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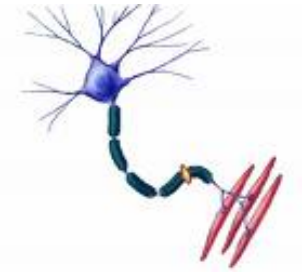
June is National Myasthenia Gravis Awareness Month

MYASTHENIA GRAVIS and other related stuff … Myasthenia Gravis (MG) is a chronic autoimmune neuromuscular disorder characterized by fluctuating weakness of the voluntary muscle groups caused by the failure of neuromuscular transmission, which results from the binding of autoantibodies to proteins involved in signaling at the neuromuscular junction (NMJ). The term comes from the Greek and Latin words meaning "grave muscular weakness." MG can be controlled with medications to improve the weakness and reduce the autoimmune process.
Conti-Fine BM, Milani MK. Myasthenia gravis: past, present, and future. *J Clin Invest*. 2006 Nov;116(11):2843-54.

IMPORTANT FACTS ABOUT MG:

- Prevalence: 20/100,000 people
- There are multiple genetic and environmental factors which may predispose a person to autoimmune disorders, however much remains unknown
- Occurs in all races, both genders, and at any age
- Not thought to be directly inherited nor is it contagious
- Occasionally occurs in more than one member of the same family
- Common symptoms can include:
  - A drooping eyelid
  - Blurred or double vision
  - Slurred speech
  - Difficulty chewing and swallowing
  - Weakness in the arms and legs
  - Chronic muscle fatigue
  - Difficulty breathing



National Institute of neurological disorders and Stroke. [homepage on the internet]. Maryland: NINDS; [updated 2007 Feb 14; 2007 May 28]. Available from: http://www.ninds.nih.gov/disorders/myasthenia_gravis/detail_myasthenia_gravis.htm
Muscular Dystrophy Association MDUSA.org [homepage on the Internet] c 2006 [updated 2006; cited 2007 May 28]. Available at : http://www.mdausa.org/publications/fa-mg-qa.html

DIAGNOSIS: Diagnosis of myasthenia gravis includes blood tests, clinical and neurological exam, imaging tests (e.g., x-ray, CT scan), intravenous anticholinesterase (Tensilon test), neurological tests (e.g., electromyography) and medical history. Blood tests are performed to determine serum levels of certain antibodies (e.g., AChR-binding antibodies, AChR-modulating antibodies, antistriational antibodies). High levels of these antibodies may indicate MG. Neurological examinations involves testing muscles and reflexes, observance of abnormal eye movements, and fatigability of the muscles. Chest x-ray and CT scan may be performed to detect enlarged thymus, which is common in MG.

In MG, there are few acetylcholine receptor sites (AChR) on the muscle and acetylcholine is broken down before it can fully stimulate the muscle, resulting in muscle weakness. The Tensilon® test involves intravenous administration of edrophonium chloride (Tensilon®), a drug which temporarily blocks the action of acetylcholinesterase. This allows for increased amounts of acetylcholine to stimulate the muscle and temporarily improve muscle strength. Side effects of this test include fluctuating abnormal heart rhythms such as atrial fibrillation and bradycardia.

Myasthenia.org [homepage on the Internet]. Myasthenia Gravis Foundation of America, Inc. c 1998-2007 [updated 2007 Feb 15; cited 2007 May 28]. Available from: http://myasthenia.org/amg_testsdiagnostics.cfm
National Institute of neurological disorders and Stroke. [homepage on the internet]. Maryland: NINDS; [updated 2007 Feb 14; 2007 May 28]. Available from: http://www.ninds.nih.gov/disorders/myasthenia_gravis/detail_myasthenia_gravis.htm
The Merck Manuals Online Medical Library. Neurological disorders. Merck & Co., Inc. c 1995-2005. [updated 2005 Nov; cited 2007 May 28]. Available from: http://www.merck.com/mmpe/sec16/ch223/ch223g.html

INFORbits on MG … Differential Diagnosis:

- Disorders that may cause symptoms similar to MG include botulism, congenital myasthenic syndromes, myopathies or muscular dystrophy and Lambert-Eaton syndrome.
- Some medications can exhibit non depolarizing blocking actions which may block the neuromuscular junction causing symptoms similar to MG. These drugs include:
- Antibiotics (e.g., ciprofloxacin, erythromycin, ampicillin)
- Antispasmodic drugs (e.g., trihexyphenidyl; used to treat movement disorders)
- Beta-adrenergic receptor blocking agents (e.g., propranolol, timolol)
- Cardiac drugs (e.g., procainamide, verapamil, quinidine)
- Lithium (used to treat bipolar disorder)
- Penicillamine (penicillin metabolite; used as an immunosuppressant to treat rheumatoid arthritis and as a heavy metal chelator)

Myasthenia.org [homepage on the Internet]. Myasthenia Gravis Foundation of America, Inc. c 1998-2007 [updated 2007 Feb 15; cited 2007 May 28]. Available from: http://www.myasthenia.org
Jason JS, Barton M, Fouladvand M. Ocular aspects of myasthenia gravis. *Semin Neurol* 2000; 20 (1):7-20. Available at: http://www.medscape.com/viewarticle/410859_5

TREATMENT: Neostigmine (Prostigmine®) and pyridostigmine (Mestinon®), cholinesterase inhibitors, are used to improve muscle weakness. By inhibiting cholinesterase at a higher level, acetylcholine is maintained in the neuromuscular junction and able to stimulate the receptors enhancing communication between nerves and muscles. These drugs improve muscle contraction and strength. Side effects include diarrhea, diaphoresis, and other typical cholinergic effects. Side effects are often counterbalanced by the use of atropine. Immunosuppressive drugs are utilized to reduce the autoimmune process involved in myasthenia gravis. Combination therapy with cholinesterase inhibitors and immunosuppressive agents is often required to achieve the best results. The most common immunosuppressive drugs used for myasthenia gravis include prednisone, cyclosporine, mycophenolate mofetil, and azathioprine. Treatment with these drugs require weeks to months for effects to be seen.

Jaretzki A 3rd. Barohn RJ. Ernstoff RM. Kaminski HJ. Keesey JC. Penn AS. Sanders DB. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Neurology. 2000 Jul 12;55(1):16-23. Available at: http://www.neurology.org/cgi/reprint/55/1/16?cookietest=yes
Mayo Foundation for Medical Education and Research. [homepage on the Internet] c 1998-2007 [updated 2007 Jan 19, cited 2007 May 28] Available at: http://www.mayoclinic.com/health/myastheniagravis/DS00375/DSECTION=6

OTHER TREATMENT OPTIONS: … Plasmapheresis is a treatment option used to remove the reputed antibodies from the circulation. Intravenous immunoglobulins are similarly used to bind the circulation antibodies. Both of these treatment options present only short-term benefits and must be repeated. It has been suggested that an abnormal thymus gland plays a significant role in the pathogenesis of MG. Surgical removal of the thymus (a thymectomy) has been shown to improve symptoms in greater than 50% of patients suffering from MG. Although some patients have been cured by this procedure, it is not considered a definitive cure.

Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America; Jaretzki, A., Barohn, R. J, Ernstoff, R. M, Kaminski, H. J, Keesey, J. C. MD; Penn, A. S. Myasthenia gravis: Recommendations for clinical research standards. Neurology 2000; 55(1):16-23.
Zinman L, Ng E, Bril V. IV immunoglobulin in patients with myasthenia gravis: a randomized control trial. Neurology 2007; 68: 837-841.

SO WHAT'S THE PROGNOSIS ... Myasthenia gravis is a chronic autoimmune disease, however patients may experience periods of remission. With treatment, the prognosis for most patients with MG is good. Patients can expect to see significant improvement of muscle weakness and are usually able to lead near normal lives. Remission, although temporary, may occur with complete resolution of muscle weakness and discontinuation of medications. Complete remissions are the goal of thymectomy and have been achieved in some patients. Approximately 60% of patients may experience remissions after having a thymectomy.

In severe cases of MG, termed myasthenic crisis, respiratory failure may occur as a result of extreme muscle weakness. Emergency medical treatment involving intubation and mechanical ventilation may be necessary. In some instances symptoms worsen even with aggressive treatment. As a result, generalized weakness and disability may occur. It is rare for MG to cause early deaths with the exception of myasthenia crisis resulting in respiratory failure.

National Institute of neurological disorders and Stroke. [homepage on the internet]. Maryland: NINDS; [updated 2007 Feb 14; 2007 May 28]. Available from: http://www.ninds.nih.gov/disorders/myasthenia_gravis/detail_myasthenia_gravis.htm
Aggarwal AN, Gupta D, Behera D, Prabhakar S, Jindal SK. Intensive respiratory care in patients with myasthenic crisis. Neurol India 2002;50:348-51
Berrouschot J, Baumann I, Kalischewski P, et al. Therapy of myasthenic crisis. *Crit Care Med* 1997;25(7):1228-35
Fischer JE, Grinvalski HT, Nussbaum MS, Sayer HJ, Cole RE, Samaha FJ. Aggressive surgical approach for drug-free remission from myasthenia gravis. *Ann Surg 1987; 205 (5): 496-501*.

FROM THE LAY LITERATURE: Did you know … The stress of illness can often be eased by involvement with support groups. Sharing in the experiences of others with the same illness can help ease some of the burden of the disease. Support groups can provide another important avenue for learning about new research and treatment programs aimed at myasthenia gravis. Some notable groups involved in MG include the Myasthenia Gravis Foundation of America and the Muscular Dystrophy Association. The Myasthenia Gravis Foundation of America maintains over 30 chapters located throughout the country. These chapters offer a variety of services including education forums, local help lines, local support group information, and newsletters. Patients and family members are able to gather information and resources. For more information on research on myasthenia gravis or other neurological disorders, you may contact:

NIH Neurological Institute
P.O. Box 5801
Bethesda, Maryland 20824
(301) 496-5751 or (800) 352-9424

http://www.ninds.nih.gov/; www.myasthenia.org ;www.mdausa.org ;
http://www.myasthenia.org/

FROM THE MEDICAL LITERATURE:

There are nine core autoimmune diseases:

- rheumatoid arthritis (RA)
- systemic lupus erythematosus (SLE)
- type 1 diabetes (DM1)
- multiple sclerosis (MS)
- autoimmune thyroid disease (Hashimoto's thyroiditis or Graves disease)
- juvenile RA
- inflammatory bowel disease (Crohn's disease or ulcerative colitis)
- psoriasis
- primary Sjögren's syndrome

Epidemiologic studies have demonstrated that genetic factors are crucial determinants of susceptibility to autoimmune disease. There is familial clustering, and the rate of concordance for autoimmune disease is higher in monozygotic twins than in dizygotic twins. Even in a genetically predisposed person- some trigger- an environmental exposure or a change in the internal environment, is usually required for frank autoreactivity. Studies of genetically similar populations living in different conditions strongly suggest the importance of environmental triggers. In the case of most autoimmune diseases, however, the trigger is unknown.

Criswell LA, Pfeiffer KA, Lum RF, Gonzales B, Novitzke J, Kern M, et al. Analysis of families in the multiple autoimmune disease genetics consortium (MADGC) collection: the PTPN22 620W allele associates with multiple autoimmune phenotypes. *Am J Hum Genet*. 2005;76.
Davidson A, Diamond B. Autoimmune diseases. *Adv Imm.* 2001; 345(5):340-50.
Noseworthy JH, Lucchinetti C, Rodriguez M, Weinshenker BG. Multiple sclerosis. *N Engl J Med.* 2000;343:938-952.

Other Important Topics and Dates in June

National Aphasia Awareness Month
National Safety Month
Vision Research Month
National Headache Awareness Week 3-9th
National Men's Health Week 11-17th

The last "dose" …

Medical science has proven time and again that when the resources are provided, great progress in the treatment, cure, and prevention of disease can occur.

Michael J. Fox
Actor suffering with Parkinson's Disease

An electronic bulletin of drug and health-related news highlights, a service of …
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Bernie R. Olin, Pharm.D., Director