

# Acetylcholine Receptor Antibody Testing

## *FOR CONFIRMATION AND MONITORING OF AUTOANTIBODIES IN PATIENTS WITH MYASTHENIA GRAVIS*

### Disease Overview

- Myasthenia gravis (MG) is characterized by sporadic, fatigable muscle weakness that usually presents first in the extrinsic ocular muscles, progressing to muscles in the extremities.
- Autoantibody-mediated loss of muscle acetylcholine receptor and complement-mediated destruction of the neuromuscular junction morphology prevent the transmission of motor nerve impulses across the neuromuscular junction. Autoantibodies associated with MG include anti-AChR antibodies, anti-muscle-specific kinase (MuSK) antibodies, and striated muscle antibodies (including titin antibodies).
- AChR antibodies are further characterized into three categories; binding, blocking, and modulating.
  - AChR-binding antibodies are detected in 90% of patients with severe, generalized MG, and 50% of patients with ocular MG. AChR-modulating antibodies and AChR-blocking antibodies are detected in approximately 65% to 70% of MG patients.
- Approximately 40% of AChR antibody-negative MG patients possess autoantibodies to MuSK, an AChR complex-associated protein.
- MG patients lacking AChR and MuSK antibodies are described as having seronegative MG.
- While disease severity and AChR-binding antibody titer may be positively correlated in MG patients as a population, this is not necessarily true for individual patients.
- MG is a paraneoplastic disease, with 20% to 30% occurrence of thymoma reported in MG patients. This increases to approximately 80% if both AChR and striated muscle/titin antibodies are detected.
- Acetylcholine receptor (AChR) antibodies are not detected in healthy individuals; however, AChR antibodies and striated muscle antibodies have been detected in patients with thymoma without neurological symptoms, and in patients with other autoimmune diseases, including, for example, Lambert-Eaton disease, myasthenic syndrome, rheumatoid arthritis, systemic lupus erythematosus, Graves disease, and autoimmune liver disease.

### Epidemiology

- The reported prevalence of MG varies widely but is estimated to be 77 per million, with a slight female prevalence.
- The annual incidence is estimated to be 4 to 6 per million, but chronic muscle fatigue is common to many diseases, which increases the importance of AChR antibody testing.

### Indications for Ordering

- Assist with diagnosis of MG.

- Assessment and patient management following immunosuppressive treatment or plasmapheresis.
- Prognosis of disease progression, particularly in paraneoplastic MG.
- A combination of binding and blocking AChR antibody testing will identify 99.6% of the patient population possessing AChR antibodies and can be used to screen for the presence of AChR antibodies.
- Reflex testing for AChR-modulating antibodies in serum testing positive for either binding or blocking AChR antibodies may be useful in predicting MG patient prognosis. Serum lacking binding and/or blocking AChR antibodies is rarely positive for modulating antibodies alone (0.4%).
- Reflex testing algorithm: If the Acetylcholine Receptor Binding Antibody test result is greater than 0.4 nmol/L, or if the Acetylcholine Receptor Blocking Antibody test result is greater than 15%, then the Acetylcholine Receptor Modulating Antibody (ARUP test code [0099521](#)) assay will be added. For the Myasthenia Gravis Panel, a titer to endpoint will be added if the Striated Muscle Antibody assay is positive at the initial 1:40 screening dilution.

### Interpretation

- The presence of AChR antibodies confirms a diagnosis of MG.
- AChR-binding antibody titer of 0.5 nM or greater is considered positive.
- AChR-blocking antibodies demonstrating 25% or greater inhibition/blocking is considered positive.
- AChR-modulating antibodies demonstrating 26% or greater modulation is considered positive.
- The absence of AChR antibodies does not rule out a diagnosis of MG, as 10% to 15% of MG patients lack detectible AChR antibodies.

### Limitations

This panel is not recommended as a screening test for MG; however, it may be used for screening patients with chronic muscle fatigue that is suggestive of MG. Antibodies are restricted to neuromuscular (alpha-1) AChR and will not detect ganglionic neuronal (alpha-3) antibodies.

### Methodology

- Acetylcholine Receptor Binding Antibody: quantitative radioimmunoassay
- Acetylcholine Receptor Blocking Antibody: semi-quantitative radioreceptor assay
- Acetylcholine Receptor Modulating Antibody: semi-quantitative radioreceptor assay

### Related Tests

- Acetylcholine Receptor Binding Antibody (0080009)
- Acetylcholine Receptor Blocking Antibody (0099580)
- Acetylcholine Receptor Modulating Antibody (0099521)

### References

1. Agius MA, Richman DP, Vincent A. Autoantibody testing in the diagnosis and management of autoimmune disorders of neuromuscular transmission and related disorders. In *Myasthenia gravis and related disorders*, 2nd ed. HJ Kaminski, ed. 2009; New York City: Humana Press, 143–56.
2. Conti-Fine BM, Milani M, Kaminski HJ. Myasthenia gravis: past, present, and future. *J Clin Invest*. 2006;116 (11):2843–54.
3. Haven TR, et al. An algorithm for acetylcholine receptor antibody testing in patients with suspected myasthenia gravis. *Clin Chem*. 2010;56:1028–9.
4. Carr AS, et al. A systematic review of population based epidemiological studies in Myasthenia Gravis. *BMC Neur*. 2010;10:46.
5. Chen J, Wang P. Assessment of multimodality therapy for thymoma. *Chin Med J*. 2010;123:1295–8.

### Test Information

- 2001571**      **Acetylcholine Receptor Antibody Reflex Panel**  
**2002666**      **Myasthenia Gravis Panel (Acetylcholine Receptor Antibody Reflex Panel and Striated Muscle Antibody, IgG with Reflex to Titer)**

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).

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