HEALTH & NUTRITION

Environmental Health and Disease

Myasthenia Gravis

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If the 1960's in the United States could be considered the decade of access to health care and if the 1970's, in a similar fashion, could be considered the decade of primary care, then it may be said the 1980's is the decade of environmental health. There has been a remarkable increase in interest in environmental health and I view this as a new development and a new specialty in medical care delivery. In light of environmental health and in consideration of the entire subject, I have become interested in diseases that may develop secondary to environmental factors such as pollution, the use of insecticides and pesticides and complications from certain medications that are used to treat other conditions. In light of this latter interest, many drugs have been described to cause a worsening of certain conditions such as myasthenia gravis.

These medications by their action or pre- or post-synaptic structures can impair an individuals functioning. This weakness most likely will happen to patients who are already receiving some other drug or drugs, or suffering from hepatic or renal disease. It is also possible that a medication of drug may induce an immunologic reaction. Some have also described that a drug may unmask a latent neuromuscular disease. Interestingly, the myasthenic state (muscular weakness) in all these conditions is acute and lasts hours or days providing the patient does not succumb to respiratory failure.

In these conditions, the eyes, face, and the bulbar muscles are involved as well as the muscles of the arms and legs. The treatment in all instances is to provide respiratory support, discontinue the offending drug, and attempt to reverse the block by infusions of calcium gluconate, a supplementation of potassium and anticholinesterases. It is known that there are probably over 30 medications and drugs in current use as well as multiple anesthestic agents that may interfere with neuromuscular transmission. Antibiotics lead the list. It has been said that any antibiotic that ends with mycin is suspect.

Myasthenic weakness has been reported with 18 different antibiotics such as Neomycin, Panamycin, Streptomycin, as well as certain Tetracyclines. I have been told by at least one patient that Serapes has also been known to cause weakness. These drugs impair transmitter release by interferring with calcium-ion fluxes at nerve terminals. Several of the immunosuppresant drugs such as ACTH, Prednisone, and Azothiaprin worsen Myasthenia temporarily by depolarizing nerve terminals or impairing release of acetylcholine. Anticholinesterase drugs, and insecticides, and nerve gas may cause paralysis by binding to cholinesterase and blocking the hydrolysis of acetylcholine. In other words, they impair the breakdown of the neurotransmitter agent. The end plate remains depolarized. D-penicillamine has also caused a type of Myasthenia. Rest increases the strength of Prostigmin and Tensilon. The electrophysiologic findings are also typical in such cases as anti-ACh receptor antibodies in the serum are found. In this case, it differs from the weakness caused by the antibiotics previously mentioned.

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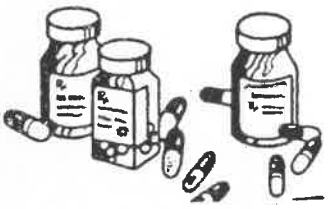

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With that introduction, I wish to briefly review a condition that was first described by Thomas Willis (of the Circle of Willis fame) in 1685. He was the first to give an account of this disease. Wilks, in 1877 pointed out that the medulla was free of disease. This fact was very important for it highlighted a condition that even though the doctor saw abnormalities that were potentially referable to a part of the central nervous system, once that part of the central nervous system was studied post mortum, no abnormalities could be found. This suggested back over a hundred years that the problem was not in the central nervous system but rather at the other end, namely at the neuromuscular junction.

The word myastenia is a Greek word meaning muscle; and the word gravis is a Latin word meaning severe. Some have referred to Myasthenia Gravis as either severe muscle disease or one with grave prognosis. Myasthenia Gravis is a group of illnesses rather than a single illness that has as the main characteristic a fluctuant weakness of certain voluntary muscles, particularly those that are innervated by motor nuclei of the brain stem (ocular, masticatory, facial, deglutitional, and lingual). The main feature of this condition is progressive weakness which is manifested or observed by the physician during some kind of continued activity. Frequently, I will ask the patient to look up at the ceiling for approximately 2 minutes and note the weakness of the eyelids with marked drooping of the eyelids. After asking the patient to rest for a minute, the eyelids recover their strength. Another way of documenting this weakness is to ask the patient to grip a ball or a manual device and after the weakness is manifested with the patient taking a brief break for 5 minutes, the strength returns. There is also a dramatic improvement in strength following administration of anticholinesterase drugs such as Tensilon (Edrophonium) or Mestinon (Pyridostigmine), Neostigmine may also be used (Prostigmine).

Jolly, in 1895, was the first physician to use the name Myasthenia Gravis. It was Jolly who originally demonstrated that the myasthenic weakness of muscles could be reproduced by faradic stimulation of its motor nerve in that the fatigued muscle would then respond to galvanic stimulation. He suggested the use of Physostigmine as a form of treatment, however, the use of Physostigmine did not come into vogue for another 40 years. The relationship between Myasthenia Gravis and the thymus gland was first noted by Laqure and Weigert in 1901. In 1949, Castleman and Norris described in great detail the pathologic changes in the gland. In 1960, Simpson and Nastuk theorized that an autoimmune mechanism must be operative in Myasthenia Gravis. It was in 1973, that Patrick and Lindstrom along with others, created an experimental form of Myasthenia Gravis that showed the mechanism of the block in neuromuscular transmission was due to antibodies to receptor substance at the end plate.

The neurologist in examining the patient usually notes muscular weakness involving the muscles of the face and eyes, leading to progressive paresis. With rest, however, the muscle strength improves. The onset is usually insidious. Occasionally, it may be fairly rapidly progressive. Sometimes, the weakness in this condition is initiated by an emotional upset or an infection. Occasionally, symptoms may appear during pregnancy or the puerperium, or in response to medications, drugs, or anesthesia as I described in my first paragraph. Once started, slow progression follows. Usually the muscles of the eyes, face, jaws, throat, and neck are the first to be affected.

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deficiency of end plate acetylcholinesterase was found. Acetycholinesterase is the enzyme that breaks down acetyclcholine. In another type of Congenital Myasthenia, there was a selective amyotrophy of scapular and forearm muscles with variable involvement of ocular facial muscles. In this case, the myasthenic weakness was attributable to a prolonged open time of the acetylcholine induced ion channel (slow channel syndrome). The unique electrophysiologic and ultrastructure characteristics of these disorders and other types of congenital myasthenia such as a defect in acethycholine synthesis or mobilization and to end plate acetylocholine deficiency are quite exciting in the entire field of myasthenia.

Type III is Ocular Myasthenia. This has a benign outlook and is seen mostly in older individuals and mostly males. Type IV ia mild generalized myasthenia with slow progression usually not associated with crises and is drug responsive. Type V is a moderate generalized myasthenia with severe skeletal and bulbar involvement but no crises, drug response is usually satisfactory. Type VI is an acute fulminating Myasthenia, rapid progression of severe symptoms with respiratory crisis and poor drug response. There is also a high incident of thymoma, a tumor of the thymus gland and it is associated with high mortality. Type VIII is a late severe Myasthenia with progression over a 2 year period from ocular to a generalized Myasthenia.

(To Be Continued in the April Newsletter and will discuss causes and treatment.)

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