

THE VIRGINIAN

SERVING VIRGINIA & WEST VIRGINIA

VIRGINIA CHAPTER NEWSLETTER

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FROM THE PRESIDENT

Joe Powers

Spring Chapter Meeting A Success

We would like to give a big thanks to **Anita Steele and the Northern Virginia Support Group** for hosting our Spring Chapter Meeting.

Our guest speaker was **Dr. Simon Fishman of the Integrated Neurology Services** in the Northern Virginia area. Among other topics, he spoke to the membership about types of MG, the difficulty in diagnosis and treatment, and strategies for daily management. After speaking, he was available for an extensive question and answer session for more individual and specific information. We certainly thank him for sharing his time and expertise.

After the Chapter meeting, a Board Meeting was held with the attending membership invited to stay and share their input on several topics of interest. These included a discussion on the need to increase membership dues, especially in light of the increased costs of producing the newsletter and materials purchased to be included in new patient information packets. Unfortunately, almost 50% of our membership has not sent in their renewal dues for 2004 – and now 2005 renewal fees are due!

We continued our discussions on fundraising. In order to continue as a Chapter, we must come up with creative ideas together. It need not be a huge event, but an event that would draw interest in your area. We need your ideas – and Phyllis Birkhead, our Program Director, will be happy to coordinate and help advertise. If you would be interested in being a part of a Fundraising Committee, please contact Phyllis at 2304 Angus Road, Charlottesville, VA 22901 or email at pma8n@adelphia.net. We need your ideas and help!

To be an effective and successful Chapter we desperately need our Board and membership to take an active role with a sense of ownership in Board and Chapter activities.

This summer we will be sending out a direct mailing to the membership outlining Board decisions and issues we need to work on together as a Chapter.

MGFA's Patient Advocacy Program

It's really good news that MGFA celebrated its 50th Anniversary by establishing a Patient Advocacy Program. As you know we've encouraged MGFA to become more active in support of the NIH Autoimmune Research Plan – and it couldn't happen at a better time. The updated plan has been given to the Director, NIH, and to the Secretary of Health and Human Services for review and approval – thus it has not yet been publicly released or given to Congress to be considered as part of the budget process.

We again delayed this edition of the newsletter, expecting the plan's release momentarily – it was supposed to have been delivered to Congress in January 2005. As soon as it is released copies will be given to MGFA and the newly established Advocacy Committee – and its new Chairman, Damon Wainscoat (our Vice President) who was also elected to MGFA's Board of Trustees at the recent conference. And so, congratulations to Damon are mightily in order!

The advent of the new plan will give all autoimmune patients hope for the future in improved therapies, diagnostic tools and at some point a cure. Dr. Noel R. Rose, M.D., chaired the NIH Autoimmune Diseases Coordinating Committee at the invitation of Dr. Elias Zerhouni, the NIH Director. Dr. Rose is also Director of the Autoimmune Research Center at Johns Hopkins University. **Certainly every MG patient can say a prayer of thanks for Dr. Rose, and for all the other doctors who are so dedicated to the service of others.**

But you've heard that expression, "God helps those who help themselves." Although we depend upon the dedication and knowledge of physicians, it's expected that as patients we accept responsibility for our own healthcare. As myasthenic patients, it's up to us individually to be informed about our health, and to play an active role in managing our care. And certainly one of the best ways to doing that is to play an active role in your MG Chapter.

The Advocacy Program will provide a unique opportunity for each of us to easily participate – and to influence those issues that have a direct bearing on the health of our families and ourselves. After all, that's one of the great things about this country – it's a representative democracy in which it's expected that ordinary citizens have a say in their government – and the need to adequately support medical research through their taxes.

As you know, our country is going through a pretty tough time now. Between Iraq, the war against terrorism, recession recovery – and many competing social demands, funds are not as easily available as in the past. For that reason, it will be vitally important that we individually and collectively let our representatives know the importance and priority that health issues and medical research need.

Advocacy has nothing to do with "politics" – or being a Democrat or Republican issue. Supporting the need for medical research is a non-partisan, non-political issue that affects each of us irrespective of "party" affiliation. Not to participate and play an active role in issues affecting your own health is to abdicate a basic right and obligation of citizenship.

In our next newsletter, we hope to summarize the "soon to be released" NIH Research Plan and to share with you how we can and need to support its funding.

Myasthenia and autoimmune research have been under-funded for years – in spite of the Congressional intent that NIH pursue a more vigorous

program. **It's time that you – and I – decide to change that by working together as strong advocates for medical research. Can we count on you to do your part?**

Northern Virginia Support Group

The next Northern Virginia Support Group Meeting is scheduled for **Saturday, June 4, 2005, from 1-3 p.m.** As usual, the meeting will be held in the **Community Room at the Central Library in Manassas, VA.** If you have not attended a previous meeting, the address is 8601 Mathis Avenue. **Contact Anita Steele at 540/891-1736 or Phyllis Birkhead at 800/728-4405 if you need directions to the library. You can also directions via email: pma8n@adelphia.net.**

MGFA Celebrates Its 50th At National Conference

The Myasthenia Gravis Foundation concurrently celebrated its 50th anniversary as part of the Annual Membership Meeting held this April in Grand Rapids. **To appropriately celebrate, a total of \$71,000 was contributed or pledged toward MG Postdoctoral Fellowships – including \$1000 from your Virginia Chapter!** Dr. James (Chip) Howard, Jr., M.D., spoke urgently of the competition to secure and develop young doctors to take the challenge of MG Research and Neuromuscular Specialties.

Dr. Howard, Chairperson for the National MGFA Medical & Scientific Advisory Board, and Distinguished Professor of Neuromuscular Disorders at the University of North Carolina, Chapel Hill, reviewed a wide range of topics including research underway not only in the U.S., but also in Canada, United Kingdom, Netherlands, Germany, Israel, Brazil, and Ukraine. Specific topics included:

- Bio-statistical analysis of the effectiveness of Thymectomy surgery
- Recent studies showing evidence of MuSK, an enzyme in Seronegative MG patients
- CellCept therapy and other studies of Prednisone,

Monarsen (like Mestimon) and Aspreva WX17798 – an “orphan drug” now being evaluated in 68 centers worldwide.

Dr. Howard noted that he met with 60-70 neurologists in Florida recently to encourage their participation in MGFA activities and research projects.

Other presentations were made including one by Dr. Nicola Pardo, M.D. – a recipient of the Osserman Fellowship – who reviewed her research in gene therapy as related to the Lambert Eaton Myasthenia Syndrome (LEMS), a neuromuscular disorder similar to Myasthenia and associated with malignancy in 50% of patients diagnosed.

One of the most significant presentations was given by our own Vice President, Damon Wainscoat, in describing the proposed MG Advocacy Program that was endorsed by the National MG Board of Directors and adopted by the membership present representing their Chapters. The presentation followed earlier discussions with MGFA's President, Ms. Esther Land, and the Executive Director, L.J. Taugher. The Advocacy Program would be “member driven” at the Chapter level with coordination provided by National MGFA's Board of Directors. The Advocacy Program will emphasize support needed to adequately fund the NIH Autoimmune Research Plan.

In view of his experience and commitment to an advocacy role for MGFA, Damon was asked to serve on the Board of Trustees and to chair a newly formed MGFA Committee for Advocacy Programs. Accordingly, Damon has submitted a proposed plan for implementing the program.

A Medical Panel Review followed the presentation covering a wide range of questions and topics – from congenital MG to Sleep Apnea. Four Working Group Sessions were also held that included:

- Chapter and Support Group Development
- MG From a Nursing Perspective

- Aging Successfully With a Chronic Disease
- Tips for Managing MG – Nutrition, Exercise, Learning All About MG and Available Therapies.

A request was made by Marcia Lorimer for Chapters to check with local medical facilities for nurses who may wish to train for MG care. An “on-site” training program is being made available. More detailed information will be given in our next newsletter!

Conference proceedings were videotaped and broadcast live over the Internet to five countries and 18 U.S. States via MGNet.org's chat room. Copies of the video presentations will be made available shortly and given to the Support Groups for their review.

MGFA sponsors two other conferences. The next meeting for the Medical Science Board will be conducted as part of the Fall Conference in San Diego, 23-24 September. The next International Symposium will be held in 2007. Medical scientists from around the world are invited to present their research projects and findings at the International Conference. Papers presented are then published through the New York Academy of Science.

MGFA Implementing Autoimmune Advocacy Program

The Advocacy Program adopted by the recent National MGFA Conference will emphasize the need for adequate funding of MG research and support for the NIH's Autoimmune Plan. To date, NIH support for all autoimmune research has been less than 2% of the NIH budget in spite of the fact that their budget was doubled by Congress in the last five years and now approaches \$30 billion annually. MG research at NIH is just over \$1 million – barely surviving!

Private foundations, like MGFA, do not have sufficient resources to fully fund comprehensive research programs – or develop a sufficient number of projects that will attract young scientists and physicians to autoimmune research and clinical practice. Accordingly, NIH was established by Congress to lead the way

in medical research and training. Nearly every national patient group (Cancer, Heart, Arthritis, and Lupus) has an advocacy program that is active on behalf of their members. In addition, they coordinate their efforts in support of NIH funding through AARDA (the American Autoimmune Related Diseases Association) and the National Coalition of Autoimmune Patient Groups. **MGFA has now committed to a more active advocacy role on behalf of its members.**

The proposed program being implemented will be chapter driven by members. Each chapter will be given webpage tools to initiate their own action, and access to an internet Congressional Directory including copies of all pending legislation, resolutions and upcoming budget issues.

The program will be managed by MGFA's Board of Directors by establishing a Government Advocacy Committee, chaired by an MGFA Board member. Each Chapter will be represented on the committee and invited to participate in scheduled workshops providing information on "how to be an effective advocate" as well as the legislative/budget process.

MGFA has requested Damon Wainscoat, the Virginia MG Chapter Vice President, to chair the initial Advocacy Committee. Damon has had extensive experience as an advocate for Veterans affairs and has been a participant in advocacy efforts sponsored by NCPAG on Capitol Hill. He has recently retired as an Information Systems Manager for the Defense Department. A highly decorated Vietnam veteran, Damon contracted a severe form of MG that has frequently required hospitalization. His injuries in Vietnam were so extensive (he spent two years in a military hospital) that a Thymectomy (thoracic surgery to remove the Thymus) was not possible. He remains active also in support of his old Army unit, the 173rd Airborne Brigade, now serving in Afghanistan.

Congress Briefed on AI Research

A Congressional Briefing was held March 16, 2005, in support of the NIH Autoimmune Research Plan with over

100 in attendance. The Briefing was held in the Dirksen Senate Office Building on Capitol Hill. The National Coalition of Autoimmune Patient Groups (NCPAG) sponsored the Briefing. MGFA and your Virginia Chapter are active members of the coalition along with 23 other patient groups. **Cosponsors of the Briefing from Virginia included Senators George Allen and John Warner and Representatives Virgil Goode and Bob Goodlatte**

Representative Patrick Kennedy opened the meeting emphasizing the need for awareness, research and prevention of autoimmune diseases. **Kennedy has introduced legislation, HR3359, cosponsored by Rep. Fred Upton that calls for specific funding of autoimmune research.**

The keynote speaker was Dr. Bhagirath Singh, Ph.D. – the Scientific Director of the Institute of Infection and Immunity that is part of the Canadian Institutes of Health Research (CIHR). Since 2000-01, Dr. Singh pointed out that the Canadian government has doubled its expenditures in support of autoimmune research in view of the high costs associated with these diseases. Canada spends a greater percentage of its research budget on autoimmunity diseases than the United States.

Two patients shared their experience of living with autoimmune diseases. Leslie Sue Betterman said, "I'm one of 22 million Americans struggling to be functional on a daily basis..Autoimmune diseases are chronic, disabling and lifelong." Betterman suffers from multiple autoimmune disorders including Sjorgren's Syndrome and Rheumatoid Arthritis.

Cecilia Ristau (age 13), also with multiple autoimmune diseases, described how everyone's life changes when that happens – and how it affects the entire family. Cecilia said, "There are tons of other children praying that every night their diseases will vanish", and that she "would give up anything, an arm or a leg if I need to, just to cure my lifelong disease, because childhood is supposed to be fun, not filled with needles and pain. There is not a day in

my life that I don't wonder what it feels like to be normal."

Dr. Noel R. Rose, M.D., Ph.D. provided an update on the NIH Autoimmune Research Plan indicating a number of key research opportunities existed that could provide hope for the future. Dr. Rose chaired the NIH Autoimmune Diseases Coordinating Committee that developed the Plan.

Dr. Stanley Finger, Ph.D., Board Chairman of AARDA (American Autoimmune Related Diseases Association), wrapped up the program by emphasizing that it costs \$120 billion a year to treat autoimmune diseases, and the National Coalition of Autoimmune Patient Groups' 2005 legislative initiatives were critical to making progress in the approximately 100 different interrelated autoimmune diseases. Accordingly, AARDA has submitted language for the FY2006 appropriations bill in both the Senate and the House – and testified subsequently on 21 April 2005 in support of the NIH Appropriation. Both Cecilia Ristau and Dr. Finger provided the Congressional testimony.

Separately, AARDA is requesting help in securing co-sponsors for the Kennedy/Upton Autoimmune Bill. If you can help call or write to either of the following:

Damon Wainscoat – 703/730-0505
djwainscoat@comcast.net

Joe Powers – 434/589-3704
pma8n@adelphia.net

Note related article in this newsletter regarding MGFA's newly established Advocacy Program that all members, including family and friends, can participate in as partners!

Israeli Drug Eases Suffering of Myasthenia Gravis Patients

An Israeli company is in the advanced stages of developing an effective treatment for Myasthenia Gravis (MG).

MG is a chronic and debilitating disease, which affects about 100,000 people worldwide, characterized by muscle weakness especially inability to open one's eyes, and hand and leg muscle problems. The body's immune system attacks acetylcholine receptors at

the neuromuscular junction, interfering with normal muscular function. In severe cases the disease can involve the respiratory muscles, causing potentially life-threatening respiratory failure.

Ester Neurosciences, based in Herzliya, has recently completed a successful Phase Ib trial for its drug Monarsen - an orally-administered anti-sense therapy for the neurological disease. As a result, The U.S. Food and Drug Administration have granted Orphan Drug Designation status for Monarsen, (formerly known as EN101).

"Obtaining orphan drug designation marks an important step in our regulatory strategy for Monarsen," said Dr. Eli Hazum, CEO of Ester Neurosciences. "Current MG treatments which include anti-cholinesterases, steroids and immunosuppressants, offer limited efficacy and often cause unpleasant and sometimes dangerous side effects. Monarsen offers the prospect of an efficacious and safe product that can address a very large market," added Hazum.

Orphan drug designation is granted by the FDA for treatments that might provide significant benefit to patients with serious, life-threatening diseases that affect less than 200,000 persons in the United States. The Orphan Drug Act was created by Congress to provide assistance and incentives for sponsors to develop drugs judged to be of potential benefit for a qualifying disease.

Orphan Drug Designation status gives Ester, upon marketing approval, the exclusive right to market a drug of this kind for MG in the US for seven years. In addition to marketing exclusivity, the advantages of the designation include eligibility for research grants to conduct clinical trials, certain tax benefits, and an exemption from certain user fees at the time of submission for marketing approval of a new drug application. A similar Orphan Drug application has been made to European regulatory authorities.

The prevalence of myasthenia gravis in the United States is estimated at 14/100,000 population, approximately 36,000 cases in the United States. However, myasthenia gravis is probably under diagnosed and the prevalence is

probably higher. Previous studies showed that women are more often affected than men. The most common age at onset is the second and third decades in women and the seventh and eighth decades in men. As the population ages, the average age at onset has increased correspondingly, and now males are more often affected than females, and the onset of symptoms is usually after age 50.

Ester's Phase Ib results for Monarsen were presented at a special session of the National Academy of Neurology earlier this year. The breakthrough study was the first demonstration of the safe and effective use of an orally-administered anti-sense therapy for a neurological disease.

This study, where sixteen patients received oral liquid Monarsen, demonstrated significant improvement in MG symptom severity, with no cholinergic effects, nor significant adverse events. Fourteen out of sixteen patients had better scores on the Quantitative Myasthenia Gravis (QMG) scale on the last day of dosing as compared to the initial baseline. Improvement of total QMG score for these days ranged from 27.8% to 53.4% (p less than 0.01). The Phase Ib trial results showed that Monarsen appears to have superior efficacy, longer duration of action and a more favorable side effects profile than currently used medications. Patient recruitment for extended clinical trials with Monarsen is underway.

Neurologist Jon Sussman, lead investigator at the Greater Manchester Neuroscience Centre, a UK trial site told Bio World, "We were very impressed with the striking improvement in the condition of our patients. Monarsen even enabled some patients with limited mobility to regain their ability to stand and to walk without aids."

The current means for treating MG is mainly a drug called Mestinon. While Mestinon is effective it deals only with symptoms of the disease and it has a short span of effectiveness. Mestinon works for only about two hours which means it must be administered up to six

times a day. It also has side effects such as diarrhea.

Monarsen on the other hand, is an antisense drug and works completely differently. Antisense technology was first developed about 10 years ago but first generation drugs started coming out only about four years ago. Monarsen is a third generation antisense drug and the first able to be administered orally instead of injected into the vein.

Antisense drugs have better penetration of the blood-brain barrier which many conventional drugs find difficult to cross. Thanks to its antisense technology, Monarsen need be administered only once a day, is more effective than Mestinon and has no known side effects.

According to Hazum, the same technology used in Monarsen can eventually be used to treat much more widespread diseases like Alzheimers and Multiple Sclerosis (MS). The company chose to target MG at first, because in US, drug markets of less than 100,000 potential patients, companies get exclusivity and the approval time is faster.

In addition, Alzheimers and MS are more complicated diseases which require testing on thousands of patients requiring tens of millions of dollars. In addition, approval takes longer - in this case up to three years more. Ester decided to initially target their concept on treating MG and then eventually partner with bigger companies for Alzheimers and other more widespread diseases.

"The next step is the Phase II study which we're preparing for, in which we'll compare head to head the efficiency of Monarsen versus Mestinon. The studies will likely be held in the U.S. and Europe beginning at the end of the first quarter of 2004," Hazum told ISRAEL21c. According to Hazum, if testing continues to go well in the second and third phases the drug could be ready for market in 2005.

Monarsen is based on pioneering research carried out by Prof. Hermona Soreq of the Hebrew University. Ester Neurosciences was established in 1997 by Medica Venture Partners, to commercialize discoveries pioneered by

Soreq, who is the company's Chief Scientific Advisor.

Source: ISRAEL21c staff, 12/04/03

Diagnosing Myasthenia Gravis

The final diagnosis of Myasthenia Gravis may take one or two years and sometimes longer from initial complaints. Because weakness is a common symptom of many other disorders, the process often becomes one of excluding other conditions, especially in individuals who experience mild weakness or in those whose weakness is restricted to only a few muscles.

The process of diagnosis includes a review of medical history and physical and neurological examinations. The signs a physician looks for are evidence of eye movement or weakness without any impairment of feeling of loss of tendon reflexes. As a general rule, a firm diagnosis is based upon a characteristic history and physical examination, and two positive diagnostic tests, preferably serological (blood) and electro-diagnostic.

Anti-AChR Antibody Test

This is a blood test that measures the level of the acetylcholine receptor antibodies that are often found in patients with autoimmune MG. These antibodies attack receptors for the neurotransmitter acetylcholine, which in the body, sends signals from nerves to the voluntary muscles. The antibody prevents adequate reception of the signal at the muscle and results in muscle weakness.

Patients negative for this test, but suspected of having myasthenia on clinical grounds, should be tested for antibodies for other determinants of muscle weakness, as they may have antibodies to other neuromuscular junction antigens.

Anti-AChR antibodies occur in:
Adults with generalized MG: 85 to 90%
Childhood MG: 50%
Ocular MG: 50% to 70%

MuSK Test

If the Anti-AChR test is negative, but there is reason to suspect Myasthenia Gravis, a recent test has been developed that tests for Muscle Specific Tyrosine Kinase (MuSK) antibodies. About half the generalized MG cases that test

negative for AChR antibodies will test positive on the MuSK test (and defines Seronegative Myasthenia). At this time only one commercial company and several hospitals can offer the test in the United States.

Tensilon Test

A short acting anticholinesterase drug (edrophonium) is given to the patient in the form of an injection into the vein. Initially, usually 2 mg is administered. If no clear response is observed in 2 minutes, up to an additional 8 mg is administered. In the patient with MG, this may result in a temporary increase in muscle strength. The effects of the drug are often evident within 30 to 45 seconds and are short lasting. Strength returns to pre-testing status usually within 5 minutes. This drug is often administered as a double blind study.

Repetitive Nerve Stimulation

The nerve to be studied is electrically stimulated six to ten times at 2 or 3 hertz. The compound muscle action potential (CMAP) is recorded with surface electrodes over muscle. In normal muscles there is no change in amplitude, but in myasthenia gravis there is a progressive decline with the first 4 to 5 stimuli. For the test to be positive there should be at least 10% reduction in amplitude. **This test will be positive in approximately 75% of patients with generalized MG, but only about 50% of those with ocular MG.**

Single Fiber EMG (electromyography)

This is a test in which small needle electrodes are inserted into a muscle to record the function of muscle fibers. This test simultaneously records potentials of two muscle fibers innervated by an individual axon. The variability is recorded as "jitter", which is increased in Myasthenia Gravis. The test is about 95% positive in generalized myasthenia, but not specific for myasthenia and requires significant expertise by the administering physician.

(Source: *Upstate New York Chapter, MGFA, Vol. 1, Issue 2, Jan. 2004*)

Book Bytes: An Indispensable Booklet

AARDA has just announced the availability of an important booklet,

"Autoimmune Diseases – The Enemy From Within" by Dr. Yehuda Shoenfeld and Gisele Zandman-Goddard. It is published by Bio-Rad Laboratories, 2003, www.bio-rad.com.

Only 82 pages in length, it still provides the reader with a very comprehensive picture of autoimmunity from how the immune system works (fascinating!) to an explanation of causes and alternative therapies. Of particular interest is his discussion of the "genetic factor" and the relationship to environmental triggers or drugs that may induce autoimmunity.

Dr. Shoenfeld notes that autoimmunity "clusters" in families, although there is some evidence of skipping a generation.

Myasthenia is briefly discussed as a "very interesting disease". He points out the dangers of MG in the mother during pregnancy: thrombocytopenia, shortage of platelets in the newborn – or neonatal myasthenia in the baby that could paralyze the child's respiratory muscles requiring artificial respiration and/or other medical interventions. So forewarned is forewarned!

Profiles of 11 of the more evident diseases are profiled demonstrating a wide spectrum of disorders from those that attack at the cellular level (hemolytic anemia) to those that affect the central nervous system (multiple sclerosis).

Both old and new treatment therapies are reviewed, some of which may have definite promise for MG patients. These include not only steroids and immunoglobulin (IVIG) and Plasmapheresis, and still newer ones like "Oral Tolerance", "Molecular Targeted Therapy" and "Stem Cell Transplantation."

This is an indispensable, "handy-dandy" guide to understanding MG and its place in the family of autoimmune diseases. **Copies can be ordered directly from AARDA at 586/776-3900 or aarda.org. Cost is a pittance - \$7.00 plus shipping for a very valuable "must read" book.**

Reviewed by Joe Powers

If you see someone who needs a smile, give them one of yours!