Overview

Useful For
Evaluating patients with suspected necrotizing autoimmune myopathy
Measuring 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) antibodies

Method Name
Chemiluminescence Immunoassay (CIA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Ordering Guidance
NMS1 / Necrotizing Myopathy Evaluation, Serum is the preferred first tier test for identification of antibodies specific for necrotizing autoimmune myopathy (HMGCOA-IgG and SRP-IgG). This initial evaluation includes signal recognition particle (SRP) antibodies performed using tissue indirect immunofluorescence, which increases the clinical sensitivity as compared to SRP immunoblot methodologies.

Specimen Required
Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Specimen Volume: 2 mL

Reject Due To
- Gross hemolysis: Reject
- Gross lipemia: Reject
- Gross icterus: Reject

Specimen Minimum Volume
1 mL

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>28 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
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Clinical & Interpretive

Clinical Information
Necrotizing autoimmune myopathy (NAM) is a serious but rare muscle disease strongly associated with autoantibodies to either signal recognition protein (SRP) or 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR). (1) NAM typically manifests with subacute proximal limb muscle weakness and persistently elevated serum creatine kinase (CK) concentrations, but slower onsets can occur and complicate diagnosis. Muscle biopsies in affected patients can demonstrate necrotic and regenerating myofibers without inflammatory infiltrates, suggesting the diagnosis. (2) However, sampling issues and lack of access to persons having expertise in obtaining, preparing, and interpreting muscle biopsy specimens may delay a diagnosis. (3)

Early identification of NAM and subsequent aggressive immune-modulating therapy is critical. (1,3) Discovery of SRP- or HMGCR-IgG autoantibodies can aid in establishing an earlier diagnosis and treatment initiation. In addition, the discovery of SRP or HMGCR autoantibodies should prompt a search for an underlying malignancy. (4) Serial testing for these autoantibodies may delay diagnosis with the discovery of either antibody aiding in establishing an earlier diagnosis and treatment initiation. (1,3)

The clinical onsets are not specific to NAM, consisting of proximal limb weakness in association with an elevated serum creatinine kinase, with or without exposure to lipid-lowering statin medications. (1,3-9) The clinical presentation can be confused with forms of inflammatory (dermatomyositis, polymyositis), toxic, metabolic, or even neurodegeneration (ie, muscular dystrophy) and the diagnosis delayed without serological testing by SRP- or HMGCR-autoantibody testing. Panel testing of both HMGCR and SRP autoantibodies is the preferred strategy for the best patient care.

Reference Values

Seropositivity for 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR) autoantibodies supports the clinical diagnosis of necrotizing autoimmune myopathy (NAM). Confirmation with muscle biopsy is recommended. A paraneoplastic basis should be considered, according to age, sex, and other risk factors. (4) In cases of NAM, immune therapy is required and often multiple simultaneously utilized immunotherapies are needed to successfully treat patients.

Cautions
Negative results do not exclude the diagnosis of necrotizing autoimmune myopathy (NAM). Only approximately 35% of cases of NAM are associated with autoantibodies against 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR). The remainder of cases are either positive for signal recognition protein (SRP) autoantibodies (approximately 20%-30%) or are seronegative (approximately 35%). Very rarely HMGCR antibodies can be detected in diseases other than NAM. A muscle biopsy is recommended.

Clinical Reference
2. Emslie-Smith AM, Engel AG: Necrotizing myopathy with pipestem capillaries, microvascular deposition of the complement membrane attack complex (MAC), and minimal cellular infiltration. Neurology 1991;41(6):936-939
myositis specific antibody. Brain 2016 Aug;139(Pt 8):2131-2135

Performance

Method Description
IgG antibodies to 3-Hydroxy-3-Methylglutaryl Coenzyme A reductase (HMGCR) are detected by a chemiluminescent assay using the Inova BIO-FLASH instrument. HMGCR antigen is coated on to paramagnetic beads, which are stored in the reagent cartridge lyophilized. When the assay cartridge is ready to be used for the first time, a buffer solution is added to the tube containing the beads, and the beads are resuspended with the buffer. The reagent cartridge is then loaded onto the BIO-FLASH instrument. A patient serum sample is diluted 1:17 by the instrument in a disposable plastic cuvette. An aliquot of the diluted patient serum, HMGCR-coupled beads, and assay buffer are combined into a second cuvette, and mixed. This cuvette is incubated at 37 degrees C. The beads are then magnetized and washed several times. Isoluminol conjugated anti-human IgG antibody is then added to the cuvette, and incubated at 37 degrees C. Again, the beads are magnetized and washed repeatedly. The isoluminol conjugate produces a luminescent reaction when "Trigger" reagents are added to the cuvette. The light produced from this reaction is measured as relative light units (RLU) by the BIO-FLASH optical system. RLU values are proportional to the amount of bound isoluminol conjugate, which in turn is proportional to the amount of anti-HMGCR antibodies bound to the antigen on the beads. The QUANTA Flash HMGCR assay utilizes a predefined lot specific Master Curve that is uploaded into the instrument through the reagent cartridge barcode. Based on the results obtained by running two calibrators, an instrument specific Working Curve is created, which is used by the software to calculate chemiluminescent units (CU) from the RLU value obtained for each sample. (Package insert: QUANTA Flash HMGCR 701333 Inova Diagnostics, Inc, San Diego, CA V04, 09/2018)

PDF Report
No

Specimen Retention Time
28 days

Performing Laboratory Location
Rochester

Fees & Codes
Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer’s instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
82397