Overview

Useful For
Confirmaing the autoimmune basis of a defect in neuromuscular transmission (eg, myasthenia gravis: MG, Lambert-Eaton syndrome: LES)

Distinguishing LES from 2 recognized autoimmune forms of MG

Raising the index of suspicion for cancer, particularly primary lung carcinoma (N-type calcium channel antibody)

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

Profile Information

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<td>CCPQ</td>
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Reflex Tests

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<td>CRMP-5-IgG Western Blot, S</td>
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<td>GANG</td>
<td>AChR Ganglionic Neuronal Ab, S</td>
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Testing Algorithm

If acetylcholine receptor (AChR) modulating antibodies are $>\text{ or }=90\%$ and striational antibodies are $>\text{ or }=1:120$, then AChR ganglionic neuronal antibody and CRMP-5-IgG Western blot will be performed at an additional charge.

This evaluation is recommended for patients presenting with an acquired defect of neuromuscular transmission in whom the differential diagnosis includes Lambert-Eaton syndrome (LES). It is not recommended for patients with a
past history of, or risk factors for, lung cancer and/or concurrent neurological symptoms/signs not attributable to LES; for those situations, order PAVAL / Paraneoplastic Autoantibody Evaluation, Serum. Testing for a newly recognized alternative antibody of myasthenia gravis (MG) (muscle-specific receptor tyrosine kinase) is indicated when all tests are negative.

See Myasthenia Gravis/Lambert Eaton Syndrome Diagnostic Algorithm in Special Instructions.

Special Instructions

- Myasthenia Gravis/Lambert Eaton Syndrome Diagnostic Algorithm

Method Name

CCN, CCPQ, ARBI, ARMO, GANG: Radioimmunoassay (RIA)

STR: Enzyme Immunoassay (EIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 3 mL

Additional Information: Patient should have no general anesthetic or muscle-relaxant drugs in the previous 24 hours.

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

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<td>Gross lipemia</td>
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<td>Gross icterus</td>
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Specimen Stability Information

Document generated August 20, 2020 at 12:56pm CDT
Test Definition: MGL1
MG/LES Evaluation

### Clinical and Interpretive

#### Clinical Information

Myasthenia gravis (MG) and Lambert-Eaton syndrome (LES) are acquired disorders of neuromuscular transmission. MG is caused by pathogenic autoantibodies binding to muscle's nicotinic acetylcholine receptor (AChR) or, in a small minority of patients, muscle-specific receptor tyrosine kinase (MuSK); LES 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 LES can affect children (see MGP1 / Myasthenia Gravis [MG] Evaluation, Pediatric) as well as adults, although LES is very rare in children. In adults MG is 10 times more frequent than LES, but it is sometimes difficult to distinguish the 2 disorders, clinically and electromyographically. In adults with MG, there is at least a 20% occurrence of thymoma or other neoplasm.

Neoplasms associated with LES or MG are an endogenous source of the antigens driving production of the autoantibodies that characterize each disorder. LES is frequently associated with small-cell lung carcinoma (SCLC). Thus far, MuSK antibody has not been associated with any neoplasm.

Autoimmune serology is indispensable for both the initial evaluation and monitoring of patients with acquired disorders of neuromuscular transmission. The neurological diagnosis depends on the clinical context and electromyographic findings, and is confirmed more readily by a serological profile than by any single test.

Not all of the antibodies in this profile impair neuromuscular transmission (eg, N-type calcium channel antibodies, antibodies directed at cytoplasmic epitopes accessible in detergent solubilized P/Q-type calcium channels and muscle AChRs, or antibodies against sarcomeric proteins that constitute the striational antigens).

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

See [Myasthenia Gravis/Lambert Eaton Syndrome Diagnostic Algorithm](#) in Special Instructions.

#### Reference Values

**ACh RECEPTOR (MUSCLE) BINDING ANTIBODY**

< or =0.02 nmol/L

**ACh RECEPTOR (MUSCLE) MODULATING ANTIBODIES**

0-20% (reported as __% loss of AChR)

**N-TYPE CALCIUM CHANNEL ANTIBODY**

< or =0.03 nmol/L

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<td></td>
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P/Q-TYPE CALCIUM CHANNEL ANTIBODY

< or =0.02 nmol/L

STRIATIONAL (STRIATED MUSCLE) ANTIBODIES

<1:120

**Interpretation**

A patient's autoantibody profile is more informative than the result of any single test for supporting a diagnosis of Myasthenia Gravis (MG) or Lambert-Eaton syndrome (LES), and for predicting the likelihood of lung carcinoma. Muscle acetylcholine receptor (AChR) and striational antibodies are characteristic but not diagnostic of MG. One or both are found in 13% of patients with LES, but calcium channel antibodies are not found in MG (with exception of rare non-thymomatous paraneoplastic cases).

Muscle AChR binding antibody is found in 90% of nonimmunosuppressed MG patients who have thymoma, and 80% have a striational antibody. Calcium channel antibodies have not been encountered with thymoma. The likelihood of thymoma is greatest when striational antibody is accompanied by a high muscle AChR modulating antibody value (> or =90% AChR loss). Detection of CRMP-5-IgG also is consistent with thymoma in patients not at risk for lung carcinoma.

N-type calcium channel antibodies are more highly associated with primary lung cancer than P/Q-type. One or all of the autoantibodies in the MG/LES evaluation can occur with neoplasia without evidence of neurological impairment. Calcium channel antibodies may disappear soon after commencing immunosuppressant therapy. Other serological markers of lung cancer also may disappear.

One or both calcium channel antibodies (P/Q and N) can occur with paraneoplastic and idiopathic cerebellar ataxia, encephalomyeloneuropathies, and autonomic neuropathy.

Titers are generally higher in patients with severe weakness, but severity cannot be predicted by antibody titer.

AChR and striational 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 LES onset. Only about 5% of nonimmunosuppressed adult patients with generalized MG remain seronegative for muscle AChR and striational autoantibodies beyond 12 months.

The alternative muscle autoantigen, MuSK, accounts for approximately 1/3 of seronegative MG cases with predominantly oculobulbar symptoms.

**Cautions**

Antibodies may disappear with immunosuppressant therapy; the neurological diagnosis is further confounded if steroid myopathy develops.

Unexplainable positive muscle acetylcholine receptor (AChR) or striational antibody values occur in 40% of patients with autoimmune liver disorders, approximately 10% of patients with lung cancer, and in patients with graft-versus-host disease and recipients of D-penicillamine.

Low false-positive values for calcium channel antibodies may occur with hypergammaglobulinemia.

False-positive results are most frequent in the bioassay for AChR modulating antibodies; 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 AChR modulating antibody results.
Seropositive rates differ in different laboratories.

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 1 week and assayed if sufficiently decayed, or canceled if radioactivity remains.

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

**Clinical Reference**


**Performance**

**Method Description**

Calcium channel binding antibodies (IgG and IgM) are measured quantitatively by immunoprecipitation assays. Selective high-affinity ligands labeled with (125)I are complexed with cation channel proteins detergent-solubilized from membranes of pig cerebral cortical synaptic membranes: omega conopeptide GVIA identifies neuronal N-type Ca(++) channels; omega conopeptide MVIIC identifies neuronal P/Q-type Ca(++) channels; (125)I-alpha-bungarotoxin identifies muscle acetylcholine receptor (AChR), fetal and adult, detergent-solubilized, acetylcholine receptors (extracted from cultures of rhabdomyosarcoma [RD] cells) AChR modulating antibody is detected in a bioassay: following 14 hours of incubation with patient's serum, viable, noninnervated, monolayer cultures of human muscle cells are probed with (125)I-bungarotoxin to quantitate percent loss of surface AChR. Striational antibodies (IgG, IgM, and IgA) are detected by EIA using as antigen a mixture of sarcomeric proteins extracted from healthy adult rat skeletal muscle. (Griesmann GE, Kryzer TJ, Lennon VA: Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In Manual of Clinical and Laboratory Immunology. Sixth edition. Edited by NR Rose, RG Hamilton, B Detrick. Washington, DC, ASM Press, 2002, pp 1005-1012)

**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.
Test Definition: MGL1
MG/LES Evaluation

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.

P/Q-type calcium channel antibody; N-type calcium channel antibody:
Monday through Friday; 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](#).

**CPT Code Information**

83519 x 4

83520

83519 (if appropriate)

84182 (if appropriate)
## LOINC® Information

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