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Key Inforbits

- Introduction to Myasthenia Gravis
- Symptoms of Myasthenia Gravis
- Diagnosis of Myasthenia Gravis
- Management of Myasthenia Gravis
- Living with Myasthenia Gravis
- Recent Developments

June is…

Myasthenia Gravis Awareness Month

About Myasthenia Gravis

In the United States, approximately 20 people per 100,000 have Myasthenia Gravis (MG), but is thought to be under-diagnosed.[1] Myasthenia Gravis comes from the Latin and Greek words that mean "grave muscular weakness." MG is characterized by varying degrees of voluntary muscle weakness. This muscle weakness increases during periods of activity and improves with rest. It occurs in all ages, genders, and races. MG patients have a normal life expectancy.[2]

Nerve impulses from the brain control the voluntary muscles of the entire body. Nerve impulses cause acetylcholine (ACH) to travel to the nerve endings where it is released into the neuromuscular junction between the muscle fibers. ACH binds to many receptors on the muscle and causes muscle contraction when enough receptors have been activated. In MG, up to 80% of these receptor sites can be depleted due to an antibody that destroys or blocks the receptor site.[1]

Antibodies are major proteins of the immune system that are usually directed at antigens, foreign proteins that attack the body. Antibodies help protect the body from foreign proteins such as viruses and bacteria. In patients with MG, the immune system makes antibodies directed against the receptors of the neuromuscular junction. The reason for this is unknown. The antibodies destroy the receptors faster than the body can replace them. These abnormal antibodies can be measured in the blood. When the ACH cannot activate enough receptors in the neuromuscular junction (NMJ), muscular weakness occurs.

1. Complementary/Integrative Medicine [Internet]. Houston: Myasthenia Gravis Foundation of America, Inc.; c2010 [cited 2013 May 22]. Available from: http://www.myasthenia.org/Home.aspx
2. NINDS Myasthenia Gravis Information Page [Internet]. Bethesda: National Institutes of Health; c2013. National Institute of Neurological Disorders and Stroke; 2012 Dec 4 [cited 2013 May 31]; [about 2 screens]. Available from: http://www.ninds.nih.gov/disorders/myasthenia_gravis/myasthenia_gravis.htm

Symptoms of Myasthenia Gravis

Muscle weakness caused by MG comes and goes. The more you use a muscle, the weaker it becomes; therefore, rest tends to improve symptoms. Symptoms tend to progress over time and usually peak several years after disease onset.

- **Eye muscles**: The eyes are typically the first muscles affected in half of MG patients.[1]
  - Drooping of the eyelids (one or both)

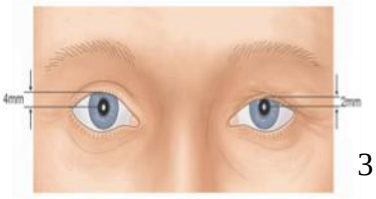
    - Double vision
- **Face and throat muscles** are the first affected in 15% of MG patients.
    - Altered speech - can become very soft
    - Difficulty swallowing - may cause choking
    - Problems chewing - muscles used to chew can become worn out
    - Limited facial expression - facial muscles may become weaker
- **Neck and limb muscles**: Neck, arms, and legs (arms are usually affected more than legs)

CALL A PHYSICIAN IF: you have trouble breathing, swallowing, seeing, walking, using your arms or hands, or holding your head up

1. Myasthenia Gravis [Internet]. Jacksonville: Mayo Clinic; c1998-2013. Symptoms; 2013 Apr 23 [cited 2013 May 22]; [about 2 screens]. Available from: http://www.mayoclinic.com/health/myasthenia-gravis/DS00375/DSECTION=symptoms

Diagnosis of Myasthenia Gravis

In addition to a detailed physical and neurological exam, there are several tests that are used by physicians to diagnose myasthenia gravis. One of the main symptoms of MG is muscle weakness following sustained activity that is relieved by rest. There are two quick approaches that can be done in a physician's office when MG is initially suspected, testing for weakness and testing the recovery of strength after rest.[1] Weakness can be evaluated by asking the patient to complete a continual activity for several minutes. Having the patient rest after activity and watching to see if strength improves checks for recovery of strength. For example, ask the patient to look up at the ceiling for several minutes and assess to see if their eyelids start to droop. This will check for muscle weakness. Next, ask the patient to lie down, close their eyes and use an ice pack, and rest for several minutes to see if lid function improves with rest. This is called " the ice pack test."


3

There are five main ways to diagnose myasthenia gravis. They include the following...

Diagnostic Tests	Description
ACH Receptor Antibody Test[1]	• Blood test that checks for the presence of antibodies; 85% of patients will test positive for this antibody • Highly predictive of MG • One of the primary tests to confirm diagnosis
Anti-MuSK Antibody Test[1]	• Blood test for the 15% of patients that test negative for the ACH receptor antibody • MuSK is a protein responsible for formation and maintenance of the NJM; attack against the receptor causes ineffectiveness
Office Tests	• Simple tests to check for weakness after activity and improvement after rest • Examples- Edrophonium test (IV ACEI that will temporarily increase ACH and relieve weakness) and ice pack test
Electromyography	• EMG provides support for diagnosis through repetitive nerve stimulation to see if symptoms worsen with fatigue
Single Fiber EMG	• Single fiber EMG provides support for diagnosis • One of the primary tests to confirm diagnosis

1. Complementary/Integrative Medicine [Internet]. Houston: Myasthenia Gravis Foundation of America, INC.; c2010 [cited 2013 May 22]. Available from: http://www.myasthenia.org/Home.aspx
2. Myasthenia Gravis [Internet]. Jacksonville: Mayo Clinic; c1998-2013. Tests and diagnosis; 2007 Mar 26 [cited 2013 May 22]; [about 2 screens]. Available from: http://www.mayoclinic.com/health/myasthenia-gravis/DS00375/DSECTION=tests%2Dand%2Ddiagnosis
3. Source: Assessment of ptosis [Internet].Denver: BMJ Publishing Group Limited; c2011.Best Practice; 2012 Sept 17 [cited 2013 May 31]; [about 2 screens]. Available from: http://bestpractice.bmj.com/best-practice/monograph/1168/diagnosis.html

Management of Myasthenia Gravis

There is currently no cure for Myasthenia Gravis, but the symptoms are treatable and manageable. No controlled trials have reported that a particular therapy is superior. Experts cannot agree on a treatment of choice. Thus, treatment decisions are patient specific. Factors that should be weighed when choosing a treatment option include the patient's age, gender, and the severity of impairment. Assessing a patient's response to therapy is complicated because the severity of symptoms can fluctuate daily. Patients will even experience remissions with no relation to a particular drug therapy. Therapies are listed in no particular order. Treatment will vary on a patient to patient basis.

Myasthenia Gravis Therapy	
Treatment	**Clinical Use**
Acetylcholinesterase Inhibitors	• **Pyridostigmine** and **neostigmine** are the most commonly used agents[3] • No fixed dosage schedule works for all patients[1] • The need for therapy will vary daily and in response to factors such as stress, infection, & menstruation[3]
Thymectomy (removal of the thymus gland)	• Maximum response usually occurs 2 to 5 years after surgery[3] • Best responses occur in young people early in the disease course[3] • If disease onset has occurred after age 60, patient will rarely have improvement with thymectomy[3]
Corticosteroids	• Improvement or complete symptom relief occurs in more than 75% of patients given prednisone[3] • Most improvement happens within the first 6 – 8 weeks of treatment[1] • **Prednisone** treatment can be initiated with a daily dose of 1.5 – 2 mg/kg/day and titrated up until improvement occurs[2]
Immunosuppressant Agents	• **Azathioprine** will reverse most symptoms; however, the effects may not be seen for 4-8 months[3;] One-third of patients will experience mild dose-dependent side effects and require a decrease in their dose[1] • **Cyclosporine** is occasionally beneficial typically showing improvement in 1 to 2 months after initiation with maximum improvements seen in 6 months • **Cyclophosphamide** can be used either IV or PO for treating MG ○ More than ½ of patients become asymptomatic after only a year of therapy[3] • With all immunosuppressant therapies, patients are at an increased risk of infection, side effects, and these agents are likely to interact with other medications[1]
Plasma Exchange	• Short-term intervention for abrupt worsening of MG • Almost all patients will improve temporarily • Max improvement can be seen anywhere from the 1st to the 14th exchange • Improvement can last for weeks or months[3]
Intravenous Immune Globulin	• Mechanism of Action is unknown, but is thought to be related to the down regulation of antibody production • Improvement occurs in 50 – 100% of patients which typically starts within the 1st week and lasts for several weeks or months • Side effects normally are related to the rate of infusion[3]

1. Micromedex [AUHSOP Intranet]. Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. [updated 2013, Cited 2013 May 29]. [about 5 p.]. Available from: http://www.micromedexsolutions.com/micromedex2/librarian/
2. Clinical Pharmacology [AUHSOP Intranet]. Tampa, FL: Gold Standard/Elsevier [updated 2013, cited 2013 May 29]. [about 5 p.] Available from: http://www.clinicalpharmacology-ip.com/default.aspx
3. Complementary/Integrative Medicine [Internet]. Houston: Myasthenia Gravis Foundation of America, INC.; c2010 [cited 2013 May 22]. Available from: http://www.myasthenia.org/Home.aspx

Living with Myasthenia Gravis - Insight into the life of Jessica Hoover, Myasthenia Gravis Patient and Pharm.D. Candidate 2014

- **What is day-to-day life like?**

"Day-to-day life is very similar to that of someone without MG. Compared to others, I don't feel restricted in my activities. The main difference is having to stop every 2-3 hours to take my medication to help manage my symptoms. Although it is a quick process, I have trouble remembering so I use phone alarms to remind me when I need a dose and put tick marks on my hand to track the number of doses I have had that day. In a normal day, I aim for 7-8 doses."

- **Have you found that anything helps better manage your MG?**

"At first, I was only taking pyridostigmine, but began to notice neck weakness, slurring of speech, and an inability to swallow. My neurologist recommended beginning the azathioprine and since initiating the new medication, I feel much better and have noticed an improvement in my symptoms. Rest is also imperative because fatigue is a common symptom in MG patients."

- **Do you have any advice for newly diagnosed patients?**

"First, listen to your body! I knew something was wrong and was told by several doctors that I was crazy before I finally found one that was willing to listen and run the necessary tests. Second, come up with a way to remember your medications because medication adherence is essential for symptom relief. The best advice I got from my doctor is to continue living life as normally as possible, but know my limitations!"

1. (Personal communication: Jessica Hoover, Myasthenia Gravis patients, Pharm.D. candidate 2014, hoovejl@auburn.edu, May 28, 2013.)

Recent Developments

Thymectomy and prednisone in MG patients for controlling symptoms… The thymus is an organ located in the chest that is responsible for the production of T cell and WBCs that make up the body's defense system. Removal of the thymus has been done for many years for treatment of MG, but new studies are seeking to understand if thymectomy plus prednisone is more effective than prednisone used alone. Patients will be followed for three years during this trial.[1] There are many current clinical trials that are currently going on that are looking at new medications and different treatment options.

1. Complementary/Integrative Medicine [Internet]. Houston: Myasthenia Gravis Foundation of America, INC.; c2010 [cited 2013 May 28]. Available from: http://www.myasthenia.org/Research/Latestnews.aspx
2. ClinicalTrials.gov [Internet]. U.S. National Institutes of Health; c1993-2012. Myasthenia 2102 Sep. [cited 2013 May 28]; [1 screen]. Available from: http://clinicaltrials.gov/ct2/results?term=myasthenia&recr=Open
3. Thymus Gland Function [Internet]. Study Health.com. c2012 [cited 2013 May 31]. Available from: http://ic.steadyhealth.com/thymus_gland_function.html

OTHER IMPORTANT DATES IN JUNE

- Men's Health Month
- Cataract Awareness Month
- National Scleroderma Awareness Month

The last "dose" …

"Although the world is full of suffering, it is also full of the overcoming of it."- Helen Keller
[American author and political activist, 1880 – 1968]

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