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RESEARCH/CLINICAL UPDATE

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2012: Sweeping Advances Made in MS Research

MS research continued to advance on many fronts in 2012. This year saw:

- The approval of a second oral therapy for relapsing forms of MS and other emerging treatments progressing through the development pipeline;
- The launch of the International Progressive MS Collaborative, the largest effort to date to speed research to stop progressive forms of MS;
- The discovery of what could be a target of the immune attack in people with MS may lead to new understanding of the disease and new treatment strategies;
- The completion of the first human trial of an experimental therapy targeting myelin repair;
- Progress in restoring functions using innovative rehabilitation techniques, including memory enhancement using a technique involving stories and imagery to solidify learning, and improving balance and mobility with specific exercises; and
- Advances in uncovering MS triggering factors, bringing us closer to finding ways to prevent the disease; and many other advances pushing us closer to a world free of MS.

The National MS Society continues to propel research forward with a comprehensive strategy aimed at stopping MS, restoring function and ending MS forever

(<http://www.nationalmssociety.org/research/index.aspx>):

- This year we invested \$44 million in over 350 new and ongoing projects;
- Projects include everything from discovery research to the Society's drug development efforts through Fast Forward[®] (www.fastforward.org).
- Read about recently launched research projects (<http://www.nationalmssociety.org/research/about-our-research-programs/download.aspx?id=44468>).

In the world's largest meeting dedicated to MS research, over 7,000 scientists convened in Lyon, France to present findings atECTRIMS (European Committee for Treatment and Research in MS). Over 1250 studies covering virtually every aspect of research were presented:

- Read a summary <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7052> and blogs <http://blog.nationalmssociety.org/search/label/ECTRIMS>
- View videos on specificECTRIMS topics <http://www.youtube.com/playlist?list=PLnPWMdCPZiBbT4OEEunsWbzFTkWNoguQD&feature=addto>

PROGRESS TOWARD STOPPING MS

The Society continued to invest in research to stop MS, including:

- Funding of clinical trials:
 - ✓ Testing whether vitamin D, or the sex hormone estradiol, or the probiotic approach of a sports drink containing parasite eggs, can reduce MS immune attacks
 - ✓ Determining if treatments available for other disorders, such as riluzole (a treatment for ALS or Lou Gehrig's disease) or phenytoin (a treatment for epilepsy), or the antioxidants lipoic acid or green tea extract, can protect the nervous system from damage.
 - ✓ Supporting a syndicate formed in the United Kingdom to conduct innovative clinical trials of neuroprotective drugs in secondary-progressive MS.
- New projects focusing on discovering "biomarkers" to aid better diagnosis and treatment decisions;
- Collaboration in a cross-disease drug screening initiative aimed at discovering the potential of compounds to stop nerve degeneration and protect the brain from harm;
- In partnership with Merck Serono, Fast Forward provided funding for lab research to discover small molecules that can deliver therapies to areas of nervous system damage and protect against that damage in MS.

Other important 2012 results toward stopping MS include:

TREATMENT PIPELINE

FDA Approves Oral Aubagio® (Teriflunomide, Genzyme, a Sanofi company)– The once-daily pill was approved as a disease-modifying therapy for relapsing forms of MS. Aubagio is the second oral disease-modifying therapy approved for the treatment of MS, and it became available for prescription in October 2012 in the U.S.

<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6864>

Two potential therapies are before FDA –

- Biogen Idec applied to the FDA for approval of BG-12 to treat relapsing MS. This oral therapy showed benefits against relapses and other MS activity in recent trials. The FDA

review is underway (<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6015>).

- Genzyme applied for approval of alemtuzumab to treat relapsing MS, based on positive results from several clinical trials. It is given by a cycle of IV infusions once per year. The FDA asked the company to resubmit its application. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6496>

Tysabri® label updated to include lab test to enhance treatment decisions – The test detects antibodies to the JC virus and can help determine a person’s risk of developing PML, a severe brain infection that has emerged in some people who have taken Tysabri (natalizumab, Biogen Idec and Elan). The test should enhance the ability of people with MS to weigh risks and benefits of this therapy. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5887>

Clinical trials discussed at ECTRIMS 2012 – Positive results from trials of statins (cholesterol-reducing medication) and Tysabri in progressive forms of MS, a new approach called AIN457 for treating relapsing MS, and results from phase II and III clinical trials of therapies were among results presented at ECTRIMS focusing on stopping MS. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7052>

Phase II results of ocrelizumab in relapsing MS – Experimental ocrelizumab (Genentech), given intravenously, significantly reduced disease activity on MRI scans in a study of 218 people with relapsing-remitting MS. One person died due to brain edema; the relation of this death to the medication is unclear. Additional research, now going on in primary-progressive MS and relapsing-remitting MS, is needed to further determine this therapy’s safety and benefits. <http://www.nationalmssociety.org/research/research-news/news-detail/index.aspx?nid=5659>

Another step toward personalized medicine in MS – Harvard researchers discovered that differences in active genes that are detectable in blood samples may be used to group people with MS into categories that predict disease course and response to therapy. Further research is needed, but it represents an early step toward personalized medicine in MS. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6941>

New approach to stopping MS – Researchers at Northwestern University have developed an innovative strategy for selectively inhibiting the immune attack in MS using tiny “nanoparticles” that were able to reduce disease activity in mice. The team is now planning a phase I clinical trial of this new technology. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7126>

UNDERSTANDING MS

Possible target of immune attacks in some people with MS identified – An immune response to a protein – called “KIR4.1,” which is found on several types of brain cells – was observed in the serum of 47% of people with MS. Further research is needed to confirm and understand these findings, which were the result co-funding by the National MS Society. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6619>

MS Societies worldwide collaborate to stop MS progression – The newly formed International Progressive MS Collaborative published a paper outlining challenges and identifying key research priorities to propel efforts to stop MS progression. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6847>

Stress management reduces MS activity – A 24-week stress management program reduced disease activity on MRI scans significantly more than in a control group, in a study at Northwestern University involving 121 people with relapsing MS. However, the benefits appeared to disappear after the weekly in-person stress management sessions were completed. Future studies should provide more clarity for optimizing the potential benefits of stress management. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6629>

Society launches project to change how MS disability and progression are measured – This cross-sector collaboration has the goal of developing new or improved tools that will be able to track benefits of therapies more quickly in people so that new therapies to stop MS progression may be tested using better assessment tools that are accepted by drug regulatory agencies. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6777>

Researchers co-funded by the National MS Society discover possible mechanism for MS damage to nerve tissue – The University of California, San Francisco researchers found that a blood-clotting protein called fibrinogen may play an early role in triggering inflammation that damages nerve fibers in a mouse model of MS. This points to a role for fibrinogen in stimulating inflammation by cells called microglia. If confirmed, targeting the interaction of fibrinogen and microglia may prove to be a novel strategy for stopping MS damage in its tracks. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7157>

PROGRESS TOWARD RESTORING WHAT'S BEEN LOST

The Society supported new and ongoing initiatives to propel efforts to restore function to people with MS through its Discovery and Fast Forward research programs, including:

- New studies into the potential of adult skin cells and umbilical cord cells as a source of nervous system repair cells;
- A new pilot research program to tap MS-specific funds from the Illinois Lottery, with a focus on nervous system repair and novel rehabilitation approaches;
- Cutting-edge research to discover new targets to stimulate myelin repair and early testing of new approaches to treating MS symptoms;

- Clinical trials testing the ability of cannabis to treat spasticity, aspirin to fight fatigue, and innovative rehabilitation and exercise programs aimed at improving mobility, fatigue, spasticity and cognitive problems;
- A study using advanced MRI analysis to determine how the brain regions associated with pain are affected by MS.

Other important 2012 results toward restoring function include:

NERVOUS SYSTEM PROTECTION AND REPAIR

First trial of experimental anti-LINGO to stimulate myelin repair – This first human phase I trial of BIIB033 (Biogen Idec), an immune antibody that inhibits LINGO-1, involved 64 healthy adult volunteers and 42 people with relapsing or secondary-progressive MS. There were no serious adverse events; headache was the most frequently adverse event reported. The authors concluded that the results support advancing this myelin repair strategy into a phase II clinical trial. Reported at the American Academy of Neurology annual meeting <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377>

Trial of patients' own adult stem cells appear safe and hints of benefit – Researchers in the UK published results of a small clinical trial involving 10 people with secondary-progressive MS, reporting that injecting a person's own bone marrow stem cells appeared safe and possibly beneficial in helping to protect the nervous system from injury. Further trials are now underway to establish its safety and potential benefit. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5951>

Collaboration to find new therapies to repair the nervous system in people with MS – Fast Forward is funding research at the Universities of Cambridge and Edinburgh, UK to screen for compounds that can stimulate myelin repair in MS. The project grew out of findings from a Nervous System Repair and Protection Initiative funded through the Society's Promise 2010 campaign. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6767>

REHABILITATION AND MANAGING SYMPTOMS

Study suggests balance/eye movement training improves MS symptoms – University of Colorado researchers found that a 6-week balance and eye movement-focused exercise program improved balance, reduced fatigue, and reduced disability due to dizziness or disequilibrium, lasting for at least 4 weeks. A larger and longer study is now getting underway with National MS Society support. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6119>

Rehabilitation technique improves memory – Learning and memory improved in people with MS with a technique that uses stories and imagery to cement learning. This was accompanied by increased activation of areas in the brain related to memory and learning. The Kessler Foundation Research Center investigation was funded in part by the Society's Mentor-Based Postdoctoral Fellowship program in rehabilitation research.

<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5962>

Hotter days may make mental tasks harder – This Society-co-funded study, which needs further exploration, may help people plan activities and may improve the design of future clinical trials. The study was done by Victoria Leavitt, PhD, and colleagues through a Mentor-based rehabilitation postdoctoral fellowship award to John DeLuca, PhD at the Kessler Foundation Research Center in West Orange, NJ. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6208>

Weight training improves walking and quality of life in small study of women with MS – The University of Arizona/University of Georgia study, funded by the National MS Society, used standard measures to evaluate the effects of the progressive resistance program, along with in-depth interviews to determine effects on quality of life.

<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7027>

Fast Forward and Concert Pharmaceuticals collaborate on MS spasticity and pain – the new collaboration funds the preclinical advancement of C-21191, a substance with the potential for treating spasticity and pain in MS. Fast Forward is committing up to \$750,000 to help its advancement toward clinical trials. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6034>

Small study reports benefit of marijuana on MS spasticity – California investigators found some benefit of smoked marijuana against spasticity and pain in people with MS in a small clinical trial. Participants also experienced reduced thinking ability after smoking marijuana, highlighting the need for research on cannabis products or other treatments that can more selectively reduce painful symptoms without producing adverse effects on cognitive function. Additional research is being supported by the Society and others.

<http://nationalmssociety.org/news/news-detail/index.aspx?nid=6374>

Study suggests Latinos with MS experience worse pain and other symptoms – A National MS Society-supported study at the Mississippi State University found that a sample of Hispanics/Latinos with MS reported more pain, fatigue, cognitive problems, mental health problems, and dissatisfaction with their access to mental health care than the general MS population, calling attention to the need for more accessible and culturally relevant mental health and social services. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6044>

CCSVI research continues –

- The 7 research projects investigating MS and CCSVI (chronic cerebrospinal venous insufficiency, <http://www.nationalmssociety.org/ccsvi>) that were launched with a \$2.4 million investment by the National MS Society and the MS Society of Canada, reached the two-year milestone, and most are in the process of completing their projects. <http://nationalmssociety.org/news/news-detail/index.aspx?nid=6803>.
- The Canadian Institutes of Health Research announced that a research team has been chosen to conduct a phase I/II clinical trial to determine the safety of venous angioplasty and obtain evidence on patient outcomes in people with MS. This initiative is also being supported by the MS Society of Canada. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6260>
- At ECTRIMS 2012, results were presented of a large prevalence study in Italy suggesting that CCSVI occurs at a low frequency in those with MS and in others without MS. Research on this phenomenon is still ongoing. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7052>

PROGRESS TOWARD ENDING MS FOREVER

To drive efforts to understand what triggers MS and ways to prevent it, the Society:

- Convened an international summit on vitamin D in MS;
- Renewed funding for an enhanced MS DNA core resource bank to foster better understanding of genes that make people susceptible to MS and may also control the course of an individual's MS.
- Supported several new research projects aimed at:
 - ✓ Understanding how risk factors such as vitamin D levels and genes to contribute to a person's susceptibility to developing MS
 - ✓ investigating how bacteria that naturally live in the human body, including in the intestines, may influence MS susceptibility and disease activity
- Launched a new, \$100,000 annual cash prize to recognize scientists whose inventive work is propelling measurable MS research progress. The Barancik Prize for Innovation in MS Research is the largest ever cash prize for MS research, and is made possible by the generosity of the Charles and Margery Barancik SO Foundation. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7096>

Other important 2012 results toward ending MS include:

Breakthrough in understanding gene activities – A government-supported, global study called the ENCODE project has mapped out specific biological functions of more than 80% of the human genome (genetic material), bringing into sharper focus the complex controls over the turning on and turning off of genetic information within cells. This leap-frog advance will greatly enhance efforts to understand the influence of genes on human diseases like MS. <http://www.genome.gov/27549810>

Studies further understanding of vitamin D and MS risk –

- Researchers in the United Kingdom and Canada reported an association between a rare variation of a gene that controls vitamin D levels and the development of MS in rare families with multiple members who have the disease. This gene variation causes dysfunction that leads to vitamin D deficiency.
<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5778>
- In a separate study, Swedish investigators found that high levels of vitamin D in the blood of pregnant women was associated with reducing their risk of developing MS later.
<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=7127>
- Men with low blood levels of vitamin D may be more susceptible to MS disability, according to a University of Utah study of 500 people with different types of MS. Read more results from the American Academy of Neurology meeting
<http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=6377>

How Epstein-Barr virus may play role in MS – This virus has been linked to increased risk for MS. In active brain lesions in people who had MS in their lifetimes, an international team found high levels of a chemical that helps the body fight viruses, and nearby, immune B cells latently (inactively) infected by Epstein-Barr virus. There was no sign of active viral infection. This may point to a possible mechanism for how the virus might indirectly stimulate MS disease activity. <http://www.nationalmssociety.org/news/news-detail/index.aspx?nid=5836>

Lives were changed in 2012 with the introduction of a second oral MS therapy, the launch of new collaborative research efforts, and significant results of recent studies promising more options in 2013 for people living with MS.