Myasthenia Gravis Testing

The presence of acetylcholine receptor (AChR) antibodies that block or destroy receptors for the neurotransmitter acetylcholine traditionally defined myasthenia gravis (MG), an autoimmune disease caused by antibodies to neuromuscular and intramuscular elements impairing function and leading to muscle weakness and fatigue. However, this definition has expanded to include the presence of other autoantibodies, including muscle-specific kinase antibodies (MuSK).

DISEASE OVERVIEW

Incidence
3-30 per million/year

Prevalence
14-20/100,000 in U.S.

Age of Onset
- Mean age of onset
  - Females: 28 years
  - Males: 42 years
- Individuals <50 years: female predominance
- Individuals >60 years: no gender predominance
- Incidence rate increases with age for both genders

Symptoms
Main symptom: sporadic, fatigable muscle weakness
- Begins with mild weakness in limited muscle groups
  - Initially and most severely affects in ocular and bulbar muscles
  - 40% of individuals only experience weakness in ocular muscles initially
- Almost always progresses to weakness of multiple muscle groups within first year
  - 16% of individuals only experience weakness in ocular muscles after first year
  - Most serious condition results when respiratory muscles are affected, which may result in myasthenic crisis

Diagnostic Issues
- AChR antibody
  - Specific for MG
  - Presence does not correlate with disease severity
  - Detected in ~85% of patients with MG
  - Not detected in ~15% of patients (predominantly female) with MG
    - Experience weakness in respiratory and bulbar muscles
    - Have antibodies against other neuromuscular junction proteins
- MuSK antibodies
  - Detected in ~6% of patients with MG
  - Should be assessed when patient is seronegative for AChR antibodies

TESTS TO CONSIDER

Acetylcholine Receptor Antibody Reflexive Panel 2001571
Method: Quantitative Radioimmunoassay/Semi-Quantitative Flow Cytometry
Diagnose MG or confirm a clinical diagnosis of MG
Preferred reflexive panel for MG diagnosis

Acetylcholine Receptor Antibodies and Striated Muscle Antibodies Reflexive Panels, and Titin Antibody 2005639
Acceptable panel for MG diagnosis

Muscle-Specific Kinase (MuSK) Antibody, IgG 3001576
Method: Quantitative Radioimmunoassay
Secondary diagnostic testing for patients with generalized or ocular MG and no detectable antibodies to AChR

Secondary Tests

Autoimmune Neuromuscular Junction Reflexive Panel 2005640
Acceptable panel for the differential diagnosis of acquired neuromuscular junction (NMJ) disorders

Striated Muscle Antibodies, IgG with Reflex to Titer 0050746
Method: Semi-Quantitative Indirect Fluorescent Antibody
Secondary diagnostic testing for MG
Order if the primary tests are negative
Differential evaluation of NMJ

Titin Antibody 2005636
Method: Semi-Quantitative Enzyme-Linked Immunosorbent Assay
Secondary diagnostic testing for MG
Order if the primary tests are negative
Screen for presence of thymoma in patients with MG
See Related Tests for individually orderable tests.

TESTING STRATEGY

- Acetylcholine Receptor (AChR) Antibody Reflexive Panel tests for binding and blocking antibodies and reflexes to modulating antibody, and is the most cost-effective testing algorithm for the diagnosis of MG.
- AChR testing should not be performed for patients who recently received radioisotopes for diagnostic or therapeutic reasons, due to the potential for false-positive results.
- Muscle-specific kinase (MuSK) antibody should be considered for patients who are AChR antibody seronegative.

TEST INTERPRETATION

Sensitivity
Combination of binding and blocking AChR antibody testing identifies 99.6% of population possessing AChR antibodies and is
- Positive in up to 90% of individuals with generalized MG
- Positive in 50-70% of individuals with purely ocular MG

Results
Paraneoplastic disease is likely when positive AChR modulating antibody is in conjunction with
- Striated muscle antibody titer of ≥1:80
- Titin antibody index value of 0.72
- Both antibodies (which usually indicates thymoma)

Limitations
Negative result does not rule out a diagnosis of MG

REFERENCES
Howard JF. Clinical Overview of MG. Myasthenia Gravis Foundation of America. [Accessed: Apr 2019]

RELATED INFORMATION
Myasthenia Gravis - MG

RELATED TESTS
Acetylcholine Receptor Binding Antibody 0080009
Method: Quantitative Radioimmunoassay

Acetylcholine Receptor Blocking Antibody 0099580
Method: Semi-Quantitative Flow Cytometry

Acetylcholine Receptor Modulating Antibody 0099521
Method: Semi-Quantitative Flow Cytometry