



# Looking Forward

FALL/WINTER 2010



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## Letter from the Co-Directors

Dear Friends,

The blistering heat of the summer has lifted and the short but crisp bright days of autumn are upon us. As with the seasons, our battle against MS, TM, and other dreaded neurological diseases cycles. This past year has seen highlights with the successful FDA approval of two new pills for MS. While we are thrilled with the recent approval of another prophylactic therapy for MS (fingolimod), we also are aware that we have more work to do to relieve the suffering and improve the lives of those living with these devastating diseases.

We are happy to provide this newsletter to you and have decided that with each issue, we will highlight one of our researchers or clinicians with a feature article about their area of interest and expertise.

In this issue, we highlight the work of Dr. Michael Levy who has aptly taken over much of the stem cell work and is running the neuromyelitis optica (NMO) center. NMO is an especially aggressive disease that was thought to be a variant of MS until a recent discovery proved it to be a different disease altogether.

In NMO, the immunopathology consists of an antibody mediated disease of astrocytes which are important cells in the brain that provide nutrients and support to neurons and that also regulate certain ion channels. These astrocytes are targeted and killed by the NMO antibody (called NMO-IgG), resulting in severe tissue loss and secondary demyelination. The critical lessons being learned from this rare disease are already shedding light on how we can better understand and treat antibody mediated forms of TM and MS. Dr. Levy is not only unraveling how the immune cells conspire to cause this wickedly disabling disease, but is also making inroads with understanding how stem cells may be used to repair the damage by replacing lost cells. His laboratory actively collaborates with colleagues in the laboratories of Dr. Pardo and Dr. Calabresi resulting in a synergy of ideas, which are advancing science in true Hopkins fashion!

Our basic research labs are actively looking at the pathological mechanisms of inflammatory diseases of the central nervous system. In our clinical research arena, we continue to study retinal nerve fiber changes that occur over time in MS in a large longitudinal study. In addition, we have various treatment trials ongoing that hope to establish efficacy of yet additional disease modifying therapies. We are investigating the dosage of Vitamin D, as this

vitamin has been shown to play a major role in the immune system, understanding the correct does may be critical for optimal immune system function. The TM group is studying Ampyra the newly FDA approved oral medication for walking difficulties associated with MS to see if this potassium channel blocker is useful for improving nerve transmission in TM patients. We are now using a 7 Tesla research MRI to study cognitive changes that are known to occur in at least 50 % of individuals with multiple sclerosis. This scanner allows us to visualize the gray matter; previously inadequately imaged with less powerful magnets.

Our research is incredibly exciting! We believe that with each passing day we are closer and closer to better treatments for these devastating illnesses. We are committed to better understanding these diseases, and to developing better treatments - that not only modify the disease course, but that can protect the central nervous system from damage that can one day provide active repair to damaged areas in the brain and spinal cord.

As always, we look forward to hearing from all of you and appreciate the support we have received, which comes in so many different forms. We wish you a safe and happy Holiday Season.

Warm regards,  
Carlos Pardo and Peter Calabresi

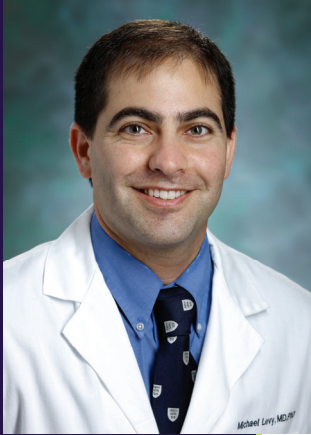


Carlos Pardo



Peter Calabresi

# Spotlight on Neuromyelitis Optica



Dr. Michael Levy

## LOOKING FORWARD

Neuromyelitis Optica (NMO) is a rare inflammatory disease that causes blindness and paralysis. NMO, formerly named Devic's disease after Dr. Devic published a case series in 1894, accounts for 1.5% of all demyelinating diseases in the United States with an incidence of approximately 300 new cases per year. The number of new patients is growing because a new test available in 2005 to identify patients with NMO has been confirmed to be specific and reliable. However, many of the symptoms of NMO are similar to multiple sclerosis (MS) and a majority of NMO patients who come to Johns Hopkins have been diagnosed with MS first. Because the medications for NMO and MS are different, we have established the Johns Hopkins NMO Clinic to specialize in the diagnosis and treatment of NMO.

NMO is a disease that preferentially strikes the optic nerve and spinal cord with frequent recurrence and devastating consequences. Before treatment became available, half of NMO patients would be blind or paralyzed within 5 years of disease onset. Until recently, NMO was thought to be an aggressive variant of multiple sclerosis but we now realize that the pathology and immunology of NMO is very different from MS. Pathologically, NMO lesions have evidence of humoral inflammation including neu-

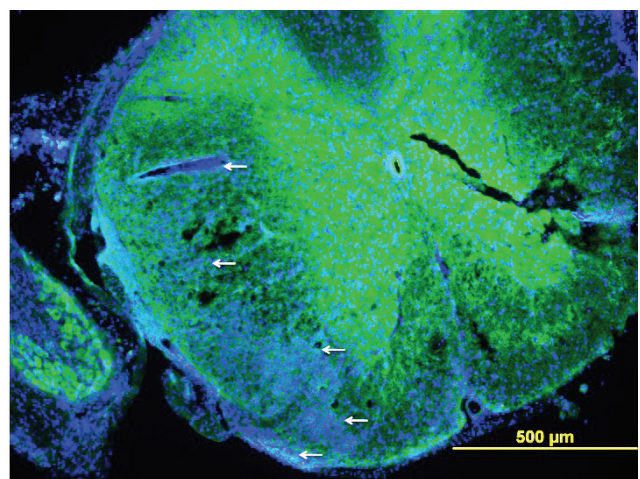
trophil infiltration, complement and immunoglobulin deposition. The lesions are also deficient in aquaporin-4 (AQP4), a protein normally found on the nervous systems' supportive cells called astrocytes. Immunologically, NMO is characterized by presence of a serologic antibody marker, the NMO-IgG, whose target is AQP4. Current models posit the NMO-IgG as the pathologic instigator of disease by binding to AQP4 on astrocytes and stimulating an inflammatory response. Ongoing research will yet determine the exact pathogenesis of disease and the roles of the NMO-IgG and AQP4, but the involvement of AQP4 and the presence of the NMO-IgG is unique in patients with NMO and helps distinguish this disease as a separate entity from all other known inflammatory diseases of the nervous system.

Most importantly, we are learning that traditional treatments for MS can be harmful in patients with NMO. Despite the recent widespread attention that NMO has received in the medical media, the delay to diagnosis for patients with NMO remains more than one year leading to

potentially harmful outcomes in these patients. The Johns Hopkins NMO clinic is focused entirely on NMO disorders with three goals: 1. Provide excellent patient care for patients with diagnosed or suspected NMO, 2. Collaborate in research efforts to understand the epidemiology, clinical course and best treatments for NMO, 3. Participate in educational program for patients and physicians on topics related to NMO.

The NMO clinic is attended by Dr. Michael Levy who has a long-standing interest in clinical NMO disease and research. In addition to attending the NMO clinic, Dr Levy also directs the inpatient General Neurology Service at the Johns Hopkins Hospital. Dr Levy completed his neurology and neuroimmunology training at the Johns Hopkins Hospital and has been working in the field of NMO research since 2005. He currently runs the NMO research laboratory at Johns Hopkins, which is dedicated to understanding the pathogenesis of NMO disease through biochemical, cell culture and animal models, and discovering safe stem cell therapies to restore neurologic function in patients with NMO.

**Spinal cord section from a mouse model of NMO showing inflammation (white arrows) similar to pathology seen in human NMO patients**



# Fundraising

# The Johns Hopkins RESTORE Team



The RESTORE Team at the Celebration Sprint Triathlon in Columbia MD on



**Hockey Fights MS** is a charitable organization whose mission is to raise money for research into the cause, cure and treatment of multiple sclerosis. To date, the Hockey Fights MS tournaments have raised nearly \$30,000 for MS research.

This event will take place in Bethlehem, PA, in August for the benefit of Project RESTORE.

The Johns Hopkins RESTORE Team exists to organize and participate in challenging sporting events, such as Triathlon, Duathlon, and road races so as to:

- Raise awareness as to the merits of physical fitness for people who are confronting challenges brought about by neuroimmunologic disorders and disability (e.g., Multiple Sclerosis)
- Raise funds and awareness for The Johns Hopkins Project RESTORE.

The Johns Hopkins RESTORE Team (HRT) is comprised of athletes who are fighting debilitating diseases such as multiple sclerosis (MS) and transverse myelitis

(TM). They are winning their battles to restore physical and athletic function thanks to the research and treatment efforts of Project RESTORE. They will be competing in multiple triathlons, duathlons and road races throughout 2010 to raise awareness as to the merits of physical fitness for others who are confronting challenges brought about by neuroimmunologic dis-

orders and disability. The team also wants to draw attention to the incredible support and breakthroughs being achieved by the Johns Hopkins Project RESTORE. All fundraising efforts of the HRT will benefit the Johns Hopkins Project RESTORE.



### *From Development: Fundraising Accomplishments!*

- Golf - 5,000
- Hockey Fights MS - \$6, 340
- Triathlon - \$27,134
- Gifts for FY10 - \$449,137.74
- Pledge payments for FY10 - \$254,000

# Thank You!

# NMO and Me: A Patient's Story

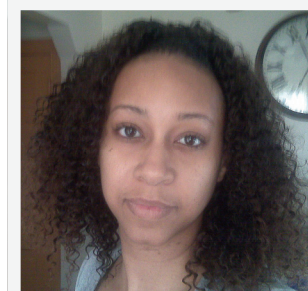
Neuromyelitis Optica (NMO) is an unfamiliar name but an unfortunate disorder that I developed at an early age. I experienced my first symptoms at age 24 with tingling, numbness, and weakness in both of my legs. This eventually developed into paralysis from the waist down. Before the NMO diagnosis, I was a dancer at Duke Ellington School of the Arts. After I graduated high school, I continued to dance with several well known established dancers. I travelled all over the United States until I was struck with NMO. I have been paralyzed on four different occasions from the waist down and had to learn the mechanics of walking all over again like a child making its first attempt.

Compared to my first episode with NMO,

the last occurrence was absolutely the worst. Just imagine waking up from your sleep and realizing that you are not able to move. Not only did it paralyze me again, but I also lost vision in my left eye. The paralysis was now from my chest down to my feet. During past NMO episodes, I was able to sit up and move the upper portion of my body with little assistance. However, with this new extended area, it was extremely difficult to sit up or even roll over on my own. To regain my strength and even walk again, I had to go back to therapy. After several months of physical therapy, water therapy, and a personal trainer; I am well on my way to being as strong as I can be. With the help of wonderful nurses, occupational and physical therapists, family and friends, I have been able to push my-

self back to regaining most of my strength after each enduring episode. All of the support and hard work, with a lot of strength, faith, encouragement, and love from family, friends and people I meet each day serves as a positive purpose in my recovery. Although NMO may be an unfamiliar name and unfortunate disorder, it does not have me. I am a determined, faith-willed person who understands that, this is just another chapter in my life.

-Trina Walker



## 10 Tips for Reducing Holiday Stress!

## Seasons Greetings

While the Holiday season can be great fun, and most of us look forward to it with great anticipation, it can be overwhelming and cause a significant amount of stress! And sometimes stress and MS are not a great combination.

One study of 32 women with relapsing-remitting MS found that 85% of clinical exacerbations were associated with stressful life events encountered in the 6 months prior to the relapse. Mohr, an MS researcher, found in a study of 36 patients that the probability of new inflammatory brain lesions was higher in the weeks following mild stress. Some researchers believe that repeated stressors have a cumulative effect on MS symptoms. From an immunological standpoint, it has been found in animal experiments that increased stress causes an increase in inflammatory immune system activity that may lead to an increase in neurological symptoms. From a patient perspective, stress seems to increase MS symptoms. From a clinical research perspective, some studies show an association between stressful events and MS exacerbations and from an immunological perspective, stress can increase inflammatory immune system activity. AND, the Holidays can be very stressful. What to do???

1. Know your expectations of the Holidays. Make a realistic plan ahead of time. How did you feel last year? If the answer is "not so

well" then this year is the perfect opportunity to scale back your expectations!

2. "Just say No" If you usually host the family for a Holiday dinner or you are involved with much of the cooking perhaps it is time to pass the torch to someone else. If you are invited to more than one Holiday event, choose one and let the others go.

3. "The Perfect Gift" Spending time searching for the perfect gift is one way of needlessly increasing stress. Ask early for gift ideas. Shop on line and you can have the gifts sent directly to the gift recipient! If you absolutely must go out to shop, make a plan ahead of time, so that your shopping can be focused and less fatiguing.

4. Budget! For many, finances are difficult! Some families draw names from a hat and reduce the number of gifts that are needed to purchase. Other families place \$\$ limits on gifts. Some only give gifts to the children in the family. We love the Holidays because it creates opportunities to spend time with those we love. This needs to be the focus, not the gift!

5. Wrapping gifts can be a difficult task if you are experiencing numbness and tin-

gling in your hands or weakness in your arms. Ask someone else to do it, or better yet, use gift bags.

6. No one can do it all! Place a moratorium on Holiday cards. If you must host the family be sure you provide the location only! Everyone comes with a food item. Have a buffet style dinner instead of a sit-down style. Designate who will be in charge of clean – up ahead of time. And make sure it is NOT you!

7. Be organized! Memory and multitasking can be difficult with MS. Do not over schedule! Limit where you will go and who you will see. Keep track using a planner or calendar. Make sure part of your planning is for rest to avoid an increase in your fatigue level.

8. Family issues do not disappear for the holidays. Set limits on the time you spend with those who you know cause you increased stress!

9. Plan for family or friends to help with decorations!

10. Try to spend time with those you love. Watch a holiday movie classic like "White Christmas" or "A Christmas Story".

**The MS and TM Centers wish you and yours a wonderful Holiday Season!**

# The Johns Hopkins Project RESTORE

Donors may be recognized in our publications. Please print your name as you wish it to appear, including your preference for Mr., Ms., Mrs., Miss. Ms. or if you wish to remain anonymous.

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*Restoring hope, function, and lives to MS & TM patients*

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I have included the Johns Hopkins Project Restore in my will

## About Project RESTORE

Project RESTORE strives to restore hope, restore function and restore the lives of patients and families suffering with transverse myelitis or multiple sclerosis. This project funds researchers to work together to discover new biological indicators of neuroimmunologic diseases, develop new imaging strategies, and conduct clinical trials to support the creation of progressive treatments.

Transverse myelitis (TM) and multiple sclerosis (MS) are the two primary disorders our team focuses on.

Both disorders attack and injure the nervous system. Although considered rare, more than 2.5 million people suffer with TM and MS worldwide. Research efforts have been limited due to limited numbers of patients at each Center.

Project RESTORE strives to accelerate this progress. Our strategy enables us to attract patients from all over the world to not only treat, but to compile the necessary data to identify common symptoms and causes and develop and offer clinical studies.

Project RESTORE is a collaborative effort between our multiple sclerosis and transverse myelitis centers.

At Johns Hopkins, we believe that without collaboration, money and effort are not spent efficiently, brilliant research is not optimized and progress is slower than it needs to be. Our goal remains to help researchers receive the needed financial support to accelerate the discovery and testing new therapies.



The Johns Hopkins  
**PROJECT RESTORE**  
*Restoring hope, function, and lives to MS & TM patients*

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