

# THE VIRGINIAN

## SERVING VIRGINIA & WEST VIRGINIA

### VIRGINIA CHAPTER NEWSLETTER

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### FROM THE PRESIDENT

#### Joe Powers

Because of its importance to the Myasthenia community, we are reprinting the lead article from INFOCUS, AARDA's June newsletter, instead of our "editorial". A real milestone has been achieved by AARDA (The American Autoimmune Related Diseases Association) and the National Coalition of Autoimmune Patient Groups (NCAPG) by succeeding in obtaining bipartisan support for a Congressional Resolution that explicitly calls for NIH to fund the Autoimmune (and Myasthenia) Research Plan.

Stan Finger, Virginia Ladd, and Kathy Hammitt of AARDA/NCAPG all deserve a really big round of applause for their efforts on our behalf. And, our Virginia Chapter members who contributed towards this effort also deserve a "pat on the back". Now we need you to continue that support by writing to your Congressional representative and letting them know how important this funding for autoimmune/myasthenia research is to you and your family. We've included a sample letter on the inside cover. The addresses of your Congressional representatives were listed in a previous issue (Spring 2003), but may also be found at [www.aarda.org](http://www.aarda.org) or call 800/728-4405 and Phyllis will help you.

As a footnote to the following INFOCUS article, it should be noted that a convergence of events now provides the MG/Autoimmune community with a unique – and critical – opportunity to possibly "jump start" needed funding for the Autoimmune Plan. Those events are:

- First, the introduction of House Resolution 610 that specifically calls for an increase in the level

of appropriations – funding – needed to implement the Plan.

- Secondly, with great good fortune, Dr. Noel Rose, M.D., Ph.D. has been selected by NIH to lead the "Autoimmune Disease Coordinating Committee". This is an outstanding selection. Dr. Rose is now Director of the Autoimmune Research Center at Johns Hopkins University, and has been Chairman of AARDA's National Scientific Advisory Board. (Note the following article by Dr. Rose).
- Also important is NIH's publication of its "Roadmap to the Future". Authored by Dr. Elias Zerhouni, NIH's Director, the "Roadmap" outlines nearly 30 different initiatives including Interdisciplinary Research, Technology, and Training. The Autoimmune Plan is a perfect opportunity for NIH to demonstrate the effectiveness of an interdisciplinary approach to finding improved therapies to chronic illnesses involving autoimmunity. Note "Science", 3 Oct. 03 or [www.sciencemag.org](http://www.sciencemag.org) for a further description of the Roadmap.
- Lastly, NIH must shortly report back to Congress as required by the original authorizing legislation on progress being made with respect to autoimmune research. Hopefully the "update: will not be merely a restatement and inventory of previously cited, on-going projects, but will describe new initiatives, new research tasks, directions, and associated funding.

Now is the time for all of us to pull together like a team. Funding for this research is long overdue and without your help, it won't happen – so make a

difference. Join the team and make it happen!

### Congressional resolution on autoimmune disease introduced A Call for Action!

A Congressional Resolution calling for funding of the National Institutes of Health (NIH) Autoimmune Diseases Research Plan is now official--a cause for celebration, and a call for action, on behalf of all of those who care about making progress on autoimmune disease. Representatives Stephen Lynch (D-MA) and Todd Tiahrt (R-KS) introduced the Resolution this spring, marking a major step forward in rallying support on Capitol Hill for a plan that will make a tremendous difference in the lives of the 14-22 million Americans who suffer from autoimmune disease. House Resolution 610 (H. Res. 610) states that Congress recognizes the importance of funding the NIH research plan.

Why is the research plan, and the Resolution that supports it, so important for all autoimmune disease patients, health care professionals, and researchers? Currently, much less federal funding goes to investigating autoimmune disease than other health issues affecting the same or fewer numbers of people. **The Resolution demonstrates a growing commitment to fund research into autoimmunity; and the more support garnered for it, the better the opportunities for funding.** The NIH plan provides the first-ever comprehensive integrated plan for research on the family of more than 100 autoimmune diseases. **Because autoimmune diseases often overlap and multiple disorders occur in families, the greatest progress will come from examining shared mechanisms in the autoimmune process, from genetics to immunology to environmental influences.** The federal initiative is the culmination of work by a wide range of experts under the auspices of the NIH Autoimmune Diseases Coordinating Committee and

includes input from federal health agencies, patient advocacy groups, medical and scientific experts around the country. It focuses on investigation into the burden, cause, diagnosis, and treatment of autoimmune disease as well as on support for professional education and public awareness.

The American Autoimmune Related Diseases Association and National Coalition of Autoimmune Patient Groups showcased the release of the NIH research plan in 2003 with its first Congressional Briefing on Autoimmune Disease. A second gathering on Capitol Hill this March focused on increasing congressional support. **The more voices that join together to call for support of the Resolution to fund the NIH Autoimmune Diseases Research Plan, the greater the likelihood of an earlier and resounding success for implementation of the plan.**

You can help! Contact your U. S. Representative and request his or her support for the House Resolution 610, sponsored by Reps. Lynch and Tiahrt. You can use e-mail or fax; or, if you prefer regular mail, your letter should be sent to your member's local office, not to Washington, D.C. Always include your name and full home address so that your congressional member knows you are a constituent. You can find your congressional members and their contact information by calling your local library or visiting [www.aarda.org](http://www.aarda.org) and clicking on "Congress Connect." See the sample letter provided. Remember to keep your message brief, state your request clearly, and add a few words about how autoimmune disease impacts your life. **Finally, watch for news of introduction of a similar Resolution in the Senate and be prepared to contact your Senators.**

**Report of the AARDA National  
Scientific Advisory Board  
Chairman Noel R. Rose, M.D., Ph.D.**

The Scientific Advisory Board of AARDA has been involved in many activities. A few general comments on the approach taken by AARDA's SAB may clarify its unique role in helping to lift the burden of autoimmune disease

from the many patients suffering from this group of disorders.

**It is generally recognized that the risk of developing an autoimmune disease is partly inherited. Unlike many other diseases, however, autoimmune disease is not due to a single gene; rather, multiple genes contribute to the overall susceptibility. Also, inheritance often involves not only one particular autoimmune disease but also a number of autoimmune disorders.**

It would be of enormous value if the genetic susceptibility to autoimmune diseases (often referred to as the "autoimmune diathesis") could be better defined. It would allow us for the first time to recognize individuals with heightened risk of later developing disease. This information would give us the opportunity of closely monitoring these individuals and perhaps initiating treatment before the autoimmune disease has had its full destructive effects. As we learn more about the fundamentals of immunologic regulation, it may even be possible to intervene in patients with the highest genetic susceptibility by instituting treatments that will alter their immune system and avoid the disease entirely.

**We also know that many autoimmune diseases are triggered by some environmental factor such as an infection, a drug, a food component, or even an environmental pollutant. Individuals with heightened genetic susceptibility may be isolated from these environmental factors and avoid the disease entirely.** Our success in overcoming the devastating effects of rheumatic heart disease in children testifies to the successful approach of prevention. In this case, we use continued treatment with antibiotics to avoid repeated streptococcal infection in children who are susceptible to rheumatic fever. Similarly, patients with celiac disease, an autoimmune disease, can be successfully treated by avoiding gluten in their diet.

**With these considerations in mind, AARDA and the Scientific Advisory Board are making special efforts to unravel the complex genetic basis of autoimmune disease. Scientists face a number of unique problems in this**

**type of study. First, the number of genes involved in autoimmune disease appears to be quite large, many more than in the simpler genetic diseases like hemophilia. The genes, in addition, heighten susceptibility to a number of autoimmune diseases rather than to a particular one.**

Special attention should be paid to the genes that relate to a number of autoimmune diseases, and therefore a premium is based on families where multiple diseases occur. These problems mean that rather large numbers of patients must be studied in order to obtain reliable genetic data. No single medical institution has enough patients with any particular disease to carry out the study. Therefore, a nationwide program is necessary.

With a great deal of urging from AARDA, the National Institutes of Health has undertaken to support a coordinated study of multiple autoimmune disease genetics. This project takes advantage of the newest knowledge and methods made available through the international human genome project.

The question then arises of where to find families with multiple autoimmune diseases. Here AARDA has stepped forth to provide essential information for pursuing this important project. It is a dramatic illustration of the value of an organization like AARDA that focuses broadly on the multiple autoimmune diseases in an effort to find the common traits that underline these devastating and often life threatening disorders.

(Note: If there are instances of multiple autoimmune diseases in your family, past or present, contact AARDA at 586/776-3900 or email at [aarda@aarda.org](mailto:aarda@aarda.org). Examples of autoimmune diseases would include MG, Lupus, Multiple Sclerosis, Rheumatoid Arthritis, Type I or Juvenile Diabetes, Inflammatory Bowel Disease, Sjogrens Syndrome, Myositis, Vasculitis – and nearly 90 others!)

**From the Program Director  
Phyllis Birckhead**

**Fall Campaigns:** Soon the Community Health Charities of VA (CHC) will begin their fall campaigns in your workplace. The local United Way

campaigns will also begin throughout the state.

**All of the CHC of VA campaigns should have us clearly listed in their brochure. Our designation code is #6037.**

**For the CHC of the National Capital Area, our designation code is #6004, and again, we should be clearly listed in their brochures.**

The United Way campaigns may work a little differently. In some of them, we will be listed in the "Local Agencies" under "Unaffiliated Organizations". In others, we may not be listed at all. **Please note that you may "write-in" your favorite charity if we are not listed.** Most United Way in Virginia honors these "write-in" designations. This alternative is not always fully disclosed by campaign assistants, but you will be permitted to exercise your choice if you are willing to insist. **You should write in Myasthenia Gravis Foundation, 6037, and add Virginia Chapter and our mailing address** United Way extracts a fee for this service, but it is a way for you to support our Chapter via your workplace campaign.

Please feel free to call me at 1-800-728-4405 or email [pma8n@adelphia.net](mailto:pma8n@adelphia.net) if you have any questions on how we may be listed in these campaigns.

**And, of course, you can always contribute directly to our Chapter by sending your tax deductible contribution to: Dan Marsh, Treasurer, VA Chapter, MGFA, 5552 Oliver Lane, Broad Run, VA 20137-1934.**

#### **Northern Virginia Support Group:**

The Support Group in Northern Virginia led by **Anita Steele** has set the dates and times for their upcoming meetings. Meetings have been scheduled for August 28, 10 am-2 pm; December 11, 1-3 pm; March 26, 2-4 pm; and June 4, 1-3 pm. Meetings are held at Community Room of the Manassas Central Community Library, 8601 Mathis Avenue (1 block West of Route 28, South of Manassas Dr.). **For information, please contact Phyllis Birkhead at 800/728-4405 or by email at [pma8n@adelphia.net](mailto:pma8n@adelphia.net).**

#### **MG Clinical Trial Set for CellCept**

Aspreva Pharmaceuticals, in partnership with F. Hoffmann-La Roche, has announced the initiation of a global phase III study of CellCept (mycophenolate mofetil) for myasthenia.

This randomized, placebo controlled clinical trial is to fully investigate the efficacy and safety of CellCept for MG patients. **No new medications for this condition have been approved since 1955.**

The CellCept MG trial, which has received health authority approval in the US, Canada and the UK, will ultimately recruit 136 patients at 22 sites in five countries. Local ethics committee approvals are pending. **Results of the study are expected in 2006.**

This study is designed to achieve regulatory approval for existing drugs for less common, often neglected conditions. Last year Aspreva announced it had acquired the rights from Roche to develop the transplant medication CellCept for all autoimmune conditions.

Physicians managing patients with less common diseases often have little or no hard clinical evidence on which to base their treatment decisions, and often have to rely on anecdotal information. Aspreva's clinical trials programs will enhance the evidence base, and will increase the availability of important medications for these patients.

#### **Current therapies for MG include:**

- Short-acting agents, such as cholinesterase inhibitors, intravenous IgG and plasma exchange. These treatments do not offer sustained symptom control or long-term remission.
- Thymectomy, surgical removal of the thymus, which can sometimes offer complete remission in a subset of young patients.
- long-term immunosuppression, which is the main-stay of current treatment.

Corticosteroids are used almost universally, along with other agents to spare steroids, such as azathioprine and cyclosporine. The damage to

the acetylcholine receptors by the auto-reactive antibodies is completely reversible if the autoimmune process can be controlled, but many patients can not achieve optimal disease control at a safe steroid dose.

**There are no approved treatments for MG with the exception of cholinesterase inhibitors. Urgently needed are new treatments that offer faster onset of action, better disease control, and superior steroid tapering with a more favorable safety profile.**

Professor of Neurology and MG clinician and researcher at Duke University Dr Donald Sanders commented: **'Patients with MG often have to sacrifice disease control in order to reduce the side effects of their treatment. The Aspreva study is of particular interest as it should allow us to see if CellCept will enable reduced reliance on steroids while maintaining effective disease control. This trial will provide the hard clinical evidence we need to make the best treatment decisions for our patients. Based on published reports, largely uncontrolled, it is highly probable that a well-designed study of MMF, such as this, will demonstrate efficacy.'**

The Myasthenia Gravis Foundation of America has welcomed the study. Chairperson Esther Land said, "This is the first phase III study of a new medication for Myasthenia Gravis for 49 years. It is so exciting for us that a company like Roche, through their partnership with Aspreva, is paying attention to the needs of MG patients. Increased disease control with reduced drug toxicity is an important goal for the MG Foundation. We await the outcome with interest."

CellCept is also currently being investigated for the treatment of a number of other neurological autoimmune conditions including multiple sclerosis.

#### **Congratulations To U.Va. Medical Center**

The University of Virginia Medical Center is again ranked among "America's Best Hospitals" by U.S. News and World Report. The July 12<sup>th</sup>

issue cited 10 of U.Va.'s Departments among the top 50 in the country. The Neurology and Neurosurgery Departments, of which Drs. Lawrence Phillips and Vern Juels, (members of our Medical Advisors Board) are members, were ranked 37<sup>th</sup> in the country. Over 6000 hospitals in the U.S. were considered – only 117 were singled out. Inova Fairfax Hospital in Northern Virginia was cited with 7 departments and Norfolk General had one department also honored. Congratulations to one and all!

### **New-Found Antibodies May Offer Hope For People With Autoimmune Disease**

Autoimmune diseases are “friendly-fire” disorders in which the body’s immune system mistakenly identifies cells or tissue as “foreign” and attacks them. Among these serious ailments are rheumatoid arthritis (RA), multiple sclerosis, **myasthenia gravis**, and Crohn’s disease. Now Dr. Nathan Karin and colleagues in the Technion Israel Institute of Technology’s immunology department have discovered that the body possesses a second set of beneficial antibodies that suppress the activity of the self-destructive ones. Furthermore, using genetic manipulation, they were able to boost the restraining activity of the beneficial antibodies.

Their work was published as the lead article in the November 03 issue of *Immunology*. Based on these findings, Karin has developed a novel platform for the development of new therapies, and has applied for a patent.

A properly working immune system is able to recognize an autoimmune attack. In response, it activates the beneficial antibodies that suppress the self-destructive immunity. But if the immune system is not working properly, the beneficial antibodies are not activated, allowing the self-destructive ones to run their damaging course.

**In trials on animals with induced RA, the researchers were able to expand the number of beneficial antibodies, which resulted in a marked suppression of the autoimmune disease; eliminating the**

### **beneficial antibodies hastened the progress of the disease.**

Most importantly, the researchers were then able to verify this process in a double blind clinical study. The study consisted of 22 patients suffering from RA, a control group of 10 with osteoarthritis (which is not an autoimmune disease), and another control group of 12 healthy patients. More than 70% of the RA patients had beneficial antibodies, which shows their systems were fighting the disease.

By contrast, none of the healthy and none of the osteoarthritis patients possessed any beneficial antibodies, presumably because they had no need for them.

**These findings will likely lead to two complementary therapies: the first will be drugs consisting of novel antibodies that will assist the beneficial antibodies. The second will be vaccines to boost the autoimmune system’s beneficial antibodies.**

*AMPS: Quest Jan-Feb, 2004*

### **Merrimack Pharmaceuticals Inc. Initiates Phase 1 Study of Immunomodulator, MM-093**

*Cambridge, MA, July/03, PRNewswire*

Merrimack Pharmaceuticals, Inc. today announced the initiation of a Phase 1 study for its immunomodulatory drug candidate, MM-093, a recombinant version of human alpha-fetoprotein (AFP).

The double blind, placebo-controlled Phase 1 study will take place at the Guy’s Drug Research Unit of Guy’s and St. Thomas Hospital in London. The study will examine the safety, toxicology and pharmacokinetic profile of MM-093 in healthy volunteers. The first part of the trial will study the effects of MM-093 after a single administration and the second part will evaluate the effects of MM-093 administered several times over a 28 day period. Both parts of the study will evaluate the administration of several different dose levels of MM-093.

“We are pleased to have advanced MM-093 into human clinical trials,” said Mr. Robert Mulroy, President and CEO of Merrimack. “Our goal is to build a substantial base of safety data to

enable our transition into patient trials in a number of autoimmune indications.”

The development of MM-093 will be focused on autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and **myasthenia gravis** – areas in which published and proprietary pre-clinical data provide a compelling rationale for its use, and in which significant unmet medical needs still exist.

For additional information please visit:

<http://www.merrimackpharma.com>

### **Immunosuppressant May Allow Reduced Steroids in MG**

The potent immunosuppressant drug Cyclophosphamide (brand names Cytoxan and Neosar), intravenously given for short bursts (two hours time) may allow people with severe MG to control their disease symptoms without high doses of corticosteroids, such as Prednisone. The findings are from a study conducted at Hospital Maria Ferrer in Buenos Aires, Argentina, and are published in the July issue of *Muscle & Nerve*.

Nestor Mofino and colleagues looked at 23 people with MG whose disease was either poorly controlled or who had developed serious corticosteroid-related side effects and gave them intravenous cyclophosphamide or placebo (inert substance with no expected effect).

After the year long study period, five subjects on cyclophosphamide were off corticosteroids, whereas no subject on placebo was. Four cyclophosphamide treated participants were off steroids three years after completing the trial.

For those on the study drug, strength improved and no significant increase in drug-related side effects occurred. However, one person developed bladder cancer two years after the study, which the investigators say may have been related to the drug.

The authors say the results support the view that pulsed-dose cyclophosphamide can be considered an effective, relatively safe, and inexpensive alternative in MG. **They caution that long-term follow-up of patients is necessary to detect any possible late-developing problems such as cancer.**

Source: *AMPS: Quest Magazine and The MG Flash (Garden State Chapter)*

### MED NOTES

#### Review Suggests Heart Checks in MG

People with myasthenia gravis (MG), a disease in which the immune system attacks the part of each muscle fiber that receives nerve signals, aren't usually told they're at risk for heart disease.

But researchers at the Cooper Hospital/University Medical Center of the Robert Wood Johnson Medical School in Camden, NJ, say they recommend that physicians set a "low threshold for pursuing cardiac investigations in patients with MG with unexplained fatigue or exercise intolerance, especially if disproportionate to other signs of MG."

**In a comprehensive review of some 60 studies of MG and heart abnormalities conducted since the early 20<sup>th</sup> century, the authors found that various types of abnormalities are probably more common in this disease than they are in the general population.**

Maya Guglin and colleagues say that inflammatory heart disease (myocarditis), rhythm disturbances, blocks of conduction signals through the heart, contraction abnormalities, and cardiac disease secondary to respiratory dysfunction have all been noted in people with MG over the years.

They caution that many of the studies were conducted without taking into account the patients' ages and other factors besides their MG that may have contributed to their heart problems. And the diagnostic criteria for MG have changed, meaning some patients may have been included in MG studies in past decades who wouldn't have MG by today's criteria.

Nevertheless, the article, published in the June 2003 issue of the *Journal of Clinical Neuromuscular Disease*, sounds a cautionary note and suggests a need for further investigations to determine the scope and possible causes of heart disease in MG.

*AMPS: Quest Jan-Feb, 2004*

### NUTRI-NUGGETTS

**Vitamin D Requirements:** An NIH Conference reviewed recent surveys that

indicated Americans, particularly women, have low blood levels of Vitamin D – an essential nutrient for strengthening the immune system and for reducing the risk of osteoporosis. As folks age, the body's ability to absorb Vitamin D and calcium is reduced.

Bess Dawson-Hughes, M.D., Chief of the Bone Metabolism Lab at Tufts University reports in their *Health & Nutrition* letter that as the body metabolizes Vitamin D it forms compounds that "enhance the maturation of muscle cells and muscle functioning...perhaps explaining why people in their 70's and older have muscle weakness that make them tire easily and more prone to falls. Vitamin D deficiencies become more common with age.

Weakness occurring from a Vitamin D shortfall is often felt primarily in the legs, manifesting itself as a feeling of heaviness in the lower limbs and difficulty climbing stairs or getting out of a chair." (Note: Could this also be a factor in MG as well?)

Now Dr. Dawson-Hughes is evaluating the impact of Vitamin D deficiencies in all age groups – and in folks who are overweight. Since D is a fat-soluble vitamin, "those with extra fat tissue lose the nutrient to their fat stores rather than have enough of it circulating thru their bloodstream to the body's tissues where it is needed."

Other studies indicate Vitamin D "may also play a beneficial role in combating Inflammatory Bowel Disease (also autoimmune), high blood pressure, heart disease, some cancers, and diabetes."

In 1997, the Institute of Medicine (IOM) set the following Vitamin D requirements:

Up to age 50 – 200 IU

Age 51-70 – 400 IU

Over age 70 – 600 IU

That requirement is now being challenged by scientists, Connie Weaver, Ph.D. at Purdue University and Bess Dawson-Hughes, M.D., Director of the Bone Metabolism Laboratory at Tufts University. Their concern was further endorsed by Dr. Robert P. Heaney, M.D., Professor of Medicine at Creighton University. Consequently, the

IOM is considering increasing the daily requirement as high as 1000 IU.

Vitamin D is obtained from exposure to sunlight and from our diet – primarily fatty fish, especially salmon, sardines and herring, as well as egg yolks and organ meats – all of which are not usually high on the menu – and have lots of cholesterol. Consequently, vitamin supplements and foods fortified with Vitamin D (milk, orange juice and some cereals) are ways to increase your D intake. But a daily 10-15 minute walk in the sunlight will also help - and complement your exercise program!

*(Source: Cornell University, Weil Medical College, "Food & Fitness Advisor", Jan. 04) (Also, Tufts University, Health & Nutrition Letter, Summer 04)*

### Swallowing Made Easier

MG patients who may have difficulty swallowing might try a cup of "light" yogurt mixed with crushed fruit – berries, bananas or applesauce. If you have a blender, add peaches or even melon. For an extra dose of "good stuff" try a "scant" (1/2) teaspoon per cup of soy powder that provides calcium, phosphorus and protein. Twenty-five grams, or less than 1/3 of a cup of soy, will give you 50% of your daily protein requirements – and can be included in soups or "smoothies" as well. A "scant" teaspoon of soy or flax powder may also be included in yogurt, soups, smoothies, or cereal with milk and even cottage cheese. Some flax (FiProFlax – an organic blend available from health food stores) supplies not only fiber and protein but Omega 3 fatty acids. An extension of the fruit and yogurt mixture with added orange juice provides a near instant "smoothie" with lots of Vitamin C and D – and quick energy!

### *Final Thoughts*

*It's better to give others a piece of your heart than a piece of your mind.*

*The human spirit can gain new hope from an encouraging word.*