Overview

Useful For

Diagnosis for autoimmune myasthenia gravis (MG) in adults and children

Distinguishing autoimmune from congenital MG in adults and children

Establishing a quantitative baseline value that allows comparison with future levels if weakness is worsening

Highlights

Seropositivity confirms a clinical or electrophysiologic diagnosis of autoimmune myasthenia gravis (MG).

Second-line muscle-specific kinase (MuSK) antibody test positivity confirms a clinical or electrophysiologic diagnosis of autoimmune MG where first-line serological tests (acetylcholine receptor: AChR binding and modulating antibodies) are negative.

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
MGRMI	MG Interpretive Comments	No	Yes
ARBI	ACh Receptor (Muscle) Binding Ab	Yes	Yes
STR	Striational (Striated Muscle) Ab, S	Yes	Yes
ARMO	ACh Receptor (Muscle) Modulating Ab	No	Yes

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
MUSK	MuSK Autoantibody, S	Yes	No
GD65S	GAD65 Ab Assay, S	Yes	No
GANG	AChR Ganglionic Neuronal Ab, S	No	No
VGKC	Neuronal (V-G) K+ Channel Ab, S	No	No
CRMWS	CRMP-5-IgG Western Blot, S	Yes	No

Testing Algorithm

If acetylcholine receptor (AChR) modulating antibodies are > or =90% and striational antibodies are > or =1:120, then ganglionic AChR neuronal autoantibody, glutamic acid decarboxylase autoantibody, neuronal voltage-gated potassium channel autoantibody, and collapsin response-mediator protein-5 (CRMP-5)-IgG Western blot will be

performed at an additional charge.

If AChR-binding antibodies are < or =0.02 and AChR-modulating antibodies are < or =20%, then muscle-specific kinase (MuSK) autoantibody will be performed at an additional charge.

See Myasthenia Gravis Evaluation with MuSK Reflex Algorithm in Special Instructions.

Special Instructions

- Myasthenia Gravis Evaluation with MuSK Reflex Algorithm

Method Name

ARBI, ARMO, GANG, VGKC: Radioimmunoassay (RIA)

STR: Enzyme Immunoassay (EIA)

CRMWS: Western Blot

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Patient Preparation: Patient should have no general anesthetic or muscle-relaxant drugs in the preceding 24 hours.

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 3 mL

Forms

If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

2 mL

Reject Due To

Hemolysis	Mild OK; Gross reject
Lipemia	Mild OK; Gross reject
Icterus	Mild OK; Gross reject
Other	NA

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	28 days	
	Ambient	72 hours	

Clinical and Interpretive

Clinical Information

Fatigable weakness due to impaired synaptic transmission at the neuromuscular junction is characteristic of myasthenia gravis (MG). The diagnosis is made by clinical and electromyographic criteria. Positive autoimmune serology must be interpreted in the clinical and electrophysiological context and response to anticholinesterase medication. Most cases are autoimmune and are caused by IgG autoantibodies binding to critical postsynaptic membrane molecules (nicotinic acetylcholine receptor or its interacting proteins, such as muscle-specific kinase: MuSK).(1) Autoantibody detection frequency is lowest in patients with weakness confined to extraocular muscles (71% muscle acetylcholine receptor: AChR binding). Mayo Clinic's first-line serological evaluation detects muscle AChR antibody in 92% of nonimmunosuppressed patients with generalized weakness due to MG. In adults with MG there is at least a 20% occurrence of thymoma or other neoplasm. If acetylcholine receptor (AChR) modulating antibodies are greater than or equal to 90% and striational antibodies are 1:120 or greater, then there is an increased risk of thymoma, and AChR ganglionic neuronal autoantibody, glutamic acid decarboxylase autoantibody, neuronal voltage-gated potassium channel autoantibody, and collapsin response-mediated response-5-IgG may also be detected in that paraneoplastic context.(2)

MuSK antibody is detectable in more than one-third of those seronegative for muscle AChR antibody (<4% of all patients).(3-4) Physiologically, MuSK is involved in integrating and stabilizing AChR clusters in the motor endplate. MuSK is activated when the nerve-derived proteoglycan agrin binds to its receptor, lipoprotein-related protein 4 (LRP4). Antibodies to LRP4 itself have been described in rare patients.(1) Females are generally affected by autoimmune MuSK MG more often than males. Onset can occur at any age (pediatric to elderly). Patients may derive limited benefit from anticholinesterase medication. The thymus is normal, and patients are generally not benefited by thymectomy. Antibody-lowering therapies are effective. Bulbar, facial, and respiratory weakness are prominent, and crises are common.(1,3,4)

Six percent of nonimmunosuppressed patients with generalized MG lack demonstrable AChR or MuSK antibodies (double seronegative). However, as in autoimmune AChR MG and MuSK MG, testing for common organ-specific and nonorgan-specific autoantibodies is a valuable ancillary investigation in evaluating seronegative acquired generalized MG. General serological testing, coupled with family or personal history, will disclose autoimmune phenomena in 77% of those cases.(5) These disorders may include thyroid disease, type 1 diabetes, vitiligo, premature greying, rheumatoid arthritis, or lupus. Objective improvement in strength following a therapeutic trial of plasmapheresis or intravenous immune globulin would justify consideration of long-term immunosuppression.

Reference Values

ACETYLCHOLINE RECEPTOR (MUSCLE) BINDING ANTIBODY

< or =0.02 nmol/L

ACETYLCHOLINE RECEPTOR (MUSCLE) MODULATING ANTIBODIES

(reported as __% loss of AChR)

0%-20%

STRIATIONAL (STRIATED MUSCLE) ANTIBODIES

<1:120

MUSCLE-SPECIFIC KINASE (MuSK) AUTOANTIBODY

< or =0.02 nmol/L

GLUTAMIC ACID DECARBOXYLASE (GAD65) ANTIBODY ASSAY

< or =0.02 nmol/L

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5-IgG (CRMP-5-IgG) WESTERN BLOT

Negative

GANGLIONIC ACETYLCHOLINE RECEPTOR (ALPHA3) AUTOANTIBODIES

< or =0.02 nmol/L

NEURONAL VOLTAGE-GATED POTASSIUM CHANNEL (VGKC) AUTOANTIBODY

< or =0.02 nmol/L

Interpretation

A positive result, in the appropriate clinical context, confirms the diagnosis of autoimmune myasthenia gravis, with or without thymoma.

Seropositivity justifies consideration of immunotherapy.

Cautions

Immunosuppressant therapy is a common cause of false-seronegativity. Therefore, it is important to perform a comprehensive serological evaluation before initiating immunosuppressant therapy.

Seronegativity does not exclude a diagnosis of myasthenia gravis (MG).

Interpretation of a patient's serological and clinical status is further complicated when characteristic signs of MG are obscured by a superimposed steroid-induced myopathy.

Positive values for muscle antibodies (acetylcholine receptor: AChR or striational) occur in 13% of Lambert-Eaton syndrome (LES) patients, 40% of patients with autoimmune liver disorders, approximately 10% of patients with lung cancer, in patients with graft-versus-host disease, and recipients of D-penicillamine.

False-positive results occur most frequently in the bioassay for AChR-modulating antibody; serum redraw will be requested when only this assay yields a positive result. Curare-like drugs used during general anesthesia can yield transient false-positive results for AChR-modulating antibodies.

This test should not be requested in patients who have recently received radioisotopes, therapeutically or

diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given, and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimen received in the laboratory will be held 1 week and assayed if sufficiently decayed, or canceled if radioactivity remains.

The presence of alpha-bungarotoxin antibodies may interfere with the AChR (muscle)-binding antibody assay.

Clinical Reference

1. Li Y, Arora Y, Levin K: Myasthenia gravis: Newer therapies offer sustained improvement. Cleve Clin J Med 2013 Nov;80(11):711-721

2. Vernino S, Lennon VA: Autoantibody profiles and neurological correlations of thymoma. Clin Cancer Res 2004 Nov 1;10(21):7270-7275

3. Skjei KL, Lennon VA, Kuntz NL: Muscle specific kinase autoimmune myasthenia gravis in children: A case series. Neuromuscul Disord 2013 Nov;23(11):874-882

4. Hoch W, McConville J, Helms S, et al: Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. Nat Med 2001 Mar;7(3):365-368

5. Chan KH, Lachance DH, Harper CM, Lennon VA: Frequency of seronegativity in adult-acquired generalized myasthenia gravis. Muscle Nerve 2007 Nov;36(5):651-658

Performance

Method Description

Acetylcholine receptor (AChR) binding and muscle-specific kinase (MuSK) antibodies are measured quantitatively by immunoprecipitation assay. The high-affinity ligand (125)I-alpha-bungarotoxin is complexed with fetal and adult, detergent-solubilized, acetylcholine receptors (extracted from cultures of rhabdomyosarcoma [RD] cells). (125)I-labeled recombinant human MuSK is used in the MuSK antibody assay. AChR modulating antibody is detected in a bioassay; (125)I-bungarotoxin measures percent loss of AChR from viable, noninnervated, monolayer cultures of human muscle cells following a 14-hour incubation with the patient's serum. The EIA used to detect striational antibodies employs as antigen a mixture of sarcomeric proteins extracted from human limb muscle.(Griesmann GE, Kryzer TJ, Lennon VA: Chapter 113: Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In Manual of Clinical and Laboratory Immunology, Sixth edition. Edited by NR Rose, RGHamilton, BDetrick. ASM Press, Washington, DC, 2002, pp1005-1012)

PDF Report

No

Day(s) and Time(s) Test Performed

ACh receptor (muscle) binding antibody:

Monday through Friday;11 a.m., 6 p.m., 10 p.m.

Saturday; 6 a.m.

Sunday; 6 a.m., 10 a.m.

ACh receptor (muscle) modulating antibodies:

Monday through Thursday; 2 p.m.

Saturday; 8 a.m.

Striational (striated muscle) antibodies:

Monday through Friday; 4 a.m., 3 p.m.

Saturday; 6 a.m.

CRMP-5-IgG Western blot:

Monday, Wednesday, Friday; 8 a.m.

AChR ganglionic neuronal antibody:

Monday through Friday; 11 a.m., 6 p.m.

Saturday; 6 a.m.

Sunday; 6 a.m.

Neuronal VGKC autoantibody:

Monday through Friday; 11 a.m., 6 p.m.

Saturday; 6 a.m.

Sunday; 6 a.m.

GAD65 antibody assay:

Monday through Friday; 6 a.m.,4 p.m.

MUSK autoantibody assay:

Tuesday, Thursday; 6 a.m.

Analytic Time

3 days

Maximum Laboratory Time

7 days

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

83519 x 2

83520

83519 x 3 (if appropriate)

84182 (if appropriate)

86341 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MGRM	MG Evaluation with MuSK Reflex, S	53706-8

Result ID	Test Result Name	Result LOINC Value
8338	ACh Receptor (Muscle) Binding Ab	11034-6
8879	ACh Receptor (Muscle) Modulating Ab	30192-9
8746	Striational (Striated Muscle) Ab, S	94817-4
37213	MG Interpretive Comments	69048-7