



## *M.S. Circle of Friends*

Dedicated to providing a resource of friendship, information and help for those affected by Multiple Sclerosis.

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# M.S. Circle of Friends Journal

November/December 2008

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## **World Congress on Multiple Sclerosis: Researchers Report on MS from Around the World**

On September 17<sup>th</sup> – 20<sup>th</sup>, nearly 5,200 clinicians, clinical researchers and basic scientists from around the world gathered in Montreal, Quebec, to kick off the first World Congress on Treatment and Research in Multiple Sclerosis. This was the largest international conference on MS research and treatment in conducted in 2008. The four days of the World Congress offered an impressive glimpse into the fast-moving progress being made by investigators around the world, in many different fields, toward better treatments and quality of life, prevention and a cure for multiple sclerosis, including:

- new data on repairing MS damage
- new therapeutic approaches to treating MS
- new insight into cognitive problems
- reports on pediatric MS

A summary highlighting some of the presentations from the conference begins on page 10.

### **Table of Contents**

Calendar of Events	2
Humor	3
News and Tidbits	4
My Confession	8
Quizmaster Jim	9
World Congress Report	10
Search-A-Word	19
What Would You Do, If?	20
Puzzle Answers	22

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The *M.S. Circle of Friends Journal* is published every quarter, four times per year. To subscribe, please contact us at (352) 367-9660 or send an email request to: [subscribe@mcircleoffriends.us](mailto:subscribe@mcircleoffriends.us)

## Calendar of Events

### The MS Circle of Friends F.R.O.G.S. Group, Gainesville, FL

**November meeting:** Monday, November 24<sup>th</sup>, 6:00 – 8:00pm.  
Location: Trinity United Methodist Church  
4000 NW 53<sup>rd</sup> Avenue

**Holiday party:** Date and location to be announced.

**January '09 meeting:** Monday, January 26<sup>th</sup>, 6:00 – 8:00pm.  
Location: Trinity UMC

**February '09 meeting:** Monday, February 23<sup>rd</sup>, 6:00 – 8:00pm.  
Location: Trinity UMC

\*\*For more information or to RSVP, please contact Sarah Maurer at (352) 367-9660 or [maurerlady@yahoo.com](mailto:maurerlady@yahoo.com).

### National Multiple Sclerosis Society, North Florida Chapter

Teleconference Series (all begin at 7:30p.m. EST)

12/9/08 – Spirituality

1/13/09 – Diet and MS: The Nutrition Connection

2/10/09 – Relationships Matter

Live Events

**--Gainesville, FL: MS exercise class, 2<sup>nd</sup> & 3<sup>rd</sup> Mondays and every Thursday at 6:00pm, at Gainesville Physical Therapy. For more info, contact Toni Chiara at [toni.chiara5@gmail.com](mailto:toni.chiara5@gmail.com)**

12/4/08 – Gainesville Annual Awards Ceremony, 5:30pm

**\*For more info, call 1-800-FIGHT-MS or visit [www.nationalmssociety.org/fln](http://www.nationalmssociety.org/fln)**

### Multiple Sclerosis Association of America

**\*\*For more information, call 1-800-532-7667 or visit [www.msassociation.org](http://www.msassociation.org)**

### Multiple Sclerosis Foundation

**\*\*For more information, call 1-800-MSFOCUS or visit [www.msfocus.org](http://www.msfocus.org)**

### HealthTalk Programs (Teleconferences/Webcasts)

**\*\* For more information on upcoming programs, visit [www.healthtalk.com/multiplesclerosis/index.cfm](http://www.healthtalk.com/multiplesclerosis/index.cfm).**

### MS in Balance (MS LifeLines – Rebif)

Webevent Teleconference Calendar (all at 8:00p.m. EST):

11/19/08 – Tips to manage holiday stress

**\*\*For info or to register: 1-800-350-5416, [www.MSLifeLines.com](http://www.MSLifeLines.com)**

**Shared Solutions (Copaxone)***Teleconferences:*

Managing MS as Partners, 11/18 @ 8pm ET and 11/19 @ 9pm ET

Update from Shared Solutions, 12/16 @ 8pm ET and 12/17 @ 9pm ET

--No RSVP required for teleconferences. Call 1-800-823-1880 for a reminder call or simply call in on the night of the teleconference.

\*\*For more information, call 1-800-887-8100 or visit [www.sharedsolutions.com](http://www.sharedsolutions.com).

**MS Pathways (Betaseron)***Webcast/Teleconference:*

**NEW! The Real World of MS** is a series of free webcasts that provide the opportunity to learn more about multiple sclerosis. It connects people who are living with MS with MS experts who are qualified to answer their questions. Each webcast is available on demand, 24 hours a day, 7 days a week, and is a series recorded in front of a live studio audience of people living with MS.

\*\*For more information call 1-800-788-1467 or visit [www.mspathways.com](http://www.mspathways.com)

**MS Active Source (Avonex)***Tysabri Teleconferences:*

12/4/08 – Just the Facts: The Risks and Benefits of Tysabri

12/11/08 – On the Job: MS at Work

\*\*For more information call 1-866-955-9999 or visit [www.msactivesource.com](http://www.msactivesource.com)

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**A Break For Humor**

A man goes to the supermarket and notices an attractive woman waving at him and saying hello. He's rather taken aback because he can't place where he knows her from. So he says, "Do you know me?"

To which she replies, "I think you're the father of one of my kids."

Now his mind travels back to the only time he has ever been unfaithful to his wife and says, "Oh goodness, are you the stripper from my bachelor party that I made love on the pool table to after too many tequila shots?"

She looks into his eyes and calmly says, "No, I'm your son's teacher."

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## **News and Tidbits**

### **Phase 2 Results Published for Oral Drug BG00012**

10/23/08 - Results of a multicenter, controlled clinical trial of oral BG00012 (dimethyl fumarate, Biogen Idec, Inc) involving 257 people with relapsing-remitting MS have now been published, showing that, compared to inactive placebo, the highest tested dose led to a 69% reduction in active inflammation on MRI scans from weeks 12 to 24. The drug also reduced the number of other types of new or enlarging MRI lesions. No significant difference was seen in relapse rates, but the study was not designed to adequately detect clinical differences. Adverse events included abdominal pain, flushing, headache, fatigue, and feeling hot.

Although its exact mechanism of action is not known, BG00012, an oral fumarate, is thought to inhibit immune cells and molecules and may be protective against damage to the central nervous system.

The study was conducted by Dr. Ludwig Kappos and colleagues, and results are published in the October 25, 2008 issue of *The Lancet* (2008 372:1463-1472). Based on these results, the sponsor is proceeding with two large-scale, Phase 3 clinical trials for RRMS. Participants are being sought for the two trials, known as the DEFINE study and the CONFIRM study.

Source: *National MS Society*,  
[www.nationalmssociety.org](http://www.nationalmssociety.org)

### **Phase 2 Trial Results of Alemtuzumab Published**

10/22/08 - Treatment with alemtuzumab (Genzyme Corporation) reduced the accumulation of disability and the frequency of relapses in people with early relapsing-remitting MS, compared to Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer, Inc.). Alemtuzumab is a humanized monoclonal antibody directed at CD52 (a protein on the surface of immune cells) that is currently approved by the FDA as a single agent for treatment of B-cell chronic lymphocytic leukemia. Its ability to target immune cells has led investigators to test its potential as a treatment for RRMS.

Those taking alemtuzumab had a 74% reduction in the risk of MS relapse compared with those on Rebif, and a 71% reduction in the risk for sustained accumulation of disability. Those on alemtuzumab, an immune-suppressing monoclonal antibody, experienced adverse events more frequently, including immune thrombocytopenic purpura (a serious bleeding disorder), thyroid adverse events, and infections. Drs. D. Alastair Compston, Alasdair J. Coles (University of Cambridge, UK) and colleagues have published the results (*New England Journal of Medicine* 2008 359;17: 30-45), and two Phase 3 trials are currently recruiting participants with relapsing-remitting MS.

Source: *National MS Society*,  
[www.nationalmssociety.org](http://www.nationalmssociety.org)

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### **Teams Report on Key Enzymes Related to MS Progression and Nervous System Repair**

10/16/08 - Two teams of researchers funded by the National MS Society have reported findings on nerve tissue injury and repair that add important information needed to stop MS progression and develop nervous system repair strategies.

#### **Progressive MS and KLK enzymes (Conducted by Isobel Scarisbrick, PhD, Mayo Clinic and Foundation, Rochester, MN and colleagues):**

Understanding the processes that lead to tissue damage in MS is crucial to feed parallel efforts to protect and repair the brain and spinal cord. Dr. Scarisbrick previously found elevated levels of "KLK6" (a newly identified member of the kallikrein enzyme family) in areas of damage found in tissue samples from people with MS. Now, in a follow-up study, the group has studied the levels of KLK6 and other kallikreins in blood samples taken from 35 people with different clinical courses of MS and 62 controls without MS.

The results show that KLK1 and KLK6 were elevated in people with MS, with the highest levels appearing in people with secondary-progressive MS (a course of MS that initially is relapsing-remitting and then becomes progressive, with or without occasional relapses and minor remissions).

The team also exposed nerve cells isolated from mice to KLK1 or KLK6 in the laboratory, and found that the enzymes promoted nerve cell loss. Dr. Scarisbrick is continuing to study the role of these enzymes in nerve fiber

injury and hopes to find a way to target them with therapeutic strategies for people with progressive MS.

#### **Repair and HDAC enzymes (Conducted by Patrizia Casaccia, MD, PhD, Mount Sinai School of Medicine, New York and colleagues):**

MS involves immune attacks against brain and spinal cord tissues, primarily myelin, the insulation that surrounds and protects nerve fibers. Several studies have indicated that, early in the disease, immature myelin-making cells – called, "oligodendrocyte progenitors" – are recruited to generate new myelin. A sufficient number of these cells are needed so that progenitors can migrate to the site of myelin damage and develop into myelin-making cells. Then, genes that instruct the formation of myelin components are activated and myelin is formed. In MS, this process fails. Dr. Casaccia is studying whether some molecules may inhibit the activation of the genes that promote myelin formation.

In this study, Dr. Casaccia's team observed the gene activity during oligodendrocyte development in mice with damaged myelin. They found that enzymes called histone deacetylases (HDACs) were crucial to this process, particularly HDAC1 and HDAC2. Deleting these two enzymes impaired the differentiation of oligodendrocyte progenitors, that is, the process by which these cells develop a more specialized form or function. The team is studying how these findings might be translated into therapeutic strategies.

Source: National MS Society, [www.nationalmssociety.org](http://www.nationalmssociety.org)

### **New Case of PML Confirmed in U.S.**

10/31/08 - A new case of PML, or progressive multifocal leukoencephalopathy, has been confirmed in the U.S., in a patient receiving Tysabri for the treatment of MS.

After 14 treatments, the patient reported a change in health status, and the patient's physician began testing for PML. According to a statement issued by Biogen Idec, the drug's manufacturer, "clinical vigilance led to early identification of signs and symptoms of possible PML and clinical evaluation which included MRI scanning and CSF testing." The patient, who was admitted to the hospital on October 24, underwent plasmapheresis to remove Tysabri from their system and was released from the hospital on October 28. The patient is currently under the care of the treating physician.

PML is a potentially life-threatening condition caused by a common virus (Polyomavirus JC, often called JC virus), which lays dormant in 80-85% of adults, becoming reactivated in immune-compromised patients. Once removed from the market for this risk, Tysabri now carries a "black box" warning — the FDA's highest warning level — about PML risk. Since Tysabri's reintroduction to the market in 2006, patients receiving Tysabri have been required to participate in the TOUCH prescribing program, which includes careful monitoring for potential symptoms of PML. This is the third such case in the two years since the drug's reintroduction.

No changes to the Tysabri label, which warns of PML as a risk, are planned at this time. Patients taking Tysabri are encouraged to talk to their doctors about any questions they may have. Information also is available at MS Active Source, 1-800-456-2255.

Source: MS Foundation, [www.msfocus.org](http://www.msfocus.org)

### **Investigators Find No Overall Link Between Hepatitis B Vaccine and MS**

10/2/08 - A study evaluating the potential that hepatitis B vaccination increases the risk of developing MS found no general increase in risk from exposure to the vaccine. However, the investigators did find a possible hint that a specific brand of the vaccine may increase the risk of MS, but that finding requires confirmation. The study, led by Yann Mikaeloff, MD, PhD (Assistance Publique-Hôpitaux de Paris, INSERM), evaluated vaccination records of 349 children in France who had experienced a neurologic episode. Most previous studies have found no link between MS and hepatitis B vaccine, which can prevent serious health problems associated with hepatitis B virus infection. The study will appear in the journal *Neurology*.

Source: MS Foundation, [www.msfocus.org](http://www.msfocus.org)

### **Phase IIB Trial Results for Tovaxin**

10/31/08 - Phase IIB trial results for Tovaxin showed that people with early relapsing-remitting MS (RRMS) taking the investigational anti-T cell therapeutic vaccine had an improvement in brain atrophy, demonstrated less reactivity to T cells

and experienced fewer relapses, as compared to placebo. The trial also met its primary endpoint of reducing the number of gadolinium-enhanced brain lesions seen on MRI.

An analysis of the trial results showed that 28.1 percent of 100 people treated with Tovaxin showed an improvement on the Expanded Disability Status Scale, compared to 5.6 percent of 50 people in the placebo group. Those taking Tovaxin also showed an 88 percent reduction in the level of brain atrophy and a 55 percent reduction in the annualized rate of relapse.

No serious side effects were reported. Mild injection site reactions were experienced by some.

Tovaxin is a subcutaneous injection that uses a person's own T cells and uses them to manipulate an immune response. It has a dual mechanism of action. The first involves the depletion of myelin-reactive T cells in the peripheral blood. The second regulates anti-inflammatory T cells to rebalance the immune system of a person with MS, according to Opexa Therapeutics, which is developing the drug.

For more information, visit <http://www.opexatherapeutics.com>.

Source: MS Foundation, [www.msfocus.org](http://www.msfocus.org)

### **Bayer HealthCare Pharmaceuticals Launching New Needle for Betaseron**

9/24/08 - Bayer HealthCare Pharmaceuticals Inc. will be launching a new 30-gauge needle (the same size used for insulin and pediatric injections) and new optional autoinjector (BETAJECT® LITE) at the end of

October. The new autoinjector will replace all previous autoinjectors; use of any autoinjector other than this latest version may result in people not receiving their full dose of medication. People who are currently taking Betaseron can log onto [www.betaseron.com/thinner](http://www.betaseron.com/thinner) or call BETAPLUS at 1-800-788-1467 for more information about the new needle and to request the new autoinjector.

Source: MS Foundation,  
[www.msfocus.org](http://www.msfocus.org)

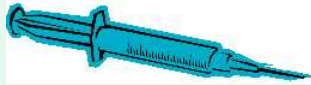
### **Kick the Habit to Help in the Fight Against MS**

Smoking and MS do not mix. Some studies have shown that lighting up can increase the risk of MS and hasten progression in people already diagnosed with the disease. It can also complicate breathing problems caused by MS and worsen fatigue.

The CDC offers these tips on quitting:

- Quit completely, don't just cut back. Smoking even a few cigarettes a day can be harmful and low nicotine options may just cause you to puff harder, longer and more often.
- Write about quitting. Give yourself a reminder about why you want to stop smoking.
- Realize it won't be easy. Most smokers go through nicotine withdrawal. It may take as long as a month to get over those feelings.

Get help. Call 1-800-QUIT-NOW or find more information on quitting as well as guides and factsheets at [www.cdc.gov](http://www.cdc.gov).



## **Confessions of a Poke-A-Holic**

By Sarah Maurer

It is well known that the available disease-modifying medications for Multiple Sclerosis are taken by injection. (The exceptions are Novantrone and Tysabri, which are administered by intravenous infusion.) For those of us on a CRAB medication (Copaxone, Rebif, Avonex and Betaseron), the poke of the needle is something we must grimace and accept in our fight against MS.

In addition to receiving a diagnosis of MS, learning that a regular injection routine would become a part of life was certainly a big shock to me, as I'm sure it was for many other people that also been diagnosed with MS. I know that I initially rejected having to do an injection, whether it would be once a week, every day, or something in between. However hard it was to become accustomed to the self-injection, I managed to accomplish it. I believe that my journey has been better for getting on and staying on a disease-modifying medication.

Many people with MS are holding out hope for the day when an oral medication becomes available. It seems that this subject has inevitably come up at almost every MS educational program I have attended. "How long until one is available?" or "Why is it taking so long?" are some of the inquiries I've heard. The general consensus seems to be that we may have an oral medication available within the next ten years.

Why am I bringing this subject up, you may be wondering. I have a confession to make. Although I understand the immense desire that a lot of people have for an oral medication, I am hesitant to get excited about this option.

I have some good reasons for feeling this way. At least, in my own mind, these reasons seem rational. The most important is that I am admittedly inadequate when it comes to remembering to take anything orally. I don't have an aversion to swallowing a pill or anything to that effect. For some reason, I have always just been too forgetful, as is the case when it comes to taking my daily vitamin. Perhaps my inability to adhere to a daily pill regimen, and the fact that I find pills almost too easy to take, at least when compared to an injection, is why I have doubts about whether an oral medication would be best for me.

I know that there are things I can do to remember to take my daily vitamin. I keep the vitamins next to my coffee pot, since this is the first place I go upon waking up each morning. This hasn't worked very well. I make it a point never to put the vitamins away, in a cabinet, believing that if they are "out of sight", they will be "out of mind." Despite this, my consistency for taking the vitamins is still not 100%. Somehow I manage to defy all my careful planning and strategizing.

To me, taking a pill is not a big deal. I swallow the pill, with some water, and I'm done. My daily injection, on the other hand, is something I never forget. Trust me, I know whether or not I have poked myself yet on any given day. I feel the injection, in a way that I never would by taking a daily pill, and therefore I always know I have indeed done what I can to help fight my MS that day.

I don't have a lot of faith in my ability to organize my own mind enough to take a vitamin on a daily basis. I am afraid I will fail miserably should my disease-modifying medication be switched to an oral form. Although this is the main reason I have for being hesitant about an oral medication, it is not the only one.

As I stated previously, I know I have taken my daily injection because the process involved is more intricate. MS became a part of my life silently yet ferociously, causing damage to my central nervous system before I even knew it had moved in. Nor had I even experienced the first symptom of the disease. Taking a pill, or pills, to fight this disease seems, to me, almost too easy.

I have come to appreciate my daily injection. It makes me feel like I am actively fighting my disease. As I insert the needle and push the medication into my body, it is almost as if a warrior's cry escapes from me. "Take that, you MonSter!" I scream, albeit silently. Although administering a daily injection is never the highlight of my day, I fear that not doing the injections anymore will take away that strong warrior feeling that I have come to rely so much upon.

There you have it, my full confession. I know that I could possibly be the only person to feel this way. I truly wish and hope that an oral option for all my wonderful friends and fellow MS'ers will be available very soon. However, please don't think me too strange for not being quite ready for a switch.

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## Quizmaster Jim's Quiz

*Questions 1-5 are multiple choice and 6-9 are in the form of a Jeopardy question. Answers are on the back pg.*

1. How old was the youngest person EVER to have graduated from the Mt. Sinai School of Medicine in New York City? a. 15 b. 16 c. 17 d. 19
2. Which King in a standard deck of playing cards has NO mustache? a. Hearts b. Spades c. Clubs d. Diamonds
3. Where were potato chips invented? a. Saratoga Springs, NY b. Paris, France c. Boise, Idaho d. Chicago, Illinois
4. In what year were toys added to boxes of Cracker Jacks? a. 1893 b. 1901 c. 1912 d. 1921
5. Who was the first American president to have a telephone on his desk? a. Wilson b. Coolidge c. Hoover d. F. Roosevelt
6. PRIME TIME Three word phrase that follows "running" in a Bob Seger song lyric and "walking" in a famous mime routine...
7. SCIENCE From the Latin for "how much", it's an indivisible physical amount...
8. BEVERAGES The "new" formula for this soda was announced on April 23, 1985; the "classic" formula was back within three months...
9. SCIENCE HISTORY It's the simple six-letter name of the journal that published the 1953 paper revealing the structure of DNA...

## **World Congress on Multiple Sclerosis**

Here is a summary of just some of the nearly 1,000 studies presented at the conference.

### **MS and the Mind**

Cognitive and emotional problems are somewhat common in people with MS, and are a major reason why people with MS leave their jobs, or have trouble in social situations or at school. Research on how to identify and treat these problems is increasing worldwide.

- Dr. Audrey Henry (Hôpital Maison Blanche, Reims, France) and colleagues examined whether people with MS had difficulties with "theory of mind" – the ability to attribute beliefs, desires and emotions to others, and distinguish them from one's own beliefs, desires and emotions. A group of 70 people with MS scored significantly lower on six theory of mind tests, and on a test of interpreting others' facial expressions, than 30 controls without MS. Dr. Henry's team believes that people with MS may experience problems with social behavior because of these deficits.
- As imaging technology leaps forward, so does the ability to pinpoint areas where MS damage may be causing cognitive problems. Kyle Kern, BS, and colleagues (University of California, Los Angeles) used high-resolution MRI to study the structure of the hippocampus, a region of the brain that is important in memory processes, in 26 people with RRMS or progressive MS and 19 controls without MS. They took images while people were completing verbal memory tests and found that, unlike controls without MS, people with MS did not show normal activation patterns in the hippocampus during both learning and recall.
- A study using an advanced MRI technique (double inversion recovery) to evaluate the presence of lesions, or damaged areas, in the gray matter parts of the brain (cortex), and their possible association with cognitive problems was described by Massimiliano Calabrese, MD (University of Padova, Italy). The team administered cognitive tests and also evaluated fatigue and depression in 70 people with MS, and compared the results to their images of intracortical lesions. They found that cognitive impairment, but not fatigue or depression, was associated with high volumes of intracortical lesions.
- In a related study, Flavia Nelson, MD (University of Texas Health Science Center, Houston, Texas) and colleagues also showed a link between intracortical lesions and cognitive impairment. These types of lesions are not well detected using conventional MR imaging. More research is needed on the detection, treatment and prevention of cognitive impairment in MS.

### **Seeking Clues to MS**

MS is notoriously unpredictable in its course. Some people experience a benign course of MS, which generally refers to individuals who have had MS for an extended period of time but whose disability continues to be very mild. There currently is no way to predict a benign course, though.

- Emilio Portaccio, MD (University of Florence) and team examined 63 people with benign MS (defined here as having minimal disability after having MS for at least 15 years) and followed them for approximately five additional years. They found that cognitive impairment, male gender, and tissue damage in the cortex were the main predictors that people would progress from benign MS to active disease.

### **Giving Repair a Boost**

The central nervous system has the ability to repair itself, but these capabilities fail in people with MS. Why this happens and how to reverse it is the focus of intense investigation.

- Jin Nakahara, MD, PhD (Keio University, Tokyo) and colleagues studied why immature brain cells that could foster repair fail to do so in MS. The team examined brain tissue from 10 people with MS and five controls obtained via autopsy. Their results show that a molecule called TIP30 may inhibit these cells. This research not only provides a clue that may help to develop repair strategies: It also highlights the value of tissue banks that collect the specimens used in such studies.

### **Atlas of MS**

A major effort has been launched to reach out to people with MS in all corners of the globe, and gather the data necessary to provide the best health care services and form the best health care policies. Alan J. Thompson, MD, FRCP (National Hospital for Neurology and Neurosurgery, London) and colleagues unveiled the Atlas of MS, a joint venture of the World Health Organization and the MS International Federation. The largest ever international survey of its kind reached people in 112 WHO member states, area and territories, representing 88% of the world's population, to gather data on MS prevalence and the resources available to diagnose, treat, and support people with MS.

The Atlas highlights the need for changes to improve MS care, including efforts to better inform the public and health professionals about the disease, and the need to make health services specific to MS more available and accessible. Survey results are presented in charts, maps and text on the Web site [www.atlasofms.org](http://www.atlasofms.org).

### **Repairing and Protecting Against MS Damage**

Repairing disease damage is an elusive goal of MS research – thanks to treatments currently on the market, we can often do a reasonable job of stopping the immune attack on the brain and spinal cord, but we still can't repair the damage it causes. Today, research teams from around the world reported their strides forward in this important aim.

- Evidence that an approved therapy, Copaxone® (glatiramer acetate, Teva Pharmaceutical Industries), may contribute to neural health was reported based on a subgroup of the PreCISe study (in which the drug reduced the risk of developing MS and delayed the development of MS among individuals with CIS – clinically isolated syndrome – a first event suggestive of MS). Douglas L. Arnold, MD (NeuroRx, Montreal) and colleagues used magnetic resonance spectroscopy to examine levels of NAA – a marker of nerve fiber integrity – in a subgroup of 34 people. These levels were significantly higher in people taking Copaxone compared to those on placebo at one year.
- One experimental strategy under study for repairing tissue damage in MS is cell transplants, such as “mesenchymal stem cells” which are derived from bone marrow. Antonio Uccelli, MD (University of Genoa) studied whether mesenchymal cell transplants would affect the immune attack as well as tissue damage in mice with the MS-like disease EAE. Despite finding little evidence that these cells developed into actual replacement nerve cells, they found evidence that brain tissue was protected from disease, as well as an increase in T cells that regulate the immune attack and a decrease of pro-inflammatory cells.
- People with MS have varying symptoms, which means that the underlying damage probably differs as well, and understanding these differences is a vital first step to devising repair strategies. A. Giorgio, MD (University of Siena, Italy) and colleagues examined changes in brain volume over an average time period of 18 months using MRI in 963 people with different types of early and later MS who were involved in placebo arms of clinical trials or who were not taking any disease-modifying therapy. Using a new technique to analyze brain atrophy, the investigators reported that reductions in brain volume were similar in people in the earliest stages of MS as to those in late stages. They concluded that this damage occurs steadily during the disease’s evolution. Further work is needed to verify these findings over longer periods of time.
- Dr. Hanneke Hulst (VU University Medical Center, Amsterdam) and colleagues reported on a posthoc analysis of data compiled during year one of a clinical trial of the experimental oral therapy ibudilast (MN-166, MediciNova, Inc) involving 297 people with relapsing MS. They found that the relative proportion of acute inflammatory lesions – detected on MRI scans – that evolved into destructive lesions (defined as persistent black holes on MRI scans) was significantly reduced in the treated group compared with the placebo group. This suggests a possible neuroprotective effect of this drug.

### **Off the Beaten Path**

People with MS who share anecdotes about the success of dietary supplements, or other alternative therapeutic strategies, are often frustrated by the answer, “There are not enough data to support the use of this treatment.” At the conference, several groups reported such data on MS therapeutic strategies somewhat off the beaten path.

- Growing evidence is linking increased levels of vitamin D to decreased MS risk, but one question is, "Will vitamin D supplements protect people from developing MS?" First, we'd need to know the safety of increasing supplementation in people with MS. Jodie Burton, MD (St. Michael's Hospital, Toronto) and colleagues compared administering escalating doses of vitamin D3 (the equivalent of 4,000 to 40,000 international units per day) to 25 people with MS over 52 weeks, with 24 untreated controls. Calcium levels remained within normal limits. Immune system analysis showed that reactivity of T cells – major players in the MS attack – was reduced. Trends toward clinical improvement were noted, but they were not significant. The group is now planning a phase II study of vitamin D supplementation that will focus on MRI and clinical endpoints.
- Ikuo Tsunoda, MD, PhD (University of Utah, Salt Lake City) and colleagues administered resveratrol, a component of red wine, to mice with an MS-like disease induced by a virus. Resveratrol enhances the activity of SIRT1, a molecule that might help to preserve nerve fibers. In this effort, treated mice gained more weight than untreated mice, a sign of clinical improvement that the researchers say might be attributed to nerve protection. In mice infected with a low dose of virus, fewer died with resveratrol treatment. The team is proceeding with the pathologic studies necessary to confirm this hypothesis.
- Although exercise is helpful in managing many MS symptoms, research on the type and intensity of this exercise continues. Heather Hayes, DPT (University of Utah, Salt Lake City) and colleagues compared a standard exercise program with a high-intensity resistance training program in 19 people with moderately severe MS. There were no significant differences in the improvement of strength or mobility between the two programs – fatigue improved significantly in both groups. The results showed no significant additional benefit of this high-intensity program for people with moderately severe MS – such studies help to direct exercise protocols for people with this disease.

### **Different Mechanisms at Play in African Americans with MS?**

Generally, the risk of MS in African Americans is around half that of Caucasian Americans, but research indicates that African Americans tend to have a more aggressive course of the disease. Omar Khan, MD (Wayne State University) and colleagues compared the presence of antibodies in the spinal fluid of 150 African Americans with MS and 150 Caucasians with MS, finding increased levels of antibody production among the African American population, and demonstrated correlations between antibody production and central nervous system tissue destruction. This study provides evidence that immune B cells may be responsible for exaggerated signs of inflammatory tissue destruction in African-Americans (as opposed to T cells, often blamed as the prime soldiers in the immune attack). Studies of B cell depletion therapies are underway.

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### **Reports about Pediatric MS**

- Emmanuelle Waubant, MD, PhD (Pediatric MS Center of Excellence, San Francisco) presented a study of 31 individuals whose onset of MS was in childhood versus 31 whose disease began in adulthood. Her team found that children at disease onset carry a higher disease (lesion) burden, as measured by MRI brain scans, than adults at disease onset.
- Researchers at the Pediatric Center of Excellence in Stony Brook, New York, reported on a study of fatigue in 51 children with pediatric MS. William Macallister, PhD, reported that fatigue was a major MS symptom for 43% of these children, who can experience this symptom even early in the disease and in the absence of other significant neurologic impairments. Fatigue can impact school performance and other quality of life issues.
- Mark Gorman, MD (Massachusetts General Hospital, Boston) presented a study comparing disease characteristics of adults with MS and children seen at the Pediatric MS Center of Excellence. They found that relapses were more frequent in the pediatric group, despite data that disease progression appears to be slower in pediatric-onset MS.
- Studies from National MS Society-supported Pediatric MS Centers of Excellence and others focus on characterizing MS in this understudied population. John R. Rinker, MD, and others from the University of Alabama-based Center reported that African-American children with MS in general experience more severe disease than children with MS from other racial or ethnic groups. The same team reported that out of 45 pediatric MS patients referred to their center over several months, two-thirds had psychiatric disorders in addition to MS. The most common was depression (64%), followed by anxiety and attention deficit hyperactivity disorder. A significant percentage of adults with MS also experience psychiatric disorders such as depression.

### **Women and MS**

MS typically initially affects women of childbearing age. When young women receive a diagnosis of MS, they frequently have questions about the effects of the disease on childbearing, and vice versa, making this a crucial area for research. Some brief findings reported in this area include:

- Dr. M. Mendibe (Hospital de Cruces, Baracaldo, Spain) and colleagues analyzed the evolution of disability in 451 women with MS and showed that having children did not affect the development of disability.
- Annette Wundes, MD (University of Washington, Seattle) and colleagues analyzed data from 391 women with MS and showed that significantly fewer have children than the U.S. national average. It is not clear whether this is the result of biological factors or choice.
- Chiara Rivoiro, MD (S. Luigi Gonzaga Hospital, Orbassano, Italy) and colleagues

administered gonadotrophin releasing hormone (GnRH) -analogue treatment to 12 women undergoing treatment with mitoxantrone to prevent onset of premature ovarian failure – a common long-term consequence of similar chemotherapeutic agents. So far, six women have completed treatment with both agents and have returned to normal menstrual cycles.

### **Reports on Emerging Therapies**

- More patients remained relapse-free and stable while taking experimental alemtuzumab (Genzyme Corporation) compared with those taking a standard interferon, supporting other beneficial measures previously reported from a Phase 2 study of the annual IV infusion, now in Phase 3 trials. Krzysztof Selmaj, MD, PhD (Klinika J Katedra Neurologii Akademii, Lodz, Poland) presented data on the Phase 2 study, which evaluated high and low doses of this immune-suppressing monoclonal antibody compared with Rebif® (interferon beta-1a, EMD Serono, Inc. and Pfizer, Inc.) in people with relapsing-remitting MS who had never taken any other disease-modifying therapies. Immune thrombocytopenic purpura, thyroid adverse events, and infections occurred more frequently in the alemtuzumab groups.
- First results from a one-year, multi-center trial of T-cell vaccination (Tovaxin, Opexa Therapeutics) were presented by Edward Fox, MD, PhD (University of Texas Medical Branch, Round Rock Texas). The placebo-controlled study involved 140 patients with relapsing-remitting MS and 10 patients who had experienced a neurological episode (CIS) that put them at possible risk for being diagnosed with MS. Those on treatment received five monthly subcutaneous injections of their own attenuated immune T cells and followed for one year. The treatment was found to be safe, but did not achieve statistical significance in the primary endpoint evaluating the cumulative number of active MRI lesions (gadolinium-enhanced) in those on active therapy versus those on placebo. Dr. Fox stated that additional evaluations of the immunological and other effects of the treatment are ongoing, with an eye toward the design of further clinical trials.
- A recent study found that one course of the IV drug Rituxan® (rituximab, Genentech and Biogen Idec) reduced disease activity and relapses for 48 weeks in people with relapsing-remitting MS. Robert Naismith, MD (Washington University, St. Louis, Mo.) presented results of an investigator-initiated study suggesting that this drug, which depletes immune B cells, has potential for treating “breakthrough” disease activity in people still taking a standard MS therapy. Twenty-six people who were on disease-modifying therapies but showing active MRI-detected lesions received four doses of rituximab while staying on their other therapy. At the end of 24 weeks, their disability status score (EDSS) remained unchanged, but another functional measure called the MS Functional Composite (MSFC) improved over baseline. In an earlier presentation by the same group, they also reported finding, to their surprise, that rituximab not only depleted B cells, but also T cells.
- According to investigators reporting the first results from an early, uncontrolled trial of injections of mesenchymal stem cells (grown from the patients’ own bone

marrow) in a small number of individuals with MS and ALS, this approach may warrant longer, controlled investigations. Dimitrios Karussis, MD, PhD (Hadassah-Hebrew University, Jerusalem) reported that 15 individuals with advanced MS and 14 with advanced ALS received intrathecal and intravenous injections of the cells. According to the report, the ALS patients remained stable for 6 months and MS patients showed improvement on disability status scores (EDSS) at 3 months and 6 months. Twenty patients experienced mild fever and transient meningeal irritation.

- Results of a small-scale safety trial of the experimental peptide therapy ATX-MS-1467 were presented by David C. Wraith, PhD (University of Bristol, UK). This compound is a "cocktail" of four peptides derived from human myelin basic protein, a major component of the myelin that is attacked in MS. The vaccine was tested in 6 people with secondary-progressive MS and was well tolerated. Lab tests also showed that it suppressed responses to MBP by immune T cells of the participants. This preliminary study was funded by Apitepe Ltd. According to Dr. Wraith, the company hopes to conduct a larger clinical trial in the future.

- Results of a second Phase 3 trial of sustained-release Fampridine (Acorda Therapeutics) showed that this symptomatic therapy could temporarily improve walking speed and leg strength in a subgroup of people with all types of MS. Andrew Goodman, MD (University of Rochester, New York) presented results of this trial of Fampridine-SR, a sustained-release formula of 4-aminopyridine that temporarily enhances nerve signaling. For nine weeks 120 people received fampridine versus 119 on placebo. The primary outcome measured was improvement in the time taken to walk 25 feet. About 43% of those on treatment showed consistent improvement in walking speed, versus about 9% of those on placebo. Among responders, speed improved by about 25% from baseline. The drug was well tolerated. According to the company, these results, combined with previous testing, will serve as the basis of an application for marketing approval.

- In the first attempt to apply a new "antisense" approach to treating MS, ATL1102 showed significant reduction in the accumulation of new active brain lesions over 8 weeks of treatment in a European Phase 2 trial. The study, presented by Volker Limmroth, MD, PhD (University of Cologne, Germany), was a placebo-controlled trial involving 77 people with relapsing-remitting MS who received twice weekly subcutaneous injections of the active agent or placebo. This proof-of-concept study requires followup with larger, longer clinical trials to verify this compound's clinical effectiveness and safety. ATL1102 targets CD49d, a subunit of a T cell adhesion molecule that permits immune cells to migrate into the central nervous system.

- Low-dose naltrexone, a drug that blocks opioid receptors and is normally used to combat addiction, was the subject of several reports at the World Congress. Bruce Cree, MD (University of California San Francisco) presented results of an 8-week placebo-controlled, crossover clinical trial involving 80 individuals with different types of MS. Using a quality of life inventory (MSQLI), they found that those on the

drug showed consistent improvement in mental health components of the survey, but not physical quality of life measures.

- Investigators at Pennsylvania State University (Hershey, Pa) reported that low-dose naltrexone could prevent, delay or reduce the severity of MS-like disease (EAE) in mice, but that high-dose naltrexone was detrimental, exacerbating the disease in mice.
- Disappointing results from a trial of the IV drug Rituxan® (rituximab, Genentech and Biogen Idec), which depletes immune B cells from circulation, may provide possible clues to future clinical trials in primary-progressive MS, a course of MS for which no treatments are currently on the market. Kathleen Hawker, MD (Ohio State University, Columbus, Oh.) presented results of a trial involving 439 people with primary-progressive MS, showing that the drug did not slow disease progression when compared with inactive placebo, the primary endpoint of the study. However, secondary outcome measures using MRI showed the median change in lesion volume from baseline to week 96 was significantly lower in patients on therapy. Looking at subgroups of participants, the investigators found that those who were younger and showed MRI signs of active inflammatory lesions (gadolinium enhancement) appeared to benefit most from the therapy. This suggests some impact on underlying disease activity that should be factored into future trials of therapies for this progressive form of the disease.

### **Reports on Possible MS Risk Factors**

- Investigators around the world have been focusing on the question of whether exposure to sunlight (and higher levels of vitamin D the body makes from sunlight) helps explain the fact that MS occurs with higher frequency in regions farther away from the equator. In two presentations, epidemiologist Robyn Lucas, MPH, PhD (Australian National University, Canberra) described early results from a large-scale collaborative, the "Ausimmune Study". Cases were gathered of people who've experienced a single neurological episode suggestive of central nervous system myelin damage (CIS, and are therefore at risk for developing definite MS) at various latitudes in Australia, and ultimately will track which develop MS. So far they have found early evidence that those cases who had CIS had less cumulative skin damage caused by the sun than the control cases, suggesting they had had less sun exposure. The investigators also found that the incidence of CIS cases increased by 9.2% per higher degree of latitude, and this latitude effect was different for different types of neurological episodes.
- Investigating the sunlight/vitamin D question from the angle of a high-incidence area, researchers at the Hospital for Sick Children (Toronto, Ontario) reviewed records of 35 children with MS from Canada whose serum levels of vitamin D had been tested. Naila Makhani, MD, described finding that only 34% had serum levels considered "adequate" (greater than 70 nmol/L 25-hydroxyvitamin D), while 65% were either "insufficient" (31-69 nmol/L) or deficient (0-30 nmol/L). Further studies

are needed to determine whether vitamin D supplementation alters disease susceptibility or course.

- In a related study investigating the possible link between vitamin D and risk of MS, reported earlier during the congress, Heather Hanwell, MS (University of Toronto) and colleagues in the Canadian National Pediatric Demyelinating Disease Network investigated 117 children at high risk for MS – youngsters who have had one neurologic episode. They took blood samples and then followed the children for one year or so to determine whether they developed definite MS (as determined by experiencing a second episode). They found that vitamin D levels were significantly lower in the 16% of the children who developed MS.

**Note:** Further studies are needed to determine whether vitamin supplements could reduce the risk of MS, and there is insufficient evidence yet that vitamin D supplements can affect the course of MS once it has begun. Currently, there are well-designed trials in progress that may clarify the potential value and possible risks of vitamin D supplementation in MS within a few years.

- MS has been linked to a variety of infectious triggers but to date none have been proven to cause the disease. Claude Genain, MD (California Pacific Medical Center, San Francisco) and colleagues are working on creating laboratory systems to investigate aspects of how an infectious agent could trigger the autoimmune attack on the brain and spinal cord in MS. Among the suspected infectious agents is Human Herpesvirus 6 (HHV6).

Reporting on a study, he showed that marmosets are susceptible to HHV6 infection, and that the virus could induce central nervous system symptoms and direct myelin damage. Over time, two of the infected animals developed MS-like relapsing-remitting symptoms and delayed autoimmunity was detected against myelin proteins. This study shows a direct correlation between HHV-6 and neurological disease in marmosets. Dr. Genain speculated that such delayed, secondary autoimmune reactions observed in this study would probably hold true for other viruses that have affinity to the central nervous system.

### **Progress Identifying Disease Predictors**

- Advanced imaging technologies are opening up new windows to the MS disease process and offering hope for better ways to predict individuals' disease course. Nancy Richert, MD (Neuroimmunology Branch, National Institutes of Health, Bethesda, Md.) described a study that followed 31 people with RRMS over five years, using a variety of MRI techniques and analyses. They reported that whole-brain magnetic transfer ratio (MTR, a measure of tissue integrity) at entry into the study was more predictive of clinical disability five years hence than were conventional MRI measures, including in individuals who are taking therapies that reduce the number of new lesions.

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- Results of another study focusing on finding ways to predict the future course of MS were reported by Dr. Bastiaan Moraal (VU University Medical Center, Amsterdam). The collaborators evaluated data from the large-scale clinical trial (BENEFIT study) in which treatment with Betaseron® (interferon beta-1b, Bayer HealthCare Pharmaceuticals) was shown to delay the onset of clinically definite MS in people at high-risk for the disease compared with people who did not receive treatment. In an ongoing follow-up study, the original patients who had been on placebo plus those who had been on active therapy are now receiving Betaseron. Comparing baseline brain MRIs of patients from the start of the study, the investigators were able to discern characteristics that best predicted whose disease would convert to definite MS.
- Heather Wishart, PhD (Dartmouth Medical School, Lebanon, NH) described a study that uncovered evidence that an alteration in a gene that has been linked to pain perception in healthy adults may also underlie differences in pain perception experienced by people with MS. The study involved 25 people with mild to moderate relapsing-remitting or secondary progressive MS and 12 matched controls. Alterations to this "COMT" gene may increase the amount of the brain messenger dopamine, which in turn may decrease the activity of the body's natural pain-killing opioids. Further research on the molecular and genetic bases of pain in MS may lead to new therapeutic approaches for this troubling symptom.

**Search-A-Word**

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## What Would You Do, If?

by Jim Paty



If it were possible to go back in time, with you or me at your current age and our knowledge level being as it currently is, who or whom would like to have a talk with?

That question, for me, is hard to answer because I do not think there is just a lone individual that I would like to have a discussion with. Just to mention a few people I would like to speak with I would name Samuel Langhorne Clemens, otherwise referred to by his penname Mark Twain. Another person would be William Tecumseh Sherman, a General from the Civil War, and finally I would like to speak with Dr. Martin Luther King, Jr. the famed U.S. Civil Rights leader.

Certainly those people were famous individuals, possibly more so after their deaths than in their living years, but I think I would be able to learn so much from them, in our private conversations that the opportunity to speak with them would be something I could not let slip past me.

Because I received my Bachelors Degree in Communication and I do not obviously personally know any of these men, I think that I would try to talk to them in the form of me interviewing them. In that way, I think I could ask them questions about what either they did, in their lifetimes, or what they are famous for instead of just attempting to carry on a conversation as if we were walking down a road or a pathway in a wooden area, for example.

Starting with Mark Twain, I think I would ask for information about his writings. I have not read all of his books but I think I would like to ask what inspired his writings. Did he know people like the persons he wrote about or are some of the individuals compellations of different he knew or would liked to have known? I suppose the same kind of questions would go for the different locations in his stories.

Being a person having lived in the southern part of America, I would like to ask General Sherman if he really had to ravish my home state of Georgia, during the Civil War? It seems a little too much to have done but I certainly did not live then and maybe that was what he deemed the best thing to do in the course of the Civil War, burn a good portion of Georgia.

For Doctor King, I was alive during his leadership days and I do not have a real clear memory of those days, as I was only born during the last few months of 1955. His start up the ladder of history began prior to my first days of elementary school. I do however have, very small, memories of seeing, on a black and white television, bits and pieces of his 1963 "I Have A Dream" speech at the Lincoln Memorial or the March on Washington DC he was speaking at. My recollection is that since I was less than two-handfuls of age I probably was running in and out of our house, during Dr. King's speech. I do remember that my mother had the speech on the

television and that I was too busy playing, as children do, to pay the speech any attention.

I would obviously need to have a tape recorder with me to record these discussions as my handwriting has gone by the wayside due to my Multiple Sclerosis. I don't know if I could arrange to film these conversations. I suppose I could try but would the interviewees want to be filmed? That is another question I would have to ask.

Of course, the men I have chosen to walk with are just some of the choices I could have made. That is not to say or write that those people are the best options to have a discussion with. Maybe you would select a past family member or an instructor you once had a class with or any person from your past. These people I have selected are just people I think it would be of interest to talk with.

Research would be needed to be done before I went into any kind of meeting with any of these people. I certainly would not like to be unprepared in trying to carry on a talk with any of these men. After all, I think I would have the advantage of knowing how their life and actions turned out while they, the interviewees, would not have had that same opportunity.

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### **What Would You Do, If?**

By Sarah Maurer



If it were possible to travel back in time and visit with anyone I desired, there are several people that I might choose from.

Certainly, the chance to visit with some of my historical idols, such as Eleanor Roosevelt or Helen Keller, would be an amazing opportunity. At this point in my life, however, there is only one person that I would wish to visit. That person is my grandmother, Mary Florence Rowland, who passed away in 2000 at the age of 86.

I spent many summer vacations, in Kentucky, with the woman we all called "Mamaw". She taught me how to sew and how to crochet, two things I still enjoy doing very much. On mornings that I tried to sleep in, she would wake me up with a simple song. "Lazy bones, sleeping in the sun. How are you ever going to get your day's work done?" My own children will tell you I have sung this many times to them as well.

I often think about Mamaw and I miss her so much that some days my heart aches. Mamaw always seemed to have butterscotch candies and homemade peanut butter cookies in her house. Sometimes, out of the blue, I swear I can smell these things around me.

Although I am now an adult, the child in me will never stop missing my Mamaw. My only regret is that I wasn't able to have more time with her. I would greatly cherish the opportunity to ask her questions about her childhood and her long teaching career. Perhaps this may seem a little childish, but I would like to ask her if she is proud of me, for the woman I have become. I would also tell her she was the best Mamaw in the whole world.

## **M.S. Circle of Friends**

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website: [www.mscircleoffriends.us](http://www.mscircleoffriends.us)

TO: \_\_\_\_\_

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### **Puzzle Answers:**

1. c. 17
2. a. Hearts
3. a. Saratoga Springs, NY
4. c. 1912
5. c. Hoover
6. What is "against the wind"?
7. What is quantum?
8. What is coca-cola?
9. What is *Nature*?
10. What is the Sousaphone?

