Immunological testing for Myasthenia Gravis (MG)

Myasthenia Gravis Panel 2 with Reflex to MuSK Antibody

Myasthenia Gravis Panel 2 with Reflex - Quantitative AChR Binding, Blocking, Modulating Antibodies with Reflex to MuSK Antibody Testing

Myasthenia Gravis (MG) is an autoimmune disorder characterized by muscle weakness that ranges from mild weakness of specific muscle groups to severe weakness of multiple muscle groups. MG affects approximately 20 per 100,000[1] patients and arises from antibody-mediated synaptic dysfunction of the transmission of nerve impulses to muscle fibers at the neuromuscular junction. This disruption involves either acetylcholine receptors (AChR) or muscle-specific kinase receptors (MuSK) that ultimately inhibit muscle contraction. Onset of symptoms is generally gradual, but can sometimes be acute following viral infection or pregnancy.

What are the symptoms of MG?[2,3]

- Weakness and fatigue of skeletal muscles, ranging from mild weakness to severe weakness of multiple muscle groups. 90% have ptosis or diplopia with pupillary involvement.
- MuSK antibody-positive patients experience more pronounced bulbar weakness and may have tongue and facial atrophy.

AChR Positive Patients

- Limb weakness, ptosis, diplopia, dysarthria, dysphagia

MuSK Positive Patients

- Bulbar weakness is predominant, and can include ptosis, diplopia, dysarthria, facial weakness, difficulty chewing or swallowing; other signs and symptoms may vary.

AChR testing

85% of Myasthenia patients have AChR antibodies; these antibodies are not present in healthy individuals.[1] The AChR antibodies that occur in Myasthenia Gravis patients can be binding, blocking, or modulating. The binding assay is the most sensitive and highly specific for MG while blocking and modulating assays increase the sensitivity of detection.[2]

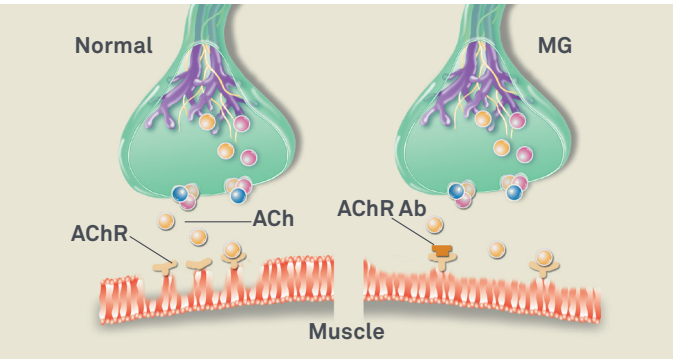

Figure 1: Diagram of the neuromuscular junction showing motor neurons transmitting acetylcholine (ACh) to receptors in the muscle tissue. (Left) ACh freely binds with the acetylcholine receptors (AChR), (Right) ACh is blocked from binding to the receptor by AChR antibodies.

Performing AChR quantification to assay the concentration may be important as AChR concentration is directly proportional to disease severity in the population, but the absolute concentration does not necessarily correspond to disease severity in individual patients. Binding antibodies were present in 82% of patients with moderate/severe generalized disease; 69% of patients with mild, generalized disease; and 59% of patients with ocular myasthenia.

MuSK

70% of seronegative[1] AChR patients have antibodies to MuSK. Overall, MuSK antibodies are seen in 5% to 10% of all MG patients. MuSK antibody-positive MG patients are also less likely to respond to acetylcholinesterase inhibitors (AChE), and symptoms may worsen with certain medications.[3] It is important that MuSK antibody-positive MG patients are identified, as 1/3 of patients experience a life threatening respiratory crisis, and long-term immunosuppression is the sole treatment.[4] Patients who test positive for MuSK antibodies are much less likely to have thymomas.

Quest Diagnostics™

How can MG be treated?

Treatment is fairly effective and leads to sustained remission.

Treatment goals: symptomatic improvement, relapse reduction and medication reductions, and medication side effect avoidance.

Treatments include:[2]

- ACh inhibitors
- Intravenous immunoglobulin (IV Ig)
- Plasmapheresis – directly removes AChR and MuSK antibodies; improvements can be seen in more than 80% of MG patients.
- Immunosuppressants

ICD-10 Codes*

H53.2	Diplopia
G70.00	Myasthenia Gravis without (acute) exacerbation
G70.01	Myasthenia Gravis with (acute) exacerbation
M62.81	Muscle weakness (generalized)
H02.409	Unspecified ptosis of unspecified eyelid
H02.403	Unspecified ptosis of bilateral eyelids
H02.402	Unspecified ptosis of left eyelid
H02.401	Unspecified ptosis of right eyelid
R53.1	Weakness
E03.9	Hypothyroidism, unspecified
E55.9	Vitamin D deficiency, unspecified
I10	Essential (primary) hypertension
E53.8	Deficiency of other specified B group vitamins
E11.9	Type 2 diabetes mellitus without complications
R20.2	Paresthesia of skin
R51	Headache
E78.5	Hyperlipidemia, unspecified
M79.1	Myalgia
G60.9	Hereditary and idiopathic neuropathy, unspecified

Ordering Information

Test Name:	Myasthenia Gravis Panel 2 with Reflex to MuSK Antibody
Test Code:	93859
CPT Codes:**	83519 (x3) without reflex 83519 (x4) with MuSK reflex
Turnaround Time:	4-7 days
Specimen Stability:	Ambient – 72 hours, Refrigerated – 14 days, Frozen – 30 days
Special Transport Requirements:	Ship refrigerated
Preferred Specimen:	3 mL serum
Minimum Volume:	0.7 mL
Specimen Container:	Plastic, screw-cap vial
Clinical Sensitivity:	AChR Binding (100%), AChR Blocking (52%), AChR Modulating (Not Established), MuSK (Not Established)
Clinical Specificity:	AChR Binding (98%), AChR Blocking (100%), AChR Modulating (Not Established), MuSK (Not Established)

Individual components may be ordered separately:
AChR Binding Antibody - Test Code: 206, CPT Code: 83519
AChR Blocking Antibody - Test Code: 34459, CPT Code: 83519
AChR Modulating Antibody - Test Code: 26474, CPT Code: 83519
Myasthenia Gravis Panel 2 - Test Code: 10104, CPT Code: 83519 (x3)
MuSK Antibody - Test Code: 18842, CPT Code: 83519

To learn more about MG testing, contact a representative at 1.866.MY.QUEST (1.866.697.8378) or visit QuestDiagnostics.com/MG.

*This list of commonly submitted diagnoses is intended to assist ordering physicians in providing ICD-10-CM codes. This is not a comprehensive list and an ICD-10-CM book should be used as the official reference. Diagnoses must always be documented in the patient's medical record. The ultimate responsibility belongs to the ordering physician to correctly assign the patient's diagnosis based on the patient's history, symptoms, and medical condition. ** The CPT code provided herein is based on AMA guidelines and is provided for informational purposes only. CPT coding is the sole responsibility of the billing party. Any questions regarding coding should be directed to the payer being billed.

References
1. Haven TR, Astill ME, Pasi BM. An Algorithm for Acetylcholine Receptor Antibody Testing in Patients with Suspected Myasthenia Gravis. *Clinical Chemistry.* 2010; 56(6): 1028-1029.
2. Yuebing Li. Myasthenia Gravis. Cleveland Clinic Center for Continuing Education Website. http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/neurology/myasthenia-gravis/. Published February 2014. Accessed April 7, 2016.
3. Shah AK. Myasthenia Gravis Workup. Medscape. http://emedicine.medscape.com/article/1171206-workup. Updated March 23, 2016. Accessed April 7, 2016.
4. Huijbers MG, Zhang W, Klooster R, et al. MuSK IgG4 autoantibodies cause myasthenia gravis by inhibiting binding between MuSK and Lrp4. *Proc Natl Acad Sci US.* 2013; 110(51): 20783-8.