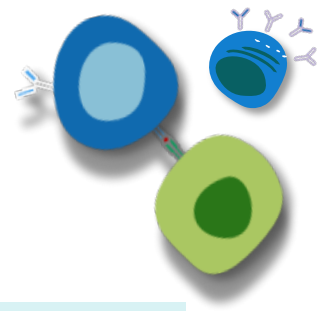
Myasthenia gravis: Diagnostic considerations

This material is intended for educational and supplemental purposes only and is not designed to be used as the sole basis for the diagnosis of myasthenia gravis. Clinical diagnosis should be based on a comprehensive evaluation by the treating physician.

Due to the similarity of symptoms with other conditions, accurate and expedited diagnosis of MG is essential[1,2]



1 Clinical evaluation[2-15]

Typical symptoms*

*MG can also present atypically, such as isolated limb/neck weakness or respiratory involvement without ocular/bulbar signs, or symptoms mimicking other neuromuscular disorders[16]

Clinical examination

Ocular	☐ Ptosis (i.e., drooping eyelid) ☐ Diplopia (i.e., double vision)	☐ Eye muscle assessment ☐ 1-min sustained upward gaze ☐ Ice pack test (improvement in ptosis after applying ice pack on eyelid for 2–5 min)
Bulbar and respiratory	☐ Facial muscle weakness ☐ Impaired speech ☐ Dysphagia (i.e., difficulty swallowing) ☐ Dyspnea (i.e., difficulty breathing), weak cough	☐ Counting slowly from 1 to 50 (1 number per second) ☐ Strength testing of neck flexion/extension ☐ Pulmonary function: FVC, MIP/MEP, SNIP, single breath count (≥25 considered normal[12])† †This is not an exhaustive list of available assessments
Muscles and limbs	☐ Weakness in the neck, arms, hands, legs, and hip flexors ☐ Impaired mobility	☐ Physical examination (fatigable proximal weakness) ☐ Improvement in muscle strength after administration of an acetylcholinesterase inhibitor

Symptoms and clinical exam positive
Proceed to step 2

Symptoms positive but clinical exam negative

Symptoms suggestive but clinical exam negative

If clinical exam **negative** but MG still suspected, proceed to **step 2**

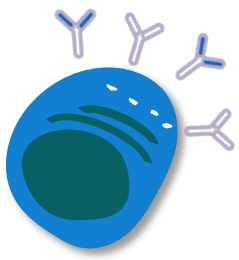
Symptoms and clinical exam negative

2 Serologic testing[3,13,17-22,‡]

‡The clinician should consider the patient's history and the benefits and limitations of each test

First-line assays: Choose available method§

§Anti-AChR testing generally recommended before anti-MuSK testing[18,19]



RIPA for anti-AChR and anti-MuSK‖

- **Established assay for anti-AChR and anti-MuSK testing**
- Radioactive labeling technique
- High specificity (nearly 100%), high sensitivity (50–100%) for AChR[18,19,23,24]

‖In this assay, it is the autoantibody from the patient sample (binding Ab) that is measured. A secondary Ab is used to detect the binding Ab[18]

OR

ELISA for anti-AChR, anti-MuSK, and anti-LRP4¶

- Alternative to RIPA, but ELISA is less specific (94–95% vs 98–100%) and less sensitive (62–77% vs 64–100%) for anti-AChR[20,24]
- Non-radioactive

¶Autoantibody testing by ELISA may be more likely to generate false positives than RIPA or CBA[25]

Positive

If **negative** but **clinical suspicion** remains high

Note: *if serology* ***negative*** *for anti-AChR and anti-MuSK, consider extending Ab panel to include anti-LRP4 and anti-agrin*[18,19,26,27]

Second-line assay

CBA for anti-AChR, anti-MuSK, anti-LRP4, anti-agrin

- Sensitive detection for anti-AChR versus RIPA and ELISA (sensitivity: 72–100% vs 64–100% and 62–77%, respectively)[20,24,25]
- **May detect Abs in individuals who would otherwise be classified as seronegative**
- Requires specialized expertise and cell-culture facilities; not commercially available

Positive

If **negative** but **clinical suspicion** remains high, proceed to **step 3**

3 Electrophysiology[3,17,28,29]

If both positive

Repetitive nerve stimulation:
☐ Decremental response
Single-fiber EMG:
☐ Increased jitter

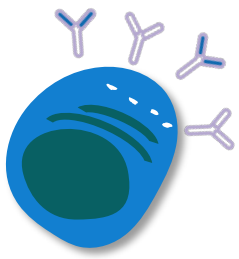
Note: *if serology* ***negative*** *for MG, but electrophysiology* ***positive****, an MG diagnosis is probable but not definitive*[30]

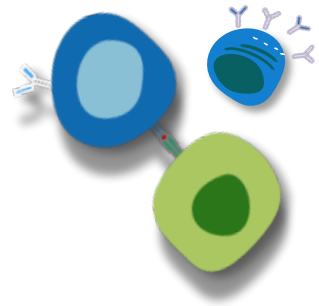
Repetitive nerve stimulation:
☐ Normal
Single-fiber EMG:
☐ Normal

MG diagnosis definitive[17]
- Chest CT/MRI recommended to assess for thymoma[2,31]

MG diagnosis unlikely[17]
- Consider further investigation for alternative diagnosis of other conditions with similar symptoms[32,33]

Myasthenia gravis: Diagnostic considerations (continued)





As part of the clinical evaluation in step 1, consider asking the following potential questions:

Do your symptoms **improve with rest** but worsen with physical activity?

Do you experience **double vision that gets worse** when you read or watch TV?

When eating, **do you have difficulty swallowing** liquids or solids?

Positive responses may align with…

Muscle weakness, ocular, and bulbar and respiratory symptoms described under clinical evaluation in **step 1**

Ab, antibody; AChR, acetylcholine receptor; CBA, cell-based assay; CT, computed tomography; ELISA, enzyme-linked immunosorbent assay; EMG, electromyography; FVC, forced vital capacity; LRP4, low-density lipoprotein receptor-related protein 4; MEP, maximal expiratory pressure; MG, myasthenia gravis; MIP, maximal inspiratory pressure; MRI, magnetic resonance imaging; MuSK, muscle-specific tyrosine kinase; OPMD, oculopharyngeal muscular dystrophy; RIPA, radioimmunoprecipitation assay; SNIP, sniff nasal inspiratory pressure.

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