

## 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  $< \text{ or } = 0.02$  and AChR-modulating antibodies are  $< \text{ or } = 20\%$ , 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 | 8097-8             |
| 37213     | MG Interpretive Comments            | 69048-7            |