MAYO CLINIC LABORATORIES

# Test Definition: MGLE

Myasthenia Gravis/Lambert-Eaton Myasthenic Syndrome Evaluation, Serum

## Overview

### Useful For

Confirming the autoimmune basis of a defect in neuromuscular transmission (eg, myasthenia gravis [MG], Lambert-Eaton myasthenic syndrome [LEMS])

Distinguishing LEMS from autoimmune forms of MG

Providing a quantitative autoantibody baseline for future comparisons in monitoring a patient's clinical course and response to immunomodulatory treatment

### Profile Information

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| MGLEI | MG Lambert-Eaton Interpretation, S | No | Yes |
| ARBI | ACh Receptor (Muscle) Binding Ab | Yes | Yes |
| CCPQ | P/Q-Type Calcium Channel Ab | No | Yes |

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| ACMFS | AChR Modulating Flow Cytometry, S | No | No |
| MUSK | MuSK Autoantibody, S | Yes | No |

### Testing Algorithm

If acetylcholine receptor (AChR)-binding antibodies are greater than 0.02 nmol/L, then AChR muscle modulating antibody will be performed at an additional charge.

If AChR-binding antibodies are 0.02 nmol/L or less, then muscle-specific kinase (MuSK) autoantibody will be performed at an additional charge.

If unable to report AChR binding antibody due to interfering substances, then AChR muscle modulating antibody will be performed at an additional charge.

If unable to report AChR binding antibody due to interfering substances and AChR muscle modulating antibody is negative, MuSK autoantibody will be performed at an additional charge.

For more information see Myasthenia Gravis/Lambert Eaton Syndrome Testing Algorithm

### Special Instructions

- Myasthenia Gravis/Lambert Eaton Syndrome Testing Algorithm

### Method Name

ARBI, CCPQ, MUSK: Radioimmunoassay (RIA)
ACMFS: Flow Cytometry
MGLEI: Medical Interpretation

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Ordering Guidance

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 specimens received in the laboratory will be held for 1 week and assayed if sufficiently decayed or canceled if radioactivity remains.

### Specimen Required

**Patient Preparation:** For optimal antibody detection, specimen collection is recommended prior to initiation of immunosuppressant medication.
**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:**
**Preferred:** Red top
**Acceptable:** Serum gel
**Submission Container/Tube:** Plastic vial
**Specimen Volume:** 3 mL
**Collection Instructions:** Centrifuge and aliquot serum into a plastic vial.

### 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

| | |
|---|---|
| Gross Hemolysis | Reject |
| Gross lipemia | Reject |
| Gross Icterus | Reject |

### Specimen Stability Information

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

## Clinical & Interpretive

### Clinical Information

Myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) are acquired autoimmune disorders of neuromuscular transmission. MG is caused by pathogenic autoantibodies binding and potentially removing (modulation) the muscle's nicotinic acetylcholine receptor (AChR) from the surface of the neuromuscular junction. Serologically, the detection of AChR binding antibody provides the best diagnostic sensitivity. However, the presence of both AChR binding and modulating activity improves diagnostic accuracy. A subset of patients who are AChR seronegative will have muscle-specific kinase (MuSK) antibodies.

LEMS is caused by autoantibodies binding to motor nerve terminal's voltage-gated P/Q-type calcium channel. Synaptic transmission fails when autoantibodies cause a critical loss of junctional cation channel proteins that activate the muscle action potential.

Both MG and LEMS can affect children as well as adults, although LEMS is very rare in children. In adults MG is 10 times more frequent than LEMS, but it is sometimes difficult to distinguish the two disorders clinically. Electrophysiological testing is extremely helpful in distinguishing these 2 disorders. MG patients have decrements of compound muscle action potential (CMAP) amplitudes on repetitive stimulation whereas LEMS has immediate and dramatic post exercise facilitation (elevation) of CMAP amplitudes. Neoplasms associated with LEMS or MG are an endogenous source of the antigens driving production of the autoantibodies that characterize each disorder. In adults with MG, there is at least a 20% occurrence of thymoma and, very rarely (<1%), extrathymic cancers. LEMS is frequently associated (80%) with small-cell lung carcinoma (SCLC). Thus far, MuSK antibody associated MG has not been associated with any neoplasm.

The diagnostic sensitivity of these tests depends on the disease severity and duration of symptoms. AChR binding antibodies may be undetectable for 6 to 12 months after MG symptom onset and similarly P/Q-type calcium channel antibody may be undetectable for 6 to 12 months after LEMS onset. Only about 5% of adult patients with generalized MG who are not immunosuppressed remain seronegative for muscle AChR beyond 12 months. Although immunotherapy is universally beneficial for MG, in LEMS resection of the identified SCLC and initiation of

3,4-diaminopyridine, which facilitates acetylcholine release by increasing presynaptic calcium concentration, is most beneficial.

Note: Single antibody tests may be requested in the follow-up of patients with positive results previously documented in this laboratory.

## Reference Values

| Test ID | Reporting name | Methodology | Reference value |
|---|---|---|---|
| MGLEI | MG Lambert-Eaton Interpretation, S | Interpretation | NA |
| ARBI | ACh Receptor (Muscle) Binding Ab | Radioimmunoassay (RIA) | < or =0.02 nmol/L |
| CCPQ | P/Q-Type Calcium Channel Ab | RIA | < or =0.02 nmol/L |

**Reflex Information:**

| Test ID | Reporting name | Methodology | Reference value |
|---|---|---|---|
| ACMFS | AChR Modulating Flow Cytometry, S | Flow cytometry | Negative |
| MUSK | MuSK Autoantibody, S | RIA | < or =0.02 nmol/L |

## Interpretation

Positive results in this antibody evaluation are indicative of an autoimmune neuromuscular junction disorder. These results should be interpreted in the appropriate clinical and electrophysiological context.

In the presence of either acetylcholine receptor antibodies or P/Q antibodies, a paraneoplastic basis should be considered with thymoma being the most commonly associated tumor with myasthenia gravis and small cell lung cancer being the most commonly associated cancer with Lambert-Eaton myasthenic syndrome. Currently, muscle-specific kinase antibody positive myasthenia gravis is not associated with a paraneoplastic etiology.

Negative results do not exclude the diagnosis of an autoimmune neuromuscular junction disorder. If clinical suspicion remains and symptoms persistent or worsen consider retesting.

## Cautions

Specimens should be collected prior to administration of immunosuppressant therapy as this may reduce the diagnostic sensitivity of the assay; the neurological diagnosis is further confounded if steroid myopathy develops.

These results should only be interpreted in the appropriate clinical and electrophysiological context and are not diagnostic in isolation.

Positive muscle acetylcholine receptor (AChR) may occur in autoimmune liver disorders and in patients with graft-versus-host disease and recipients of D-penicillamine.

Weakly positive results may occur with hypergammaglobulinemia and should be interpreted with caution in the appropriate clinical context.

AChR modulating antibodies will only be performed if AChR binding antibodies are present or if there is an interfering substance present that precludes testing for AChR binding antibodies.

Seropositive rates and quantitative results differ across laboratories and patient results tested at different laboratories should not be treated equivalently.

The presence of alpha-bungarotoxin antibodies may interfere with the AChR muscle binding antibody assay and therefore if detected, AChR binding results will not be reported.

### Clinical Reference

1. Lennon VA. Serological profile of myasthenia gravis and distinction from the Lambert-Eaton myasthenic syndrome. Neurology. 1997;48(Suppl 5):S23-S27. doi:10.1212/WNL.48.Suppl_5.23S
2. Harper CM, Lennon VA: Lambert-Eaton syndrome. In: Kaminski HJ, ed. Current Clinical Neurology: Myasthenia Gravis and Related Disorders. 2nd ed. Humana Press; 2008;209-226
3. Hoch W, McConville J, Helms S, Newsom-Davis J, Melms A, Vincent A. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. Nat Med. 2001;7(3):365-368. doi:10.1038/85520
4. Shelly S, Paul P, Bi H, et al. Improving accuracy of myasthenia gravis autoantibody testing by reflex algorithm. Neurology. 2020;95(22):e3002-e3011. doi:10.1212/WNL.0000000000010910

## Performance

### Method Description

Radioimmunoassay:
(125)I-labeled recombinant human antigens or labeled receptors are incubated with patient sample. After incubation, anti-human IgG is added to form an immunoprecipitate. The amount of (125)I-labeled antigen in the immunoprecipitate is measured using a gamma-counter. The amount of gamma emission in the precipitate is proportional to the amount of antigen-specific IgG in the sample. Results are reported as units of precipitated antigen (nMol) per L of patient sample.(Griesmann GE, Kryzer TJ, Lennon VA: Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In: Rose NR, Hamilton RG, et al. eds. Manual of Clinical and Laboratory Immunology. 6th ed. ASM Press; 2002:1005-1012; Jones AL, Flanagan EP, Pittock SJ, et al: Responses to and outcomes of treatment of autoimmune cerebellar ataxia in adults. JAMA Neurol. 2015;72[11]:1304-1312. doi:10.1001/jamaneurol.2015.2378)

Flow Cytometry:
This method uses flow cytometry to measure the loss of acetylcholine receptor (AChR) molecules expressed on the surface of live cells expressing AChR on the cell surface. The cell line used is an immortalized human rhabdomyosarcoma cell line that expresses endogenous muscle-type nicotinic AChR on its surface. Cells are plated in a 96-well plate and cultured 72 hours prior to the addition of patient sample for an additional 18 to 22 hours to enable internalization of AChR receptors (modulation). Modulation is then stopped by placing cells on ice. The amount of remaining AChRs on the cell surface is measured by flow cytometry. On ice, cells are incubated with a recombinant rat monoclonal antibody against alpha-subunit of the AChR followed by a secondary goat anti-rat IgG antibody conjugated with APC. The amount of AChR on the cell surface is proportional to the median fluorescence intensity (MFI) of allophycocyanin (APC). To calculate the amount of modulation (ie, % loss of AChR) the APC MFI is compared between cells treated with patient sample and cells treated with serum lacking AChR modulating antibodies. Background signal is established in each

experiment utilizing cells stained with secondary antibody alone (no patient sera). The percent loss of AChR is calculated as 1-[(Patient MFI-Background MFI)/(Negative calibrator MFI - Background MFI)]*100%.(Unpublished Mayo method)

### PDF Report
No

### Day(s) Performed
Profile tests: Monday through Sunday; Reflex tests: Varies

### Report Available
3 to 10 days

### Specimen Retention Time
28 days

### Performing Laboratory Location
Rochester

## Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information
86041
86596
86043 (if appropriate)
86366 (if appropriate)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| MGLE | MG/LEMS Evaluation, S | 97566-4 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 8338 | ACh Receptor (Muscle) Binding Ab | 97558-1 |
| 81185 | P/Q-Type Calcium Channel Ab | 94349-8 |

| | | |
|---|---|---|
| 34273 | MG Lambert-Eaton Interpretation, S | 69048-7 |