THE PATHCARE NEWS

Myasthenia Gravis Autoantibody Profile

Myasthenia Gravis (MG) is an autoimmune neuromuscular disorder mediated by autoantibodies that target functionally vital proteins in the post-synaptic membrane at the neuromuscular junction (NMJ).[1] MG presents clinically with a fluctuating degree and variable combination of motor weakness in the ocular, bulbar, limb, and respiratory muscles. **The detection of antibodies plays a central role in confirming MG diagnosis, defining subgroups, and guiding the management of MG patients:**[1,2]

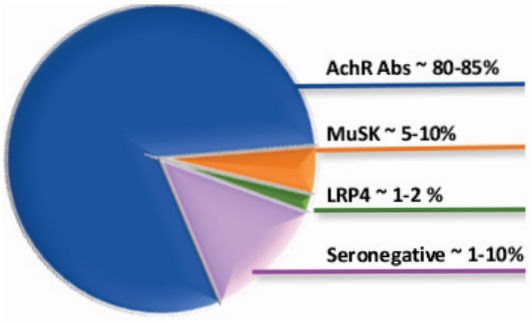

Figure 1. Prevalence of MG autoantibodies and MG subgroups.[1]

Table 1. Myasthenia Gravis subgroups[1]

Subgroup	Age at onset	Thymus	Antibody
Early onset	<50 yrs	Hyperplasia common	AchR
Late-onset	≥50 yrs	Atrophy common	
Thymoma	Any age	Lymphoepithelioma	
MuSK	Any age	Normal	MuSK
LRP4	Any age	Normal	LRP4
Ocular	Any age	Variable	Variable
Seronegative	Any age	Variable	None

MG with **Acetylcholine Receptor** antibodies **(AchR Abs)**:

Two-thirds of MG patients have generalized *early-onset* or *late-onset* disease and no thymoma. Whereas early-onset MG is associated with thymic hyperplasia and co-existing autoimmune conditions, late-onset MG is diagnosed more frequently in patients with thymic atrophy. Ten percent of MG patients have a *thymoma*, with prevalence increasing with age. In addition to the AchR Abs, thymoma and late-onset MG patients may also have Titin Abs, an indicator of more severe disease.

MG with **Muscle-Specific Kinase** antibodies (**MuSK Abs)**:

MuSK antibody-mediated MG accounts for 5-10% of MG cases. These patients may have more severe weakness, sometimes with muscle atrophy, and have marked symptoms from facial and bulbar muscles than patients with Ach-R antibodies.

MG with low-density **Lipoprotein receptor-related protein 4** antibodies **(LRP4 Abs)***:

LRP4 Abs account for 1-2% of all patients with MG and usually presents with mild-to-moderate symptoms.

Ocular MG:

In 15% of all MG patients, the disease is confined to the ocular muscles. Only half of *ocular MG* patients have detectable muscle antibodies with traditional assays. An explanation for this may include that MG patients with low-affinity clustered Abs have a higher prevalence of ocular MG. The conventional radioimmunoprecipitation (RIPA) assay is not sensitive enough to detect the low-affinity Abs. The cell-based assay (CBA) mimics the expression of native clustered antibodies on the cell surface, allowing for improved sensitivity in detecting the low-affinity AchR Abs. The fixed CBA may detect up to 20% of previously seronegative ocular MG cases.[3]

Seronegative MG:

In approximately 10% of generalized MG, the patients have no detectable muscle antibodies (seronegative MG). This classification depends on the assay type and the number of antibodies tested. With advances in assay technology, the number of seronegative MG patients may decline.

PathCare now offers an MG autoantibody test panel for improved diagnostic accuracy (Table 2):

Table 2. Myasthenia Gravis autoantibody test panel (PathCare)

Autoantibody (Method)	Description of method
AchR IgG (IIF)# *Cell-Based Assay*	Both adult AchR- and fetal AchR- are included in this fixed cell-based assay (CBA) to increase the assay's sensitivity. The cells are transfected with rapsyn to mimic the clustering of receptors on the cell surface, allowing the detection of low-affinity antibodies. This assay can also distinguish between acquired and congenital MG in the paediatric population. **The CBA may detect up to one-third of cases previously classified as seronegative.**[1,4]
AchR IgG (ELISA)	This immunoassay employs a mixture of adult and fetal AchR and allows for semi-quantitation. The ELISA assay may be less sensitive than the CBA for low-affinity AchR Abs.
MuSK IgG (IIF)# *Cell-Based Assay*	This IgG-specific MuSK fixed CBA has demonstrated good sensitivity and specificity compared with the conventional radioimmunoassay.[5,6]

Notes: # The AchR and MuSK antibodies are combined on one Cell-Based Assay (CBA) and cannot be separated.

** If LRP4 antibody testing is required, please contact the laboratory for arrangements (send-away test).*

Table 3. Test information for the Myasthenia Gravis antibody panel	
Test code	H6067
Sample type	Preferred: Serum (Yellow top tube) or Alternative: EDTA, Citrate, and Heparin plasma
Turnaround time	24 – 48 hrs after the samples reach the reference laboratory
Cost	R 1 210.90 (depending on Medical aid/payment method)

Conclusion

The combination of test methods, including the novel fixed Cell-Based assay for AchR and MuSK antibodies, will provide optimal sensitivity and specificity and may aid in more accurate diagnosis and classification of MG patients, improving disease management.

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References:

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4. Spagni G *et al*. Comparison of fixed and live cell-based assay for the detection of AchR and MuSK antibodies in Myasthenia Gravis. *Neurol Neuroimmunol Neuroinflamm* 2023; 10:e2000038; doi:10.1212/NXI.0000000000200038.
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