More gMG patients than you realize continue to

SUFFER IN SILENCE WITH SYMPTOMS

possibly including those in your practice

If your adult patients with anti-acetylcholine receptor (AChR) antibody-positive generalized myasthenia gravis (gMG) have persistent symptoms, complement may be to blame.

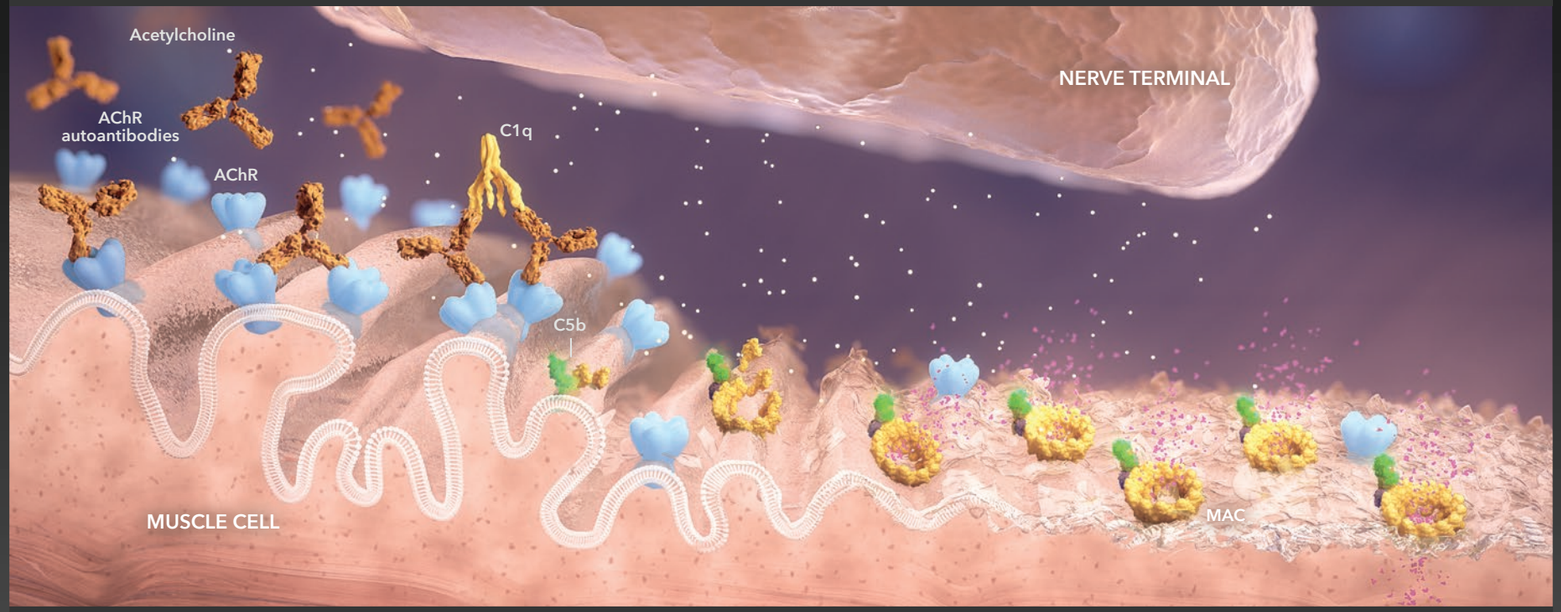
ALEXION®

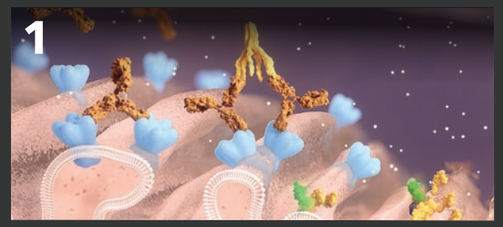
Complement may be a culprit in the UNDERLYING CAUSE of damage in your gMG patients

Up to 85% of patients with gMG are anti-AChR antibody positive[1]

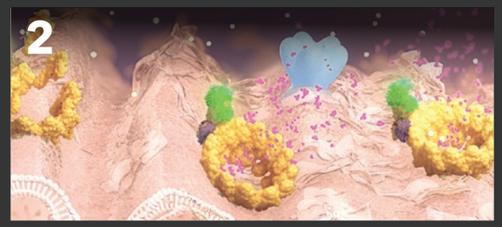
The complement cascade is a vital part of the body's immune system, but in patients with anti-AChR antibody-positive gMG, it plays a critical role in damage at the neuromuscular junction (NMJ).[2]

COMPLEMENT ACTIVATION LEADING TO MEMBRANE DESTRUCTION OVER TIME

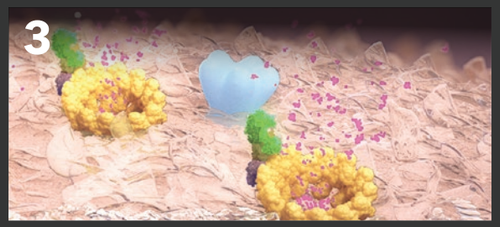




Anti-AChR autoantibodies bind to AChRs, triggering complement activation.[2,3]

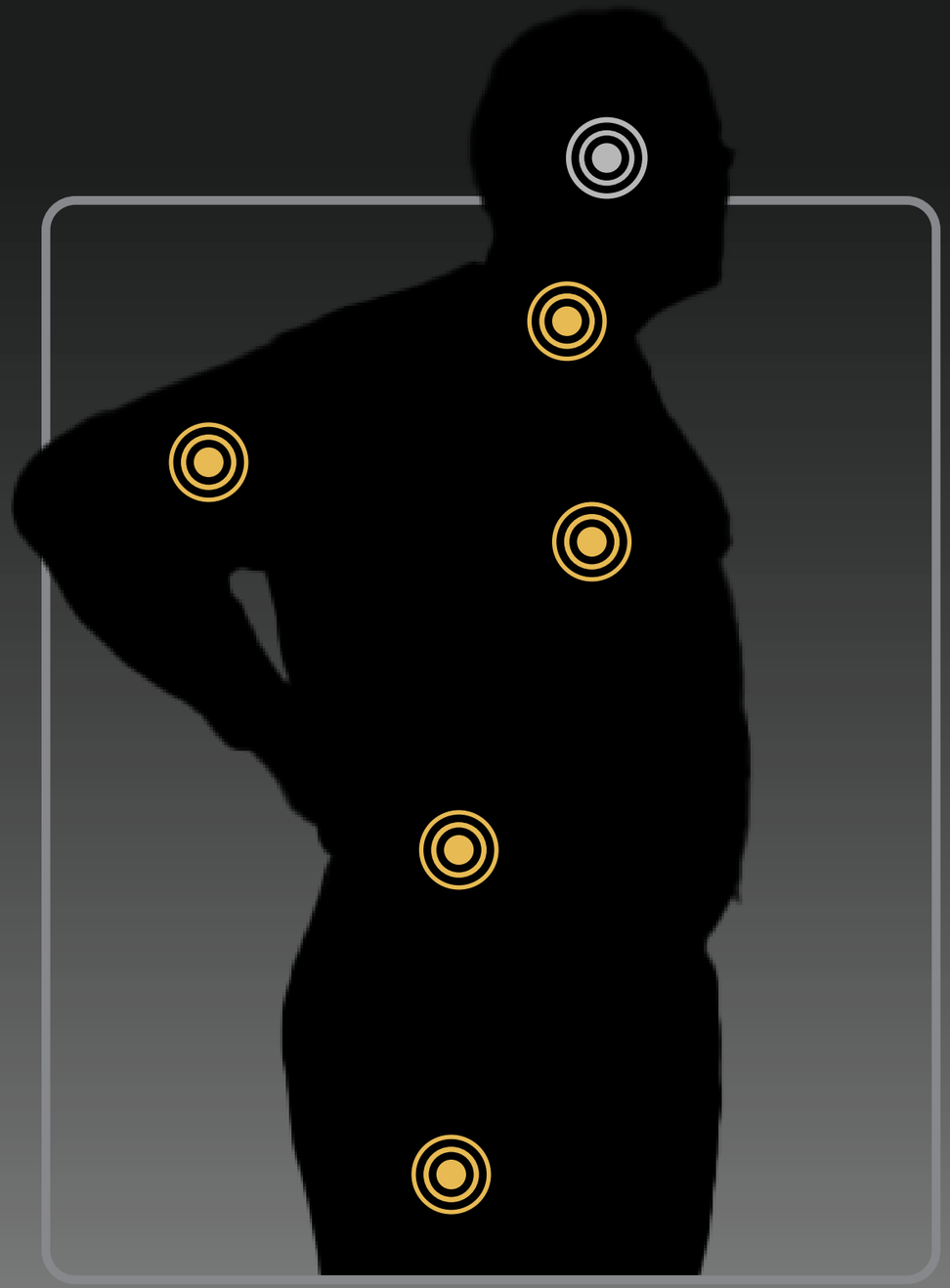


C5 in the terminal complement pathway is cleaved into C5a and C5b, resulting in inflammation and formation of the membrane attack complex (MAC).[2,3]



MAC formation causes destruction of the muscle membrane and alters the structure of the NMJ, decreasing the number of AChRs and impairing neuromuscular transmission.[3]

Did you know complement can be activated whenever anti-AChR antibodies are present?[2]



In the majority* of patients, the progression of myasthenia gravis (MG) symptoms CAN OCCUR AS SOON AS 1 YEAR

3 out of 4 Approximately 3 out of 4 patients with ocular symptoms **progress to generalized symptoms,** including bulbar, that can impact talking, chewing, swallowing, or breathing.[4-14]

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1 out of 5 1 out of 5 MG patients who went on to develop generalized symptoms did so within **1 month** of presenting with ocular symptoms.[11]*

22 out of 25 22 out of 25 MG patients with ocular symptoms who developed generalized symptoms did so **within a year.**[11]*

*Based on a study evaluating the diagnosis and treatment of 1976 patients with MG (246 with ocular MG and 1730 with gMG) between 1940 and 2000. In this study, 80% of patients who initially presented with ocular symptoms developed gMG.[11]

Do you look for signs of MG symptom progression in your practice?

Right now, there may be patients in your practice with REFRACTORY gMG

Patients may be considered refractory if they fail to respond to therapies, experience intolerable side effects, have contraindications, or are unable reduce their dose of immunosuppressive therapy.[15,16]

Are you asking your patients about subtle gMG symptoms they may still be experiencing?

In a survey, patients continued to experience the following despite treatment[17]*:

TROUBLE CHEWING
39%

TROUBLE SWALLOWING
44%

WEAKNESS OF UPPER LIMBS
71%

MUSCLE WEAKNESS AFTER PHYSICAL STRAIN
75%

WALKING PROBLEMS
70%

*These data are based on survey results of 1518 patients in the German Myasthenia Association with confirmed MG. All patients completed a questionnaire that included analysis of demographics, impairments, therapeutic course, use of complementary therapies, illness-related costs, and quality of life (SF-36).[17]

Refractory gMG can have a DEVASTATING IMPACT on your patients' quality of life

In patients with refractory gMG compared to patients with nonrefractory gMG at a 4-year follow-up[18]*:

75% HIGHER (worse) MG-ADL **ASSESSMENT SCORES**

2x as likely to experience **OVERNIGHT HOSPITALIZATION**

17x as likely to experience **INTENSIVE CARE UNIT STAY**

In a retrospective study that used claims data and health system databases to assess the clinical burden of over 4000 patients, **those with refractory gMG** compared to nonrefractory gMG (n=403) were found to be more likely to have experienced[19†]:

EXACERBATION – **4.7x** as likely

ER VISIT – **~2x** as likely

MYASTHENIC CRISIS – **4x** as likely

*This retrospective study analyzed data from adults with gMG in the Myasthenia Gravis Foundation of America Patient Registry who had completed the enrollment questionnaire between July 2013 and February 2018 and at least 1 follow-up questionnaire by February 2019. Comparisons were made between ever-refractory (n=49) and nonrefractory (n=581) patients regarding clinical and healthcare resource utilization outcomes.[18]

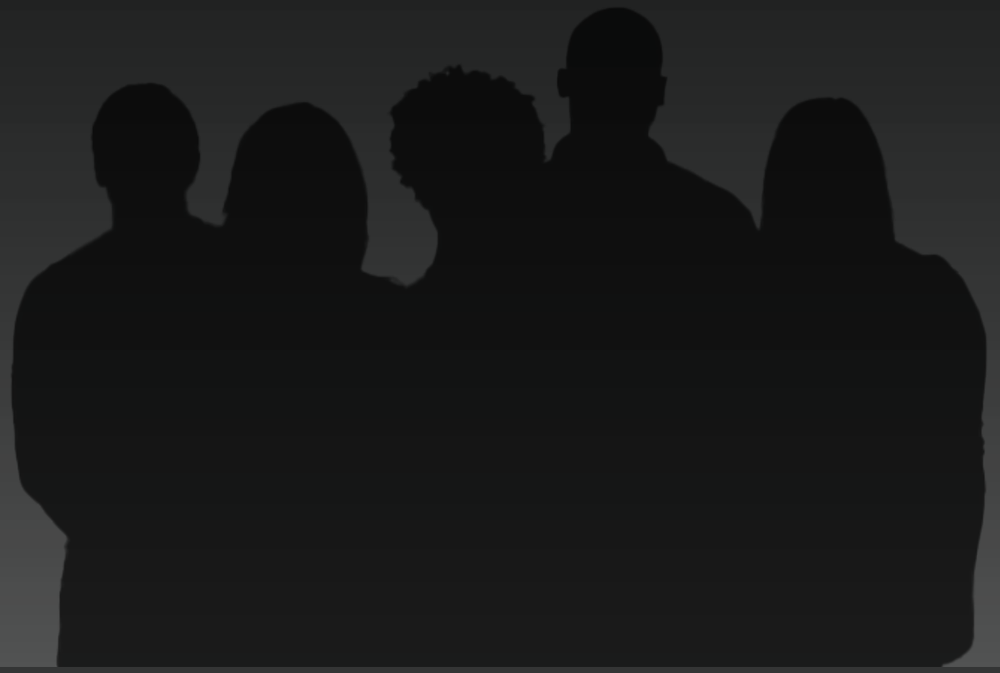
Abbreviation: MG-ADL, Myasthenia Gravis Activities of Daily Living.

†This retrospective study assessed the clinical burden of refractory MG relative to nonrefractory MG based on enrollment and claims data. Rates of myasthenic crises, exacerbations, inpatient hospitalizations, and emergency room visits over a 1-year period were measured for 403 refractory, 3811 nonrefractory, and 403 non-MG control patients from Optum Research Database and Impact National Benchmark Database between January 2000 and December 2014.[19]

What are you doing to ensure your patients' quality of life?

It's time to reevaluate the way you define and think about REFRACTORY gMG

Probe further to see if your patients are still experiencing gMG symptoms, and work together to create a new management plan



References: 1. Huijbers MG, Lipka AF, Plomp JJ, Niks EH, Maarel SMVD, Verschuuren JJ. Pathogenic immune mechanisms at the neuromuscular synapse: the role of specific antibody-binding epitopes in myasthenia gravis. *J Intern Med.* 2013;275(1):12-26. **2.** Howard JF Jr. Myasthenia gravis: the role of complement at the neuromuscular junction. *Ann N Y Acad Sci.* 2018;1412(1):113-128. **3.** Conti-Fine BM, Milani M, Kaminski HJ. Myasthenia gravis: past, present, and future. *J Clin Invest.* 2006;116(11):2843-2854. **4.** Pallaver F, Riviera AP, Piffer S, et al. Change in myasthenia gravis epidemiology in Trento, Italy, after twenty years. *Neuroepidemiology.* 2011;36(4):282-287. **5.** Lefter S, Hardiman O, Ryan AM. A population-based epidemiologic study of adult neuromuscular disease in the Republic of Ireland. *Neurology.* 2017;88(3):304-313. **6.** Joensen P. Myasthenia gravis incidence in a general North Atlantic isolated population. *Acta Neurol Scand.* 2014;130(4):222-228. **7.** Robertson NP, Deans J, Compston DA. Myasthenia gravis: a population based epidemiological study in Cambridgeshire, England. *J Neurol Neurosurg Psychiatry.* 1998;65(4):492-496. **8.** Santos E, Coutinho E, Moreira I, et al. Epidemiology of myasthenia gravis in Northern Portugal: frequency estimates and clinical epidemiological distribution of cases. *Muscle Nerve.* 2016;54(3):413-421. **9.** Zieda A, Ravina K, Glazere I, et al. A nationwide epidemiological study of myasthenia gravis in Latvia. *Eur J Neurol.* 2018;25(3):519-526. **10.** Fang F, Sveinsson O, Thormar G, et al. The autoimmune spectrum of myasthenia gravis: a Swedish population-based study. *J Intern Med.* 2015;277(5):594-604. **11.** Suh J, Goldstein JM, Nowak RJ. Clinical characteristics of refractory myasthenia gravis patients. *Yale J Biol Med.* 2013;86(2):255-260. **12.** Grob D, Brunner N, Namba T, Pagala M. Lifetime course of myasthenia gravis. *Muscle Nerve.* 2008;37(2):141-149. **13.** Li Y, Arora Y, Levin K. *Cleve Clin J Med.* 2013;80(11):711-721. **14.** Meriggioli MN, Sanders DB. Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. *Lancet Neurol.* 2009;8(5):475-490. **15.** Schneider-Gold C, Hagenacker T, Melzer N, Ruck T. Understanding the burden of refractory myasthenia gravis. *Ther Adv Neurol Disord.* 2019;12:1-16. **16.** Mantegazza R, Antozzi C. *Ther Adv Neurol Disord.* 2018;11:175628561774913. **17.** Twork S, Wiesmeth S, Klewer J, Pöhlau D, Kugler J. Quality of life and life circumstances in German myasthenia gravis patients. *Health Qual Life Outcomes.* 2010;8(1):129. **18.** Harris L, Allman PH, Sheffield R, Cutter G. Longitudinal analysis of disease burden in refractory and nonrefractory generalized myasthenia gravis in the United States. *J Clin Neuromusc Dis.* 2020;22:11-21. **19.** Engel-Nitz NM, Boscoe A, Wolbeck R, Johnson J, Silvestri NJ. Burden of illness in patients with treatment refractory myasthenia gravis. *Muscle Nerve.* 2018;58(1):99-105.

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