MESSAGE FROM THE CHIEF

As many of you are aware, the Mass General is commemorating its 200th anniversary with an array of tributes, a new patient care building and museum, and innovative outreach activities such as a scholarship program for promising high school seniors throughout 2011. At celebratory events that I had attended, I am struck by the MGH’s enduring message of "... since 1811, people have counted on Mass General for answers, innovations, and medical leadership. As our 3rd century dawns, we remain ready to serve." While our own Research Center is tender in its years compared to our home institution, we are steadfast and relentless in the pursuit to find effective treatments and ultimately, a cure for Alzheimer’s and related diseases. We are equally committed to the ‘Individual Care. Global Impact’ goals of our esteemed hospital.

We were thrilled to receive so many positive comments on our Spring/Summer 2011 newsletter, particularly on our highlight of the importance of brain donation for research. In this issue, I would like to share with you some perspectives on our efforts to find biomarkers (distinct biochemical, genetic, molecular characteristics that are indicators of a disease) for Alzheimer’s disease. Biomarkers are commonly obtained from blood or cerebrospinal fluid (the fluid around the brain or spinal cord) samples.

As in our previous newsletter, we continue to focus on our mission to engage diverse racial/ethnic minorities in research in this issue, through a conversation with one of our neurologists, Dr. Nicte Mejia, who grew up in Mexico. We also have a delightful feature of the award-winning documentary “Bicycle, Spoon, Apple” that has captured the hearts of its viewers. I won’t reveal more about it—I’ll let you read all about it in these pages—except to tell you that Dr. E. Teresa Gomez-Isla, another one of our Spanish-speaking neurologists (from Spain, of course) has a starring role in it as well.

My warm greetings to you and your loved ones for a most wonderful Fall/Winter season.

Brad
The clinical diagnosis of Alzheimer’s disease (AD) is about 90 percent accurate in centers that specialize in neurodegenerative disease, but likely much less accurate in practices outside of these centers. Having biological markers of AD that could be measured in life would greatly enhance diagnostic accuracy and likely improve clinical care. Examples of useful biologic markers abound in medicine: marking blood pressure with a cuff to detect hypertension and measuring blood sugar levels to diagnose diabetes mellitus are but a few commonly employed biological markers. Efforts to identify AD biomarkers began in earnest with the 1998 consensus report of the Alzheimer’s Association and the National Institute on Aging. The consensus panel identified several uses of biomarkers: for diagnosis, for tracking the course of disease and for detecting the effects of therapeutic interventions. The report stated that an ideal biomarker should detect a fundamental feature of the neuropathology with high sensitivity and specificity; measuring the marker should be reliable, simple to perform and inexpensive.

Since that initial report, scores of studies have been published indicating that the formula of low Aβ1-42 along with high tau and phosphotau in the cerebrospinal fluid (CSF) come closest to fulfilling the criteria for biochemical AD biomarkers. These measurements certainly meet the first and most important criterion of reflecting a central neuropathologic feature of the AD with accuracy ranging between 75-100 percent. The AD formula can also be used to distinguish individuals with MCI who will progress to AD from those destined to remain stable; further, low Aβ1-42 and high tau/phosphotau in CSF may have additional predictive value in identifying healthy non-demented individuals prior to their developing AD.

Our ADRC is in the forefront of CSF analysis in AD, as CSF collections are now embedded in several clinical research studies. The next step in biomarkers development is education. We recognize there are many misperceptions about CSF collection: patients report stories that the procedure is painful, difficult to perform and dangerous. Many physicians don’t have the time or skill to perform procedures, nor understanding how the results can affect patient care. We have therefore started to educate our patients as well as physicians that CSF collection is safe, carries minimal risk of side effects and can provide valuable information as part of the diagnostic workup for cognitive impairment and dementia. To overcome limitations on physician’s time, we’ve established a specialized outpatient facility at MGH that conducts CSF collections every Thursday morning. For now, the CSF collected is part of a research protocol, but we forecast the day when CSF biomarkers will become part of routine practice in the office assessment of individuals with MCI as well as suspected AD.
A Conversation with Nichte I. Mejia, MD

Dr. Mejia, you have a unique background in that you were born in Guatemala City but grew up and went to medical school in Mexico. Tell us more about the interesting community work you had done throughout Mexico, and how you found your way to a career in neurology at the Mass General.

Dr. Mejia: My father grew up in a village in El Salvador, and my mother in urban Mexico City. Both were first in their families to attend college. They met in grad school in California, and moved to Guatemala where my siblings and I were born. We lived in various cities in Guatemala, Mexico, and the U.S. I became a physician in Monterrey, Mexico and actively participated in community health activities including door-to-door vaccination campaigns and healthy neighborhood initiatives. I was the community service physician for a village in northern Mexico; a dentist, nurse, and I were in charge of a health center that served 6,000 people in town and its surrounding farms. Our care included chronic disease management such as treatment of hypertensive and diabetic patients, healthy child and women care, and preventive services — even rabies prevention campaigns in which we vaccinated people’s cats and dogs! I lived in the health center to provide 24/7 emergency care. I loved being part of the community I worked in and still keep great friendships from that year of service. And I lived in the health center to provide 24/7 emergency care, and preventive services — even rabies prevention campaigns in which we vaccinated people’s cats and dogs! I lived in the health center to provide 24/7 emergency care, and preventive services — even rabies prevention campaigns in which we vaccinated people’s cats and dogs!

Dr. Mejia: I wish to improve access to quality neurologic care for all, particularly the underserved. My research focuses on addressing racial and socioeconomic factors that impact neurologic care and outcomes. I study large databases to understand patterns of neurologic care across the United States. Classes at the Harvard School of Public Health gave me statistical and epidemiologic tools needed for my research. I am also actively involved in outreach initiatives, give talks about Parkinson disease to patients and providers in our community, as well as talks on pursuing health careers to youth from underrepresented communities who are connected to MGH through the Center for Community Health Improvement.

Many individuals are curious to know what a lumbar puncture or "LP" is. Can you tell us more about it, and why it is so important for research?

Dr. Mejia: I am part of a fantastic collaboration between the MGH Memory and Movement Disorders Units. We are looking for clues to the diagnosis and treatment of Alzheimer’s and Parkinson’s disease in cerebrospinal fluid. In research available to all patients by educating them of effective treatments be accessible to all racial/ethnic groups.

Are you interested in participating in a study that involves brain imaging but does not involve a lumbar puncture?

Check out:
- Brain Imaging Markers in Mildly-Impaired Cognition http://madrc.mgh.harvard.edu/brain-imaging-markers-mildly-impaired-cognition
- Evolution of Memory-Related fMRI Activation Over the Course of MCI and AD http://madrc.mgh.harvard.edu/training-memory-related-fMRI-activation-over-course-mci-ad

Lastly, we have all seen the photos of your beautiful baby, Nahia. How do you manage to juggle your personal and professional lives? Can working women really have it all?

Dr. Mejia: All men and women have to constantly balance our work, family, friends, and personal lives. Nahia has brought sunshine to my husband’s and my life. We wake up to play with her before work, give our hearts to our jobs, and return in the evening to play and grow with Nahia. Weekends are fun-filled. She is now 8 months old and has travelled with us to three neurology meetings, one while I was pregnant with her and two after her birth. She’s also spent quality time with her aunts, uncles, and grandparents. I am not sure if working women or men “can have it all,” but know life is definitely great with Nahia and my husband Alvaro on board. ♬
Pasqual Maragall i Mira is a Catalan politician and was the President of Generalitat de Catalunya (the government of Catalonia) from 2003 to 2006. He had previously been Mayor of Barcelona, from 1982 to 1997, and helped run the city's successful Olympic bid. Trained in economics and law, he was active in politics for more than three decades. Maragall presided over the organizing committee for the 1992 Barcelona Summer Olympics; served as President of the Committee of the Regions of the European Union between 1996 and 1998, and was appointed doctor honoris causa of the Johns Hopkins University in 1978.

On October 20, 2007, Maragall announced that he had been diagnosed with Alzheimer's disease, and sought treatment from the Massachusetts Alzheimer's Disease Research Center's neurologist, E. Teresa Gomez-Isla, MD, PhD. In April 2008, he was featured with Dr. Gomez-Isla in a TV documentary that won the Boehringer Journalist Prize in Medicine.


At the awards ceremony in Madrid’s Teatro Real, Maragall proclaimed that “without Diana (his wife), there is no Pasqual, without Oriol Ivern (the film producer) and his wife, this movie would not have been made and without Dr Teresa Gómez-Isla, I would not be in such stable shape.”

Here are Dr. Gomez-Isla’s personal reflections on the President’s remarkable challenges …

President Maragall contacted me by phone while I was on a brief visit to Boston 4 years ago. We soon met up in person upon my return to Barcelona, when I was then the Head of the Memory Disorders Unit at the Hospital de la Santa Creu i Sant Pau, and also ran an active research laboratory dedicated to Alzheimer's disease. He spoke to me about some mild symptoms that he had begun to notice and asked me to take care of his health from then on.

Out of respect for his privacy as a public figure, we decided to complete his neurological work-up here at MGH with the invaluable help of my colleagues in the MDU (MGH Memory Disorders Unit). It appeared that President Maragall was in the initial clinical stages of Alzheimer's disease. We also had the opportunity to visit the MIND (MassGeneral Institute for Neurodegenerative Disease) and some of the laboratories devoted to Alzheimer's research during that trip to Boston with him and his wife, Diana.

Despite the blow of the diagnosis, the journey to the MGH was very inspiring and hopeful for President Maragall and Diana. He would later make the decision to go public with his diagnosis in 2007 – something a public figure had never done before in Spain – and expressed his desire to contribute to the welfare of other patients and join the fight to find a cure for this disease. With this gesture, President Maragall has managed to challenge the stigma that the society in my home country has about the disease. He is indeed a brave and visionary man who has decided not to give up because he is convinced that “nowhere is it written that this disease is invincible.”

With the support of his family, he has launched the Pasqual Maragall Foundation which is dedicated to research on Alzheimer's disease, and I have continued to advocate for its research support in Spain as a member of the Scientific Committee of the Foundation. I keep in touch with President Maragall on a weekly basis on Skype and he follows with great interest the developments that occur here at the MIND.

President Maragall once lit the Olympic flame for the city of Barcelona when he was mayor of the city in 1992. He now has reignited the flame of hope for all patients and families waiting for a cure for this devastating disease!

The DVD “Bicicleta, Pollera, Poma” may be purchased online at Abacus Cooperativa (www.abacus.coop/es-multimedia/bicicleta-cullera-poma-dvd-cromosoma-0919390.html) for 8.45 €.
Some Thoughts from Our Participants

Ever since I suspected my husband had dementia, I have gotten him and me into any study I could find – particularly a lot of cognitive studies. Recently I was asked to have a spinal tap for the Biomarkers Study, which is part of the Memory Study. At first, I was reluctant to do it, but then I remembered that I had not had any problems with the epidural when giving birth so I agreed to do it. The doctor and his assistants were so good and patient and the best part is that the needle has gotten a lot smaller so it is not nearly as uncomfortable as in the past. I had no side effects during or after the procedure. If we all do our part in helping the research, the faster our loved ones – and we as caregivers – will have a better quality of life.

Consider volunteering.

Blossom Hoag
September 29, 2011
Hingham, MA

Greetings from the Clinical Coordinator

To all our Memory Study participants:

I hope you all had a good summer. Fall is here and we’re busier than ever with the Memory Study and all the other studies that are affiliated with it. One of the affiliated studies is the Biomarkers Study, which collects blood specimens for research. For the last year we have been asking many of you who participate in this study if you’d also be willing to take part in another specimen collection, cerebrospinal fluid (CSF). (You may know this by other names such as lumbar puncture or spinal tap.) The CSF is being collected to examine the clear fluid around the brain and spinal cord. Studying the substances in CSF will help us better understand brain disorders such as Alzheimer’s disease and other neurodegenerative diseases. This may help us find disease markers in the CSF to diagnose or make out different types of neurologic conditions. To date we have collected CSF from 60 subjects.

I want to thank all of you who have participated in the cerebrospinal fluid collection part of the Biomarkers Study … and all of you who are considering participating. It is only because of your willingness to help in this way that we can make progress toward our goal of understanding, treating, and preventing various neurodegenerative diseases.

And thank you to all of you who are in our large, longitudinal Memory Study. Your participation year in and year out is so valuable to us. YOU are the study. If there’s any way we can make your experience with us more enjoyable or rewarding, please let us know.

Jeanette M. Gunther, MS
Clinical Coordinator

A New Centralized Telephone Number For All Our Studies!

Interested in learning more about research studies and how you can get involved? Patients, caregivers, family members, and healthy volunteers can call Caroline Sullivan at 617-643-5200 to learn about all of the exciting research opportunities we have going on at the MADRC!
Thanks in large part to our longitudinal research cohort and similar programs around the country, samples from over 11,000 individuals with and without Alzheimer’s disease have contributed to the discovery of several new genes contributing to Alzheimer’s disease risk, and confirmed several others. These samples, including blood samples donated as part of our biomarkers project, and brain tissues donated under our autopsy program (see accompanying articles), were critical to these new discoveries.

The study, known as the Alzheimer’s Disease Genetics Consortium and funded by the National Institute on Aging, is led by Dr. Gerard Schellenberg at the University of Pennsylvania, and includes investigators from 44 research institutions across the country, including Mass General. The paper, appearing in the online edition of the journal Nature Genetics on April 3, had well over 100 authors, including five from our center (director Dr. Brad Hyman, founding director Dr. John Growdon, and Drs. Deborah Blacker, Rudy Tanzi, and Matt Frosch), and was widely reported in the print and electronic media. The work is buttressed by similar findings from a large European consortium that is now collaborating with the American group to form an International Genomics of Alzheimer’s Project funded by the U.S. Alzheimer’s Association and the French Foundation Plan Alzheimer. This represents an unprecedented level of cooperation in a formerly hotly competitive field, bringing together the large samples and broad expertise necessary to really get to the bottom of understanding the role of genes in this devastating disease.

Before this huge effort, variants in four genes were known to be involved in Alzheimer’s disease. Three of them lead to a rare highly familial form of Alzheimer’s disease that develops when someone is in their 40s or 50s. The other one, known as APOE-4, is a risk factor for the more typical late-onset form of the disease, meaning that it only increases the chances of getting Alzheimer’s, rather than causing it directly. Although APOE-4 is a major risk factor gene, increasing risk two-fold or more, many people who carry the APOE-4 gene do not get Alzheimer’s, and many people who do get the disease don’t carry the gene. These new genes have a considerably smaller impact on Alzheimer’s disease. The value of this new information will depend on using it to better understand how genetic and other factors such as diet, lifestyle, and health act together to contribute to disease risk, and how we can develop better treatments or prevention strategies for the disease.