

THE VIRGINIAN

SERVING VIRGINIA & WEST VIRGINIA

VIRGINIA CHAPTER NEWSLETTER

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FROM THE PRESIDENT

Joe Powers

Let me tell you, it was quite a shock! Failure to read the fine print on anything can spell disaster, especially a college catalog. But that summer, after my senior year in high school, I had 2 jobs – 16 hours a day – thinking that meant twice as much money, but little time to explore the complexities of a college program. As a consequence there would be ancient Greek, 5 days a week at 8 a.m. – followed through the week by Calculus, Chemistry, Biology, German Lit., History, Philosophy, English and Geo-Politics (for ROTC). And, oh yes, Religion. Since I continued working 30 hours a week, the days got pretty long.

Now that I'm about to mark my 72nd birthday, I occasionally look back on that period and try to evaluate lessons learned. Coming from a strongly religious family with a tradition that included a Franciscan and several nuns, it was preordained that I would attend a Catholic University.

Now if my life depended on it, I'm sure I couldn't decline a Greek verb – or solve a differential equation. But the most meaningful lesson still relevant was the concept of "serving the common good".

Rick Warren, author of "The Purpose Driven Life" makes the point that life develops in stages: there is the "Survival Stage" in which you just try to get a toe-hold on life, a beginning – followed by a "Success Stage" – where we strive to "get ahead", compete, establish security. Lastly, there's the option of the "Significant Stage" which implies making a difference in the world around you and in the lives of others. Warren's observations seem to have some validity: **"Life is a temporary assignment, a trust given to us as stewards"**.

Like Mattie or Terry (see article on inside front cover), we're here on earth with the chance to make a difference – a contribution – each in our own way:

"What matters most is not the duration of your life but the donation of it – not how long you lived, but how you lived".

No doubt it's difficult to translate that challenge into everyday life. With my retirement, and becoming an MG/Cancer patient, the equations that balanced my life changed – life's stable reference points were threatened. However, one of the best things that ever happened to me as a new MG patient (in addition to Dr. Pamela Chavis and Dr. James Brooks) was a call from Bob Colby, our past Chapter President – who volunteered to visit me. Over lunch, we talked for several hours, and subsequently he invited me to serve on the Chapter's Board. That visit helped me out of the initial depression that followed the MG/Thymoma Cancer diagnosis.

The visit gave me a starting point to confront my medical issues. It became our opportunity to "serve the common good" as an advocate for increased research – not just MG, but for a whole host of diseases. Our country really needs a "Marshall Plan for Medicine".

This is an exciting time in medicine. There are new tools for research: the Genome for genetic solutions, stem cells to replace damaged organs (eventually) and the whole new field of nanotechnology. Medical breakthroughs are possible. Both NIH and the Congress are becoming focused on MG/Autoimmune diseases. But we need to intensify our efforts supporting research – both at the Congressional level and at our Chapter/MGFA level – specifically for medical fellowships.

For us to continue, our Chapter's support of patients and research, the Chapter needs new leadership – folks who will roll up their sleeves, serve as Board members, run a committee, or help with fundraising, support groups – or our Congressional Advocacy Program.

As a Chapter, we're rapidly approaching a crossroads: we can succeed or fail. To survive we need your support and participation. Here is your opportunity to "give back" – to make a difference in your own life by helping others. You're important! We need you not just as a "member" but as a partner, an active participant in our Chapter's search for a cure. What will be your decision?

From the Program Director Community Fall Fairs

Once again, **Joan and Harry Glass** will be hosting booths at two fall fairs in the Northern Virginia area.

On **Saturday, October 1**, they will attend the **Manassas Fair** located across from the railroad station.

On **Saturday, October 8**, they will host a booth at the **Fairfax Fair** located on University Drive near Armstrong.

Our Chapter is most appreciative of Joan and Harry's time and efforts on our behalf to disseminate information and their experience with handling MG. Feedback from participants in past years has been most positive.

Please stop by to thank them and if you have time perhaps assist them. I'm sure they would welcome the help!

MG/Autoimmune Progress Report Released by NIH

Following the Autoimmune Research Plan issued in December 2000, the National Institutes of Health (NIH) has just now released its first biennial Progress Report as required by Congressional legislation. Congress instructed NIH to "expand, intensify and coordinate autoimmune research", and to establish priorities "to reflect input from a broad range of scientists, patients, and advocacy groups."

To develop the initial Plan and the present Progress Report, an Autoimmune Diseases Coordinating Committee (ADCC) was established with the participation of every NIH Institute, three federal agencies (CDC, FDA, and HHS) and 10 patient advocacy groups. Nearly 50 scientists

and physicians participated in developing the reports.

NIH invited Dr. Noel R. Rose, M.D., Ph.D. to chair the ADC Committee, for assessing progress made in the last two years, and to identify promising research directions for the future. Dr. Rose is the Director of the Autoimmune Research Center at Johns Hopkins University.

The result of this cooperative effort is a report that is intriguing – and exciting – because it reflects both the challenge and the promise of a future with improved diagnostics, therapies – and one day hopefully a world without MG.

Although the report is primarily intended for the medical professional, it is essential reading for every MG patient as well because it concerns the research needed – and the funding required to support the scientists and laboratories who head the battle against autoimmune disease.

The report identifies \$591.2 million expended by NIH in FY2003 – happily an increase of 36% over FY2000, yet still less than 2% of the total NIH budget of \$28 billion. Expenditures for MG research also increased from \$1.7 million in FY2000 to \$5 million in FY2003. Expenditures for FY2004 and 2005 were not provided – nor expected projections for 2006 and beyond.

Autoimmunity (AI) is outlined in the report as a composite of many different disorders. Just as there are many different forms of cancer or heart disease, there are nearly 80 different forms of autoimmune disease – one of which is MG. The impact of these disorders is described by the report in very stark language:

“Collectively autoimmune diseases affect 14.7 to 23.5 million people in this country – and for reasons unknown – their prevalence is rising...they are also a leading cause of death among young and middle aged women”. Although the cause of autoimmune disease remains unknown, and is not thought to be directly inherited, the report emphasizes that genetic factors play a major role in susceptibility and may be “triggered” by infections or an exposure to a wide range of environmental agents. The

seriousness of having any one of 80 different autoimmune diseases was emphasized by the report:

“Overlapping genetic traits enhance susceptibility to many of the diseases, so that a patient may suffer from more than one autoimmune disorder, or multiple autoimmune disorders may occur in the same family.”

Because autoimmune diseases have many different clinical factors that are difficult to diagnose but “share many features related to their onset and progression”, the report defines a far-reaching, many faceted research program that covers a very comprehensive range of medical issues. It is a “state-of-the-art” report on autoimmunity that is not duplicated anywhere else, thus invaluable for both patient and physician – something you definitely want to put on your “must read” list.

Copies of the report may now be accessed by way of the internet at: www.niaid.nih.gov/dait/pdf/ADCC_Fin_al.pdf

Hard copies were being printed as we “went to press” in August, and should now be available from the National Institutes of Health at National Institute of Allergies & Infectious Diseases ((NIAID), Office of Communications & Public Liaison, Center Drive MSC 2520, Bldg. 31, Room 7A50, Bethesda, MD 20892, Phone: 301/496-5717.

Current Research Projects Promise New Hope for Myasthenics

Ongoing research projects continue to improve the lives of myasthenics by enlarging the arsenal of medications that can be used to treat patients, by improving treatments and diagnostic tools, and by opening the doors to possible vaccines and innovative approaches.

The National Institutes of Health lists two current clinical trials. At present they are recruiting human volunteers for research specifically involving myasthenia gravis for tests involving the medication CellCept and the use of single fiber electromyography and macro-electromyography in diagnosis and information gathering about the progression of neuromuscular disease.

CellCept Safety and Efficacy

CellCept (Mycophenolate mofetil, MMF) modulates autoimmune responses through a unique mode of action which may be relevant for autoimmune disease patients. **The current study will test the safety and efficacy of adjunct MMF to maintain or improve symptom control with reduced corticosteroids in subjects with myasthenia gravis.** The study hopes to enroll 136 subjects. Those eligible for the study must have been diagnosed with MG, must have had the disease for 10 years or less, must require immunosuppressants, and must take prednisone for 4 weeks. Excluded are those taking CellCept or an immunosuppressant other than prednisone, those who have had a thymectomy within 6 months, those with a thymoma and those who are pregnant. There are a number of test sites throughout the United States and Canada. One is at the University of Rochester Medical Center where Dr. Emma Ciafaloni is the Principal Investigator. For more information see: www.clinicaltrials.gov/ct/show/NCT00090636?order=1.

EMG Training Program

The electromyography (EMG) 8 year study is a training program for fellows in clinical neurophysiology. They will employ electromyography to diagnose neuromuscular disorders, to provide information about disease progression, and to guide therapy. This is an ongoing program and study in which 2 adult volunteers a year participate. Healthy subjects and those with neuromuscular disorders or post poliomyelitis syndrome are recruited. The fellows in clinical neurophysiology learn and perform technically advanced electro-diagnostic studies, such as single fiber EMG and macro EMG, on patients with neuromuscular diseases. Over the eight year period, they hope to involve 30 subjects.

Monarsen Clinical Trials

In Israel, Ester Neurosciences is testing a new drug called Monarsen, proposed to be a substitute for Mestinon. In animal studies extremely low doses of Monarsen resulted in restored muscle strength. The drug proved to be extremely long acting. The

first studies in humans were conducted in the UK and in Israel and the results were positive. Currently a Phase 11a study is being conducted in Israel with a projected test group of 18. Current subjects must be sero-positive, aged 18-75. The test group receives one dose of Monarsen on a daily basis, thus reducing the amount of medication required for positive control of symptoms. At this point there have been no side effects and the single daily dose has been sufficient for symptom control in subjects. The drug has been granted Orphan Drug Status by the United States Food and Drug Administration, but testing in the United States cannot take place until the current testing of 18 patients is completed with good results. At that time the company can apply for permission to investigate the new drug in the United States. Additional information can be found at:

www.esterneuro.com/underproducts>an_tisense_drugs.

Immune System Studies

A new autoimmune tolerance technology, patented by the American Red Cross has been licensed by TolerGenics in Rockville, MD. This technology was developed by Dr. David W. Scott while at the University of Rochester, then further refined while at the American Red Cross. The technology seeks to make the immune system "tolerant", with the goal of preventing damaging attacks on the body's own tissues. In animal models the immune response has been turned off against specific proteins attacked in the autoimmune diseases: uveitis (an eye disease that causes blindness), juvenile diabetes, myasthenia gravis and multiple sclerosis. The developers felt that once these therapies are developed, they could be used to treat additional autoimmune diseases and allergies and be used in preventing organ rejection. Phase 1 trials are planned in 2005 for uveitis, but it is projected that the technology will ultimately be expanded to include additional autoimmune diseases. The company's site is:

www.tolergencis.com/. A press release announcing the trial is at: www.prweb.com/releases/2004/10/prweb_xml172286.php.

Source: *Upstate NY Chapter, MGFA, April 2005 "The Grapevine"*.

Form of Anemia Associated with MG and Thymoma

Recently published reports by four different Medical Centers in Japan have called attention to a potential association with Pure Red Cell Aplasia (PRCA) – a form of anemia – in patients with Myasthenia and Thymoma. Clinical case studies of a limited number of patients were noted. Evidence of Thymoma, bulbar involvement and high AChR antibody levels in MG patients appeared to indicate "significant risk for development of PRCA after thymectomy". Cyclosporine enhanced by erythropoietin caused hemoglobin to increase to normal levels.

Anemia reflects a decrease in red blood cells that carry oxygen throughout the arterial system, and is noted by hemoglobin content of the blood cells and their size. Depending on its severity, Anemia would likely exacerbate MG with increased fatigue, difficulty in breathing, dizziness, headache and possible insomnia. Appetite loss, gastrointestinal upsets, irregular heartbeats and murmurs may also occur. Deficiencies in Iron and Vitamin B – especially B₁₂, may be the most common cause. Blood tests are used to determine the exact type of anemia and its cause.

Sources:

(1) *Myasthenia Gravis with Thymus Hyperplasia and Pure Red Cell Aplasia*. Neurological Science, 15 Sept. 04, Suto, Y.; Sakuma, K. and others. Institute of Neurological Sciences, Tottori University, Japan.

(2) *Successful Treatment of Pure Red Cell Aplasia with Cyclosporin A and Erythropoietin After Thymectomy*. Haematologica, 1 June 04. Maeda, T.; Shiokawa, S. and others. Dept. of Molecular Genetics, Shin-Beppu Hospital, Japan.

(3) *Initial Predictors of Development of Pure Red Cell Aplasia in Myasthenia Gravis After Thymectomy*, Clinical Neurology & Neurosurgery. Dec. 03. Suzuki, S.; Nogawa, S. and others. Dept. of Neurology, Keio University School of Medicine. Tokyo, Japan.

(4) *Triad of Thymoma, Myasthenia Gravis and Pure Red Cell Aplasia Combined with Sjogrens Syndrome*. Japan Journal of Thoracic/Cardiovascular Surgery. July 04. Fujii, K.; Kanno, R. and others. Fukushima Medical University, Japan.

Note: Many thanks to Dr. Pamela Chavis, M.D. for bringing these articles to our attention.

Pesticides/Insecticides... Caution is Advised

For myasthenics there are special considerations when using pesticides.

Two of the most popular classes of pesticides are organophosphates and carbonates. Both classes inhibit the enzyme cholinesterase found in the nervous systems of insects and humans. Use of these products by those taking Mestinon or its generic, pyridostigmine bromide, may result in the same symptoms as an overdose of the medication.

In humans, to activate a muscle, an impulse travels from the brain to the nerve ending. The chemical acetylcholine carries the message across the space (synapse) between the nerve and the muscle, linking to the muscle receptors. When the muscle receptors are activated by the acetylcholine, the muscle responds. Cholinesterase is an enzyme that, in normal individuals, is produced to deactivate the acetylcholine when the muscle is activated, preventing too much acetylcholine from building up at the site.

In myasthenics, these muscle receptors may be damaged or blocked by antibodies that interfere with the acetylcholine, producing a need for greater amounts of acetylcholine to produce the desired muscle response. Mestinon or pyridostigmine bromide delays the breakdown of the acetylcholine so that more will flood the muscle receptors by inhibiting the work of the cholinesterase. The important thing to remember is that Mestinon and the pesticides in the organophosphate and carbonate classes are all cholinesterase inhibitors. So for those who take Mestinon, using these pesticides may result in exposure to excessive amounts of cholinesterase inhibitors, producing symptoms of a

myasthenic cholinergic crisis. This type of crisis is chemically induced by an overdose of medication or overexposure to an anticholinesterase agent. Symptoms are those of an overdose of Mestinon, including muscle weakness, twitching (fasciculation), excessive salivation, constricted pupils, and breathing difficulties. Organophosphate poisoning requires intervention within 24 hours to avoid permanent damage. Carbonates temporarily bind to cholinesterase for about six hours.

In addition to the organophosphates and carbonates, myasthenics should also be cautious about using DEET and permethrin. DEET is a pesticide applied directly to the skin to repel insects. It is available in sprays and in liquid and is commonly seen in household foggers, and in mosquito repellants. It is widely used to repel ticks that cause Lyme Disease. Permethrin is usually sprayed on clothing to repel insects. It is also used in household foggers and sprays, in flea dips, in termite treatments, agricultural pesticide products and in lice shampoos.

Normally the healthy immune system deactivates the pesticides. Recent investigations at Duke University Medical Center have shown that Mestinon (pyridostigmine bromide), DEET and permethrin, when used in combination can be toxic. In one experiment chickens were selected because their susceptibility to neurotoxin chemicals resembles that of humans. The chickens, when treated with pyridostigmine bromide and exposed to DEET and permethrin, developed leg weakness, difficulty with wing movement, stumbling, diarrhea and shortness of breath. Researchers hypothesized that the pyridostigmine bromide reduces the body's normal ability to inactivate the combination of DEET/permethrin, thus allowing the pesticides to travel to and damage the brain and nervous system. No comparable tests have been done on myasthenics, but caution in the use of these products is advised.

For more information, see EPA's website on organophosphates: www.epa.gov/pesticides/op/primer.htm. They also have a page that describes

DEET and their recommendations for use. See this fact sheet at: www.epa.gov/pesticides/factsheets/chemicals/deet.htm.

Permethrin is in the class called pyrethroids and there is a fact sheet that describes its uses and addresses its toxicity at: <http://npic.orst.edu/factsheets/permethrin.pdf>. For more information on pesticides that are cholinesterase inhibitors see: <http://extoxnet.orst.edu/tibs/cholines.htm>.

Effects of pesticides on human health depend on how much of the substance is used and the length and frequency of exposure. Effects also depend on the health of a person and the environment in which the exposure occurs.

Source: Upstate NY Chapter, MGFA, April 2005 "The Grapevine", Vol. 2, Issue 3.

MED NOTES

Pleasingly Plump and the Magic Number

If you've ever wondered just how "pleasingly plump" you might be, there's now a scientific measure you can use to confirm your expectations. It's called "Body Mass Index" or "BMI". As you might suspect, BMI is a number that doctors use to also assess your risk of coronary disease, but you can use the index to do your own risk assessment. It goes like this: Take your weight in pounds, divided by your height in inches – square that number and multiply the result by 704.5 (the magic number).

Unless you're a mathematical whiz, it's not recommended that you attempt this calculation off the top of your head – a calculator is much easier – and more accurate! Here's an example, submitted by an "anonymous" contributor:

Weight: 230 pounds

Height: 5 ft., 10 inches – or 72 inches

Height Squared: $72" \times 72" = 5184$

The Magic Number: 704.5 – and here's the calculation:

$230 \text{ divided by } 5184 = .04436 \times 704.5$
equals 31.257.

To interpret that number and its significance here's a tell-all table for handy-dandy reference:

18.5 or less = underweight

18.5 to 24.9 = normal (gold star for these folks)

25 to 29.9 = overweight

30 to 39.9 = obese

40 and over = severely overweight

Now that you know just how "pleasingly plump" you are, should you wish to change your category from "obese" (the above example) to "overweight", losing just 10 pounds will do it. However, to move to the most desirable category, "normal", it will take a loss of 50 pounds!! But if done at 1 pound a week, we'd have a winner – not an impossible job but one that requires daily discipline including the right nutrition (hold the carbs), exercise (30 minutes to 1 hour daily), little or no stress, and of course enough sleep (8 hours preferably).

BMI index over 35 increases the likelihood of diabetes by as much as 80%! So...

Did Someone Just Say "Exercise"?

Since the ability of a Myasthenic patient to exercise is most often compromised – depending on the severity of the MG – a specially structured exercise program should be considered in consultation with your doctor.

First, an assessment of your ability to exercise would likely be made through a series of possible tests. This may include an antigen blood count as a possible indicator of the MG's severity, as well as other tests of muscular strength or weakness, lung capacity and cardiac status, including your maximum heart rate. Knowing your maximum heart rate (a number of numerical ranges) is important since for exercise to be "aerobic" you should try to get your heart rate up to 70 or 80% of your maximum to fully exercise your heart, lungs and circulatory system.

Your doctor can schedule you for a stress test to evaluate your cardiac status and determine your maximum heart rate. Depending on your medical condition, the doctor can recommend one or more of several types of stress tests – all of which are "safe, quick and non-invasive" (per the American Medical Association). They include the standard "treadmill test" while being monitored by an electrocardiogram. Should you be unable to walk or have difficulty walking, a "chemical stress

test” can be given in which a stimulant drug called dobutamine is given intravenously to increase your heart rate. A variation of that is the “Nuclear Stress Test” in which a small amount of radionuclide (usually thallium) is injected and monitored as it circulates. Concurrently, a “gamma camera” is used to take pictures of the heart before, during, and after exercise. The resulting pictures identify any heart damage and whether normal blood flow is blocked or obstructed.

To develop an exercise program that corresponds with your physical condition, a possible “team approach” may be used by the doctor working with a physical therapist.

Another option to consider is the “Wellness Program” or “Cardiac Rehabilitation Program” that a number of hospitals sponsor. They can structure a graduated program for you and carefully monitor your performance and improvement – with reports back to you and your doctor for review. Alternatively, you may be able to work with an exercise specialist at a health club gymnasium to develop a “customized exercise program”.

In addition to commercial health clubs, some counties have gymnasiums and offer exercise opportunities through their “Parks and Recreation” programs which are quite inexpensive.

Failure to engage in some systematic exercise program, however, may further compromise and atrophy or weaken your muscles – the axiom of “use it or lose it” becomes operable.

In retrospect, for those of us who are 50 or older, the significance and importance of exercise was never emphasized to the extent that exercising became an integral part of daily life. Now however, thanks to the AMA information programs, the necessity of daily exercise is defined unequivocally as a factor in your life expectancy.

Exercise helps regulate appetite, reducing body fat – thus is essential in weight management and improved sleep. As a person ages, exercise aids in balance and coordination by helping to prevent catastrophic falls. Exercise will also directly influence your blood lipids, including your cholesterol (both LDL and HDL), and triglycerides – all factors

in the development of atherosclerosis, a major cause of heart disease or stroke. Never willing to “sugarcoat” serious issues, the AMA flatly states that an “on-going exercise program throughout a lifetime helps to prevent or delay serious diseases included some types of cancer, the most common form of diabetes, age related bone loss and osteoporosis”. The choice is pretty clear – so what will you do? But before you do anything, check with your doctor!

NUTRI-NUGGETS

Here’s a Fishy Story!

By now you may know that the American Heart Association encourages you to have at least six ounces of Omega-3 rich fish every week – higher amounts if you already have heart disease.

Omega-3’s are special polyunsaturated fatty acids that appear to inhibit the forming of blood clots that could contribute to a heart attack or stroke. Two constituents of the Omega-3’s are EPA (Eicosapentenoic acid) and DHA (docosahexenoic acid). Reportedly, they reduce the risk of arrhythmias (irregular heart beats) and lower inflammation, triglycerides, and high blood pressure, all linked to heart disease.

Omega-3’s are found both in seafood and plants. Fish contains the EPA and DHA. Plants contain another constituent of Omega-3, called ALA (Alpha-linolenic acid). The best sources of ALA are flaxseed, walnuts, and canola oil.

Although there’s no official recommended daily intake, there is reported evidence that as little as 500 milligrams of EPA and DHA, and as little as 1500 milligrams daily of ALA may be beneficial. The American Heart Association recommends 1 gram (1000 milligrams) daily of Omega-3 from fish or a supplement – but 2-4 grams a day if you have elevated triglycerides. They suggest 3 grams daily may reduce joint pain and swelling from rheumatoid arthritis – an autoimmune disease.

It’s been said that “an ounce of seafood is like an ounce of prevention and worth a pound of cure”. In part, that’s because fish is a great source of low fat protein, all 8 amino acids, and can be a good source of Vitamin B12,

calcium, phosphorus, potassium and minerals like iodine and zinc – all in addition to the Omega-3’s.

Here are some comparative Omega-3 tables:

For EPA and DHA

<u>Fish (3.5 oz. cooked)</u>	<u>Amt (mg.)</u>
Salmon	1800-2100
Herring	2000
Sardines (canned)	1000-1400
Trout	900-1200
Mackerel	1200
Bluefish	1000

For ALA

<u>Plant or Plant Product</u>	<u>Amt (mg.)</u>
Flaxseed Oil (1 tbsp)	7200
Walnut (1 oz.)	2600
Flaxseed (Ground, 1 tbsp)	2200
Walnut Oil (1tbsp)	1400
Canola Oil (1 tbsp)	1300
Soybeans (1 cup)	640
Kidney Beans	300
Tofu (1/2 cup)	230

The food industry has begun “enriching” foods with Omega-3’s including breads, cereals, waffles, granola and various spreads like butter and “mayo”.

With respect to seafood, a cautionary note is sounded: Because of environmental pollution, some types of fish may be contaminated with mercury, PCB’s, or dioxins. Toxic forms of mercury which accumulate in waterways, if ingested via fish may accumulate as a toxin in your system and remain in your body for up to a year. Remember that toxins can become “triggers” for some types of cancer and autoimmune diseases.

Women who are or may become pregnant, babies, and children younger than 5 should limit their intake of seafood, particularly shrimp, farm-raised salmon, pollock, catfish, or canned light tuna. These fish and “white tuna” or albacore should be definitely limited to no more than 6 oz. a week, if that. Wild salmon is preferred to farm-raised salmon, which may have higher levels of contaminants due to toxins in their feed. The Federal Government now requires labeling to identify farm-raised fish.

Should all this discourage you from eating fish – or if you don’t really care

for fish, The American Heart Association still recommends that at least you take a supplement – from 1 gram (1000mg) to 4 grams (4000 mg) depending on your heart health. Bon Appetite!

**Tacrolimus Continues to Show
Promise in Management
of Myasthenia Gravis**

by Curtis W. Balmer, Ph.D.

Purposely weakening the body's natural defense system hardly seems a useful strategy for combating disease, that is unless you are one of the thousands of individuals worldwide battling myasthenia gravis (MG)—a chronic and currently incurable autoimmune disorder that produces often debilitating weakness and fatigability in the muscles under voluntary control. Most cases of MG arise when the immune system—which protects the body against a constant onslaught of foreign invaders—mistakenly attacks and disables specialized receptor proteins on the surface of muscle cells that receive signals from the nervous system.

Why and how the body suddenly turns against itself in this way remains a mystery. Nonetheless, dampening immune activity with powerful “immunosuppressive” agents such as prednisolone, azathioprine, and cyclosporine has emerged as an effective and, for many people, an indispensable frontline therapy in the management of MG.

Three recently published studies add to a small body of research suggesting that tacrolimus (FK506; Prograf), a potent immunosuppressive drug used to prevent rejection of organ transplants, may also be an effective and well-tolerated treatment for MG.

In the first of these studies, researchers in Japan assessed the effectiveness and safety of long-term, low-dose tacrolimus administration in the management of generalized MG which is characterized by weakness of the arms, legs, and trunk.

At the start of the study, which appears in the March issue of the *Journal of Neurology, Neurosurgery, and Psychiatry*, all 12 participants were receiving prednisolone as well as

additional immunosuppressive agents either to enhance symptomatic relief or reduce the side effects of the prednisolone.

Study participants continued to receive prednisolone, but additional drugs which included azathioprine, cyclosporine, and cyclophosphamide were replaced with low-doses of tacrolimus for a maximum of two years. Changes in muscle strength, activities of daily living, and required prednisolone dosages were then compared with those recorded in patients who had undergone the same experimental regimen for 16 weeks.

Investigators reported that a greater percentage of participants receiving long-term tacrolimus therapy showed improvements in muscle strength or activities of daily living, and that in a few cases, improvements in activities of daily living were more pronounced than those observed in the 16 week study.

The researchers also reported that prednisolone dosages could be modestly reduced in seven of the 12 long-term study participants versus only three in the 16 week trial.

22 side effects were observed in 8 of the study participants. However, in all but one case, these effects were minor and did not require interruption of tacrolimus administration.

Another small study from Japan, published in the June issue of the journal *European Neurology*, evaluated the effectiveness of tacrolimus in patients who had recently been diagnosed with MG but who were not yet receiving treatment for the disorder.

Study participants received the immunosuppressive drug prednisolone alone or in combination with low doses of tacrolimus for a maximum of one year. Patient outcomes were then compared between the two groups.

Researchers reported that both the duration of early phase therapy and the need for additional therapeutic interventions were reduced in participants receiving tacrolimus. Furthermore, participants receiving the experimental treatment required lower doses of prednisolone to maintain “minimal manifestations” of the disease.

No significant side effects were reportedly observed in participants receiving tacrolimus.

In a much larger study appearing in the May 24 issue of the journal *Neurology*, researchers in Spain evaluated the effectiveness and safety of long-term tacrolimus administration in 79 patients with disabling MG who were dependent on and experiencing serious side effects of combined high-dose cyclosporine and prednisone therapy.

Study participants continued to receive prednisone but cyclosporine was replaced with tacrolimus for a minimum of more than one year to a maximum of more than three years.

Researchers reported that, according to the Myasthenia Gravis Foundation of America Post Intervention Status, four study participants achieved “complete stable remission” (CSR) which is defined as the complete absence of signs and symptoms of MG for at least one year and no therapy for MG during that time. 70 participants reportedly achieved “pharmacologic remission” which is defined by the same criteria as CSR except the patient continues to receive some therapy for MG. The five remaining participants had minimal symptoms.

All participants resumed full activities of daily living and in all but two patients, prednisone could be completely withdrawn.

Of the 79 study participants, five reportedly experienced side effects serious enough to require withdrawal of tacrolimus. Adverse effects included kidney problems, loss of the ability to coordinate muscular movement, nerve disorders, and dizziness. Increased rates of infection—a common complication of long-term immunosuppression—were not observed.

While the findings presented in these studies are promising, the efficacy and safety of tacrolimus in the management of MG has yet to be evaluated in large multi-center randomized, double blind, placebo-controlled studies—the gold standard of clinical research trials. Such trials are reportedly underway in Japan.