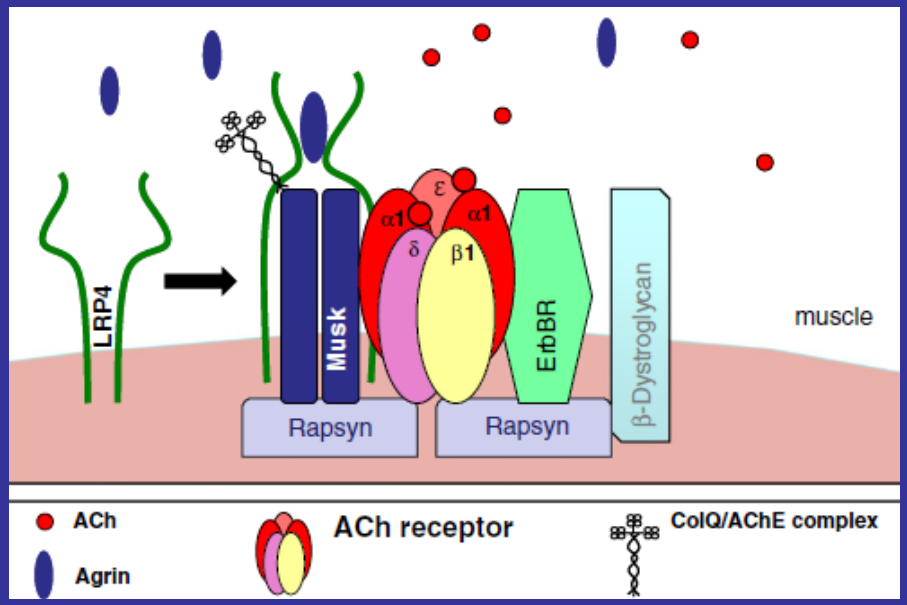
- Ocular: weakness in three muscle groups
  - Eye motility muscles: cause double vision
  - Orbicularis oculi: cause weakness in eye closure

- Generalized
  - Bulbar muscles (speaking, swallowing, chewing)
  - Axial muscles (neck, spine, respiratory)
  - Limb muscles (arm and leg), usually proximal

- Pure ocular MG: 15% of all MG patients
- Approximately two third or more of patients presented with ocular symptoms will eventually generalize.
- Generalization usually occurs within the first three years.

Subtypes of Autoimmune MG based on antibody

- AChR antibody (80-85%)
- MUSK antibody (6%)
- LRP4 antibody (?)
- Cortactin antibody (?)
- Agrin antibody (rare)
- ColQ antibody (rare)
- Other unrecognized antibodies
- More than one antibody

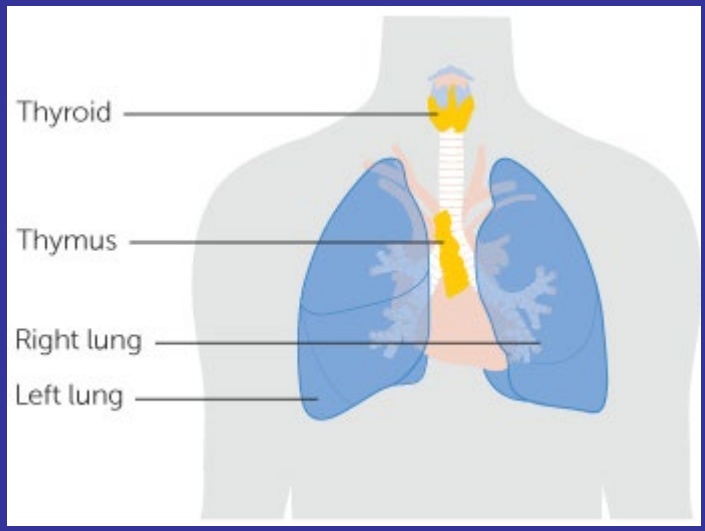


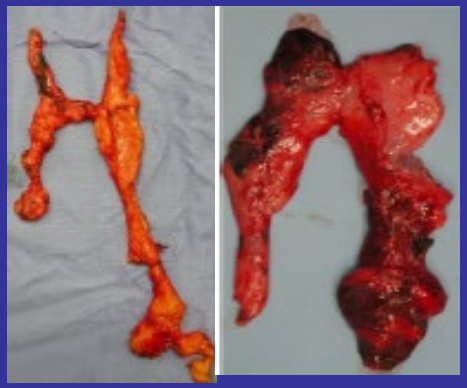
Why do you need to know antibody status?

- Antibody status may influence a physician's confidence in diagnosis MG.
  - Seronegative MG is always difficult to make. And there tend to be a lot of error in underdiagnosing/overdiagnosing seronegative MG.
- Antibody status may predict future course:
  - MuSK-MG tends to have more refractory course.
  - Antibody level may have some correlation with clinical progression.
- Antibody status may alter treatment option:
  - Eculizumab has been approved for AChR-Ab (+) MG only.
  - Rituximab is particularly effective for MuSK-Ab (+) MG.
  - Plasma exchange is particularly effective for MuSK-Ab (+) MG.
  - Thymectomy is effective for young patients with AChR-Ab (+) MG.
  - Thymectomy should not be performed for MuSK-Ab (+) MG.

Myasthenia gravis with heterogeneous thymus pathology

- Normal thymus: mostly AChR-Ab (-) MG
- Thymic hyperplasia (excessive growth):
  - <60-year-old AChR-Ab (+) MG
- Thymus involution (atrophy):
  - >60-year-old AChR-Ab (+) MG
- Thymoma: >50-year-old AChR-Ab (+) MG
- Thymus involution vs. hyperplasia (Mineo, 2015)





MGTX: Thymectomy in MG

- International study of 67 sites.
- 126 patients: AChR-Ab (+), MGFA class II-IV, < 5 years of onset, 18-65 years of age, non-thymomatous
- Results:
  - Thymectomy in early onset (<65 yo) AChR-Ab (+) generalized MG improves outcome, reduce immunosuppressant usage and improve quality of life
  - Efficacy of thymectomy seen in 6 to 12 months after surgery, and sustain for > 5 years.
  - Benefit clearly seen in <40 years of age, less clear in patients > 40 yrs, more significant in females

- Wolfe et al. NEJM 2016; 275: 511

Subtypes of MG based on treatment response

- Non-refractory MG

- Refractory MG (<10% of MG; Definition varies; Probably the following group:
  - Patients who failed corticosteroid and two other immunosuppressive agents of sufficient duration
  - Patients with clearly intolerable side effects limiting the use of immunotherapy
  - Patients with frequent relapses/exacerbation in need of maintenance IVIG or plasmaphereis therapy.

  - Usually generalized MG
  - A significant portion of MuSK-MG patients (not everybody)
  - MG with thymoma is more likely to be refractory.

Treatment options for MG

1. Document of your treatment history.
2. Aware the common side effects of each treatment.

Name	Used (yes/no)	Note (efficacy, side effect)
Pyridostigmine (mestinon)		
Corticosteroid (prednisone)		
Azathioprine (Imuran)		
Mycophenolate mofetil (Cellcept)		
Methotrexate		
Cyclosporine		
Tacrolimus (Prograft)		
Cyclophosphamide (Cytoxan)		
Rituximab (rituxan)		
Intravenous immunoglobulin (IVIG)		
Plasmapheresis (plasma exchange)		
Eculizumab (solirius)		
Thymectomy		

Guidelines on Medication Usage in MG

Avoid	Use with caution
Telithromycin	Antibiotics (fluroquinolones, aminoglycosides, macrolides)
Magnesium, intravenous	Magnesium, oral
Pencillamine	Corticosteroid
Botulinum toxin	Iodinated contrast agent
PD-1 inhibitors (nivolumab, ipilimumab, pembrolizumab)	Beta-blockers
	Procainamide
	Statins

- Sanders et al. Neurology. 2016;87(4):419-425. Table e2.

Fluctuating Course of MG

- Exacerbation (flare-ups)
  - Mostly triggered by:
    - ❖ Infection,
    - ❖ Hot weather
    - ❖ Surgery
    - ❖ Child birth
    - ❖ Medications
    - ❖ Reduction of treatment
  - Usually more frequent within first three years but can occur later in a portion of patients

Anxiety about MG crisis

- Crisis symptoms
  - Do not usually occur in isolation!
    - ❖ Usually associated with other MG symptoms.
    - ❖ Usually there is a cause (change in medication, infection, undiagnosed).
  - Do not go away without treatment adjustment!
  - Do not occur suddenly without gradual evolution for a few days to weeks, especially if already on immuotherapy!
  - Usually not manifesting as episodic shortness of breath with exertion only.
  - Usually not manifesting as a sudden episode of shortness of breath that wake you up at night.

Learn about exercise in MG

- Anziska and Inan. Semin Neurol 2014; 34: 542-556
  - MG patients may benefit from exercise by reversing their baseline reconditioning.
  - Aerobic activity at mild–moderate exertion on a regular basis seems to improve MG functional status and quality of life.
  - No adverse effects are noted on strength training. Avoid long runs at extreme temperature.
  - Respiratory training seems to improve QoL, respiratory endurance, self-perception of physical fitness, and decreased fatigability.
- Recommendations
  - Regular exercise
  - Avoiding prolonged-endurance type exercises
  - Working out only after adequate rest.
  - Exercising during cooler times of the day

Learn about your coexisting conditions

- Coexisting autoimmune conditions
  - Autoimmune thyroiditis seen in 25% patients. Lupus, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease
  - Not mixing up symptoms from these illnesses with those from MG.
  - Treatment for these coexisting conditions may help MG.

- Coexisting conditions that may influence choice of treatment
  - Diabetes
  - Osteoporosis
  - Gastrointestinal illness (ulcer, diverticulosis)
  - Liver or kidney dysfunction
  - Malignancy
  - Pregnancy and family planning

Learn about your physicians

- Work with responsible physicians
  - Care about you
  - Effective communication channel
  - Trustworthy
- Neuromuscular physicians or neurologists who know how to treat MG
- Keep your primary care physician in the loop to help monitor side effects as neurologists are generally not good in monitoring/treating these.
- Own your records!
  - Keep your previous records
  - Hand deliver your records. DO NOT RELY ON HOSPITAL/PHYSICIAN OFFICES.
  - Ask physicians to give back your records.