Overview

Useful For
Diagnosis of autoimmune muscle-specific kinase (MuSK) myasthenia gravis

Second-order test to aid in the diagnosis of autoimmune myasthenia gravis when first-line serologic tests are negative

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

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

Special Instructions
- Myasthenia Gravis Evaluation with MuSK Reflex Algorithm

Method Name
Radioimmunoassay (RIA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 1.5 mL

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

Specimen Minimum Volume
1 mL

Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
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<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>Reject</td>
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</table>
Test Definition: MUSK
MuSK Autoantibody, S

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tr>
<td>Serum</td>
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<td>Frozen</td>
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<tr>
<td></td>
<td>Ambient</td>
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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).(1) Autoantibody detection frequency is lowest in patients with weakness confined to extraocular muscles (71% muscle acetylcholine receptor: AChR binding).(2) Mayo Clinic Laboratories’ first-line serological evaluation detects muscle AChR antibody in 92% of nonimmunosuppressed patients with generalized weakness due to MG. Muscle-specific kinase (MuSK) antibody is detectable in more than one-third of those seronegative for muscle AChR antibody (less than 4% of all patients).(3) 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)

Six percent of nonimmunosuppressed patients with generalized MG lack demonstrable AChR or MuSK antibodies (double seronegative). Other rare autoantibodies no doubt remain to be discovered in such cases. 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.(3) These disorders may include thyroid disease, type 1 diabetes, vitiligo, premature greying, rheumatoid arthritis, or lupus. Testing may also reveal antinuclear antibodies, glutamic acid decarboxylase (GAD65) antibodies, thyroperoxidase/thyroglobulin antibodies, or gastric parietal cell antibodies.(3) Objective improvement in strength following a therapeutic trial of plasmapheresis or intravenous immune globulin would justify consideration of long-term immunosuppression.

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.(1,4)

Reference Values

< or =0.02 nmol/L

Interpretation

A positive result, in the appropriate clinical context, confirms the diagnosis of autoimmune muscle-specific kinase myasthenia gravis.
Test Definition: MUSK
MuSK Autoantibody, S

Seropositivity justifies consideration of immunotherapy.

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

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

Clinical Reference

Performance
Method Description
Duplicate aliquots of patient serum are incubated with I(125)-labeled recombinant human muscle-specific kinase. Immune complexes, formed by adding secondary (goat) antihuman immunoglobulin, are pelleted by centrifugation and washed. Gamma emission from the washed pellet is counted, and mean counts per minute (cpm) are compared with results yielded by high positive and negative control sera. Sera yielding cpm higher than the background cpm yielded by normal human serum are retested to confirm positivity and titrated as necessary to obtain a value in the linear range of the assay. The antigen binding capacity (nmol per liter) is calculated from the cpm precipitated at a dilution yielding a linear range value.(Lavrnic D, Losen M, Vujic A, et al: The features of myasthenia gravis with autoantibodies to MuSK. J Neurol Neurosurg Psychiatry 2005 Aug;76[8]:1099-1102)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 6 a.m.

Analytic Time
3 days

Maximum Laboratory Time
10 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 using an analyte specific reagent. Its performance characteristics were 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

LOINC® Information

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<td>MuSK Autoantibody, S</td>
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