

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Ocular Manifestations of Myasthenia Gravis

Joseph A. Pruitt and Pauline Ilse

Southern College of Optometry, Memphis, TN & Southern California

College of Optometry, Fullerton, California

USA

1. Introduction

Myasthenia Gravis (MG) is presently an incurable antibody-mediated autoimmune disorder characterized by generalized voluntary skeletal muscle weakness. Literally translated from its Latin and Greek etymological roots, myasthenia gravis means, "grave muscle weakness."

The cause of the weakness is due to a defect at the level of the neuromuscular junction in which autoimmune antibodies block the receptors responsible for initiating muscular contraction. The neurotransmitter that is subject to this competitive inhibition is acetylcholine (ACh). The muscles commonly affected include those of the neck, limbs and chest cavity with regards to breathing. The muscles of the eye, including those responsible for eye movements, as well as those involved with swallowing, chewing, and speaking, are most notably affected. Muscle weaknesses involving the eye produce symptoms of blurred vision, variable diplopia, and ptosis. Colavito et al. noted that nonstriated ocular muscles can also be involved in MG. They cautioned that when patients with myasthenia present with complaints of asthenopia and blur, resulting from accommodative dysfunction and vergence insufficiency, the underlying systemic disease process may be missed. Ptosis is defined as an abnormal eyelid "drooping" beyond the normal 1-2 mm of the upper limbus of the cornea.

Since the process in which the muscular weakness manifests is a result of competitive inhibition, the weakness observed is transient and improves with periods of rest. Likewise, muscular weakness increases during periods of increased or prolonged physical activity.

Even though MG is an antibody-mediated autoimmune disease, a reported 15% of patients with systemic or generalized MG have no detectable antibodies to acetylcholine receptors (i.e., they have "seronegative" MG). Seronegative MG is common in children; 40% of cases present before the age of 10 years.

It is estimated that 85-90% of all reported MG cases, whether seropositive or seronegative, present with ocular symptoms. Additionally, it has been reported that 20-50% of all cases of MG are purely ocular. Ocular myasthenia is considered a distinct diagnosis from generalized MG. Although there is evidence of ocular MG progressing to generalized MG, it has been reported that those with purely ocular symptoms for a period of 1-3 years have a greatly reduced chance of progressing on to generalized MG. Furthermore, a reported estimate of 55% of all cases of ocular MG are seropositive.

Two reasons have been suggested to explain the high proportion of MG cases that present with ophthalmic manifestations. The first is the susceptibility of ocular muscles to the disease process. The second reason is that ocular involvement in MG is relatively easy to recognize compared to that of other muscle groups. The exact reasoning why is unknown, but the following four reasons are hypothesized to contribute in part or in whole: First, even the slightest extraocular muscle (EOM) weakness will sufficiently misalign the visual axis to produce symptoms of diplopia. This is in contrast to an affected muscle in a limb, where an individual would not notice minute reductions in muscle-generated forces most likely.⁷ Moreover, the ocular motor system relies primarily on visual feedback, not so much on proprioceptive mechanisms, thereby making its ability to adapt swiftly to asymmetric or variable weakness more limited compared to an extremity muscle. Second, the high firing frequencies of ocular motor neurons might contribute to neuromuscular transmission fatigue. No other motor neuron in the body exhibits the rate of firing frequency of the ocular motor neurons. It is estimated ocular motor neurons fire at a frequency exceeding up to 600 Hz during saccades. Motor neurons found elsewhere in the body rarely exceed a firing frequency of 100 Hz. Therefore, any disruption in the ability of these ocular neurons to maintain a high firing rate would cause a decrease in effectiveness and appropriate output. Myasthenia gravis produces this kind of disruption. Third, several anatomic and physiologic properties of EOM fibers make them more susceptible to neuromuscular transmission blockade. EOM nerve fibers possess anatomical characteristics that possibly make them more susceptible to neuromuscular transmission block. The fibers of the EOMs have less prominent synaptic folds, and the conclusion is drawn that there are fewer ACh receptors and sodium channels on the postsynaptic membrane. Much has been previously documented in that the mean quantal content (in other words, the average number of vesicles released during a synaptic event) of ocular motor neurons is lower than motor neurons innervating other muscles. Fourth is the preferential immunologic targeting of EOM synapses. This theory remains purely speculative, but it has been observed that the sera from some MG patients bind only to multi-innervated fibers' synapses, and the use of EOM as a source of ACh receptors for ACh antibody assays leads to higher rates of autoantibody detection, which suggests that EOMs have unique antigenic targets.

Treatment for systemic or generalized MG includes a wide variety of options, but remains primarily systemic medication. First line therapy typically consists of an acetylcholinesterase inhibitor like pyridostigmine bromide (Mestinon). Although it must be noted that pyridostigmine bromide has rather variable results in pure OMG with an approximate effectiveness ratio of 1 to 2. Another option is immunosuppressant therapy such as prednisolone, cyclosporine, azathioprine, methotrexate and mycophenolate mofetil (Cellcept). Yet again, it must be noted with regards to pure OMG, it is suggested there is not sufficient evidence to warrant the routine use of immunosuppressant therapy (i.e. corticosteroids). More drastic measures attempted in the past include systemic oral medications, plasmapheresis (a.k.a. plasma exchange) and IVIG injections. Plasmapheresis is the removal of antibodies from the blood. An IVIG injection is a sterile solution of plasma proteins containing IgG antibodies from pooled human plasma. Although the mechanism of action is unknown, it is thought to down-regulate the production of antibodies. The preparation contains no less than 90% immunoglobulin consisting of all the IgG substances and trace amount of IgA and IgM. However, this treatment is usually reserved for patients

demonstrating dysphagia with an associated high risk of aspiration and those who are unable to ambulate without assistance. Although slower-acting than plasma exchange, the response is similar and offers advantages when therapeutic plasmapheresis is not available or when vascular access is problematic. Significant improvement is seen in patients whose therapy consist of an initial dose of 400 mg/kg/d for 5 days and followed by maintenance with 400 mg/kg once monthly. Furthermore, it has been noted that with regards to a similarly treated disease, Guillian-Epstein Barr Syndrome, IVIG treatment in many ways is considered to be the more effective successor to plasmapheresis.

Thymectomy, the surgical removal of the thymus gland, is also an effective and accepted treatment for generalized MG; however, while effective, it is controversial as a treatment measure in pure OMG. Recent theories suggest thymectomies could be performed on early presentations of OMG to prevent and/or slow the disease progression and immunosuppressive therapy only if proven necessary. Thymectomies are often performed on young individuals in the early stages of MG regardless of the presence of a tumor.⁸ As related to generalized MG and post-surgical improvement, it has been shown both the grade of follicular hyperplasia and density of T-cell subsets in the middle part of the thymus (space between the superior and inferior horns) had a significant correlation with the level of improvement of MG after thymectomy.

Additionally, if there is found to be thyroid involvement, a thyroidectomy is a viable treatment option.

Treatment for ocular MG specifically may include all the aforementioned options because a report 50-60% of individuals who present with purely ocular MG will eventually progress and develop generalize MG. Nevertheless, ocular MG treatments consist of both surgical and non-surgical treatments. Surgical options for myogenic ptosis are ptosis repair surgery, blepharoplasty, and frontalis suspension for which a Tutoplast sling can be utilized, external levator advancement, and tarsomyectomy. A non-surgical option is Botulinum Toxin Type A (Botox) injection to temporarily treat myogenic ptosis.

The first line of treatment should be a refraction in order to achieve the patient's best corrected visual acuity (BCVA). Assessment of accommodation and vergence testing should also be considered. As for diplopia, standard treatments such as occlusion and prisms are commonly employed. However, with prisms, the practitioner must keep in mind the variability of the disease's manifestations, thereby making it possible for the angle of deviation to fluctuate.

2. References

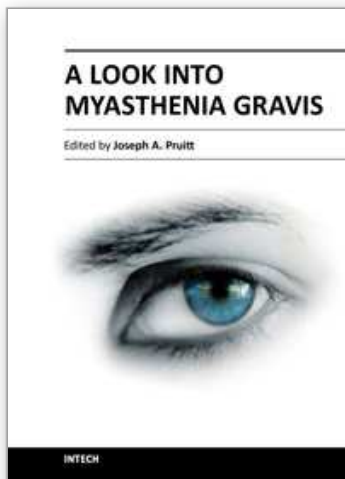
- Rowland R, Sparr S. Head-drop and shortness of breath as a presentation of myasthenia gravis. *J Am Geriatr Soc* 2007;55(4):S116
- Palace J, Vincnet A, Beeson D. Myasthenia gravis: diagnostic and management dilemmas. *Current Opinion in Neurology* 2001;14:583-589
- Horn P, Kupersmith M. Development of Generalized Myasthenia Gravis in Patients With Ocular Myasthenia Gravis. *Arch Neurol* 2003; 60(10):1491-1492
- Hilton-Jones D, Palace J. The management of myasthenia gravis. *Practical Neurology* 2005;5:18-27

- http://www.ninds.nih.gov/disorders/myasthenia_gravis/myasthenia_gravis.htm
- Golnik K. How to Diagnose and Treat Myasthenia Gravis. *Review of Ophthalmology*. 2002;9(10):219.
- Ubogu E, Kaminski H. The Preferential Involvement of Extraocular Muscle by Myasthenia Gravis. *Neuro-ophthalmology*, 2001;25(4):219-228
- Colavito J, Cooper J, Ciuffreda K. Non-ptotic ocular myasthenia gravis: a common presentation of an uncommon disease. *Optometry*. 76(7): 363-375.
- Cameron R, Loehrer P, Thomas C. Thymic Neoplasms; Neoplasms of the Mediastinum. *Principles & Practice of Oncology 7th Edition*. Chapter 28. Lippincott Williams & Wilkins. 2005.
- Donati F, Bevan D. Neuromuscular Blocking Agents. *Clinical Anesthesia 5th Edition*. Chapter 16. Lippincott Williams & Wilkins. 2006.
- Toyka K. Ptosis in myasthenia gravis: Extended fatigue and recovery bedside test. *Neurology* 2006;67(8):1524
- Reddy A, Backhouse O. "Ice-on-eyes", a simple test for myasthenia gravis presenting with ocular symptoms. *Practical Neurology* 2007;7(2):109-111
- Benatar M, Kaminski H. Evidence report: The medical treatment of ocular myasthenia (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2007;68(24):2144-2149
- Rudnicki S. Lamber-Eaton Myasthenic Syndrome with Pure Ocular Weakness. *Neurology* 2007;68(21):1863-1864
- Lapid O. Eyelid Crutches for Ptosis: A Forgotten Solution. *Plastic and Reconstructive Surgery*. October 2000. 106(5): 1213-1214.
- Scherer K, Bedlack R, Simel D. Does This Patient Have Myasthenia Gravis?. *JAMA* 2005;293(15):1906-1914
- Morris O, O'day J. Fatiguable Ptosis and Pseudoretraction Caused by Myasthenia Gravis. *Clinical and Experimental Ophthalmology*. 2004; 32:303-304
- Shaw J. When Muscles Falter: Update on Myasthenia Gravis. *Clinical Update: Neuro-ophthalmology*; <http://www.aao.org/publications/eyenet/200607/neuro.cfm>. 2006
- Golnik K, Pena R, Lee A, Eggenberger R. An Ice Test for the Diagnosis of Myasthenia Gravis. *Ophthalmology*. 1999; 106(7): 1282-1286
- Kennard C. Examine eye movements. *Practical Neurology* 2007;7:326-330 Tomelleri G, Vattermi G, Filosto M, Tonin P. Eyelid ptosis from sympathetic nerve dysfunction mistaken as myopathy: a simple test to identify this condition. *J Neurol Neurosurg Psychiatry* 2007;78(6):632-634
- Chan J, Orrison W. Ocular Myasthenia: A Rare Presentation with MuSK Antibody and Bilateral Extraocular Muscle Atrophy. *Br. J. Ophthalmol*. 2007;91:842-843
- Kubis K, Danesh-Meyer H, Savino P, Sergott R. The Ice Test versus the Rest Test in Myasthenia Gravis. *Ophthalmology*. 2000;107(11): 1995-1998
- Gilbert M, De Sousa E, Savino P, Peter J. Ocular Myasthenia Gravis Treatment: The Case Against Prednisone Therapy and Thymectomy. *Archives of Neurology*. December 2007. 64(12): 1790-1792.
- Chavis P, Stickler D, Walker A. Immunosuppressive or Surgical Treatment for Ocular Myasthenia Gravis. *Archives of Neurology*. December 2007. 64(12): 1792-1794.

- Kupersmith M, Latkany R, Homel P. Development of Generalized Disease at 2 Years in Patients With Ocular Myasthenia Gravis. *Archives of Neurology*. February 2003. 60(2): 243-248.
- Kaminski H, Daroff R. Treatment of Ocular Myasthenia: Steroids Only When Compelled. *Archives of Neurology*. May 2000. 57(5): 752-753
- Bennett D, Mills K, Riordan-Eva P, Barnes P, Rose M. Anti-MuSK antibodies in a case of ocular myasthenia gravis. *Journal of Neurology, Neurosurgery, & Psychiatry*. April 2006. 77(4): 564-565.
- Caress J, Hunt C, Batish S. Anti-MuSK Myasthenia Gravis Presenting With Purely Ocular Findings. *Archives of Neurology*. June 2005. 62(6): 1002-1003.
- Elrod RD, Weinberg DA. Ocular myasthenia gravis. *Ophthalmol Clin North Am* 2004 Sep;17(3):275-309.
- Sommer N, Sigg B, Melms A, Weller M, Schepelmann K, Herzau V, Dichgans J. Ocular myasthenia gravis: response to long term immunosuppressive treatment. *J Neurol Neurosurg Psychiatry* 1997;62(2):156-162
- Howard J. Intravenous Immunoglobulin for the Treatment of Acquired Myasthenia Gravis. *Neurology*. December 1998. 51(6) Supplement 5: S30-S36.
- <http://www.umd.nycpic.com/cgi-bin/bookmgr/bookmgr.exe/BOOKS/D971-2A/FRONT>
- Hilkevich O, Drory V, Chapman J, Korczyn A. The Use of Intravenous Immunoglobulin as Maintenance Therapy in Myasthenia Gravis. *Clinical Neuropharmacology*. May/June 2001. 24(3): 173-176.
- Meche F, Schmitz P. A Randomized Trial Comparing Intravenous Immune Globulin and Plasma Exchange in Guillian-Barre Syndrome. Dutch Guillian-Barre Study Group. *The New England Journal of Medicine*. 1992(17); 326:1123-1129.
- Roberts P, Venuta F, Rendina E, De Giacomo T, Coloni G, Follette D, Richman D, Benfield J. Thymectomy in the treatment of ocular myasthenia gravis. *The Journal of Thoracic and Cardiovascular Surgery*. September 2001. 122(3): 562-568.
- Lauriola L, Ranelletti F, Maggiano N, Guerriero M, Punzi C, Marsili F, Bartoccioni E, Evoli A. Thymus changes in anti-MuSK-positive and -negative myasthenia gravis. *Neurology*. 8 February 2005. 64(3): 536-538.
- Agius M. Treatment of Ocular Myasthenia With Corticosteroids: Yes. *Archives of Neurology*. May 2000. 57(4): 750-751.
- Mori T, Nomori H, Ikeda K, Kobayashi H, Iwatani K, Kobayashi T. The distribution of parenchyma, follicles, and lymphocyte subsets in thymus of patients with myasthenia gravis, with special reference to remission after thymectomy. *The Journal of Thoracic and Cardiovascular Surgery*. February 2007. 133(2): 364-368.
- Periman L, Sires B. Floppy Eyelid Syndrome: A Modified Surgical Technique. *Ophthalmic Plastic and Reconstructive Surgery* 2002;18(5):370-372
- Sakol P, Mannor G, Massaro B. Congenital and acquired blepharoptosis. *Current Opinion in Ophthalmology* 1999;10:335-339
- Lauriola L, Ranelletti F, Maggiano N, Guerriero M, Punzi C, Marsili F, Bartoccioni E, Evoli A. Thymus changes in anti-MuSK-positive and -negative myasthenia gravis. *Neurology*. 8 February 2005. 64(3): 536-538.
- Shields M, Putterman A. Blepharoptosis correction. *Current Opinion in Otolaryngology & Head and Neck Surgery* 2003;11(4):261-266
- Sakol P, Mannor G, Massaro B. Congenital and acquired blepharoptosis. *Current Opinion in Ophthalmology* 1999;10:335-339

- Eliasoph I. RE: "Surgical Correction of Blepharoptosis in Patients with Myasthenia Gravis". *Ophthal Plast Reconstr Surg* 2002;18(4): 312-313
- McCord C, Seify H, Codner M. Transblepharoplasty Ptosis Repair: Three-Step Technique. *Plastic and Reconstructive Surgery* 2007;120(4):1037-1044
- Seider N, Beiran I, Kaltreider S. One medial triangular Tutoplast sling as a frontalis suspension for adult myogenic blepharoptosis. *Acta Ophthalmologica Scandinavica* 2006;84:121-123
- Wong, V, Beckingsale P, Olley C, Sullivan T. Management of Myogenic Ptosis. *Ophthalmology*. 2002;109(5): 1023-1031
- Bernardini F, Concillis C, Devoto M. Frontalis Suspension Sling using a Silicone Rod in Patients affected by Myogenic Blepharoptosis. *Orbit*. 2002; 21(3): 195-198
- Gausas R, Goldstein S. Ptosis in the Elderly Patient. *Int Ophthalmol Clin* 2002;42(2):61-74
- Bradley E, Bartley G, Chapman K, Waller R. Surgical Correction of Blepharoptosis in Patients With Myasthenia Gravis. *Ophthalmic Plastic and Reconstructive Surgery*. March 2001. 17(2): 103-110.
- Morris O, O'Day J. Strabismus Surgery in the Management of Diplopia caused by Myasthenia Gravis. *Br. J. Ophthalmol*. 2004; 88: 832-850
- Takagi S, Hosokawa K, Yano K, Kunihiro N, Tateki K. Crutches Glasses For Blepharoptosis. *Plastic and Reconstructive Surgery*. June 2002. 109(7): 2605
- Frueh BR. The mechanistic classification of ptosis. *Ophthalmol* 1980; 87(10):1019-21.

IntechOpen



A Look into Myasthenia Gravis

Edited by Dr. Joseph A. Pruitt

ISBN 978-953-307-821-2

Hard cover, 106 pages

Publisher InTech

Published online 20, January, 2012

Published in print edition January, 2012

Myasthenia gravis is presently an incurable antibody-mediated autoimmune disorder characterized by generalized voluntary skeletal muscle weakness. The cause of the weakness is a defect at the neuromuscular junction level, in which autoimmune antibodies block the receptors responsible for initiating muscular contraction. Literally translated from its Latin and Greek etymological roots, myasthenia gravis means "grave muscle weakness". Fortunately, advances in modern medicine have resulted in a reduction of the truly "grave" outcomes for those inflicted but, without a cure, the gravity surrounding the disease remains

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Joseph A. Pruitt and Pauline Ilse (2012). Ocular Manifestations of Myasthenia Gravis, A Look into Myasthenia Gravis, Dr. Joseph A. Pruitt (Ed.), ISBN: 978-953-307-821-2, InTech, Available from:
<http://www.intechopen.com/books/a-look-into-myasthenia-gravis/ocular-manifestations-of-myasthenia-gravis>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen