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Believe in the Power of the Bike

MS Global 2011 was held in the Canadian Rockies on August 13 through August 21. For the 3rd year in a row Accelerated Cure Project (ACP) was the beneficiary of this event held by Tyler Hamilton Training and Bill Hamilton. Thank you to our sponsors EMD Serono, John Hancock, Express Card Systems, Inc., ClifBar, Duncan Oil and Destination Cycling. Below are excerpts from a blog written by Jupiter Bridge, a first-year fundraiser for MS Global.

Sunday – Travel day

Banff is a bustling little mountain town surrounded by jagged peaks that seem to spring abruptly from the landscape. The effect is to create a stunning view in all directions from the center of town where we are staying.

My legs feel good and I'm excited to hit the road in the morning. It is a great crew of people that have gathered. In addition to the riders like me, we have a bunch of very strong ride leaders and a support team who will accompany us in vans with food, water, our clothes, etc. Also present are representatives from ACP and EMD Serono (the lead corporate sponsor) who spoke tonight to share their appreciation for all of the fundraising efforts.

Monday – Lake Louise

Yup, we woke up to rain for the true Day 1 of the ride. From our departure around 9:00 until our arrival a few hours later at Lake Louise, the weather varied between raining and raining hard.

IT WAS FREEZING!!!!



1st row: Peter Doran; 2nd row: Chris Gorwood, Karen Crumback, Karen Gardner, Larry Vuolo, Michelle Tullie, Mark "Bunny" Schwab, Suzy Berry; 3rd row: Charlie Hicks, Jacl Seiz, Dick Tapply, Kiersten Gallagher, Patti Columbus, Mary Yokobaskas, Gord Nelson, Vito Visconte; 4th row: Adam Chapman, Jill Alford, Bill Hamilton, Leanne Duncan, Kathy Zawadzki, Jack Irving, Ethan Forman; 5th row: Tyler Hamilton, Paul Columbus, Geoff Hamilton, Scott Sherman, Jupiter Bridge; Missing from photo: Colin Eggleton

A bunch of us walked the 1/4 mile down to Lake Louise to soak in some of the views. The water, in the mid-30's, is a unique light turquoise that gives the illusion of translucence until a closer look proves that its opacity hides even the shallowest rocks under the surface.

The false sense of sunshine security then led a dozen of our party to rent canoes and go for a paddle on the lake. That was spectacular! ...for about 8 minutes. Mountain weather rules:

(continued on page 3)

A Message from Robert McBurney, Chief Executive Officer



Dear Friends and Supporters of the Accelerated Cure Project,

The two months since I joined ACP have been filled with important activities and developments.

The big event was this year's MS Global Bike Ride. A great success despite difficult weather! Read all about it in this edition of *Multiple*

Sclerosis Update. I am in awe of what our supporters will do to raise awareness of our work and provide us with the financial resources that enable us to pursue our goal. We are enormously grateful for your generosity.

Your support makes it possible for ACP to act as a catalyst for innovative approaches to understanding the causes and mechanisms of MS and related demyelinating diseases, to enable the discovery and development of new treatments, and to optimize treatment for each individual patient – all leading to cures for these diseases.

Our Repository is a unique resource that allows us to share biological samples and data with researchers all over the world to facilitate research into the causes and mechanisms of demyelinating diseases. The Repository is made possible through the efforts of a key group of clinical centers across the US that treat patients suffering from multiple sclerosis, neuromyelitis optica, transverse myelitis and other demyelinating diseases. Along with members of ACP's team, I plan to visit all of our clinical centers over the next few months. In late August, these visits began when Hollie Schmidt and I visited the UT Southwestern Medical Center. We met with Dr. Ben Greenberg, one of ACP's key advisors and champions, and the team in the Multiple Sclerosis program, including research nurse Martha Mann. Martha does tremendous work visiting patients with neuromyelitis optica to collect samples and information for our collaboration with the Guthy-Jackson Charitable Foundation.

In addition to facilitating research into causes and mechanisms of MS, we have begun to explore opportunities to catalyze and contribute to the development of online systems that provide physicians and patients with information and tools that can help them to optimize the treatment of each MS patient.

I look forward to telling you more about our visits to clinical centers, research initiatives and community activities in the next letter.

Robert A. McBurney

Robert McBurney
CEO

Site Spotlight: Barrow Neurological Institute

by Sara Loud

This is the sixth in an occasional series highlighting ACP's collection sites. In this issue we turn our attention towards the Barrow Neurological Institute (www.thebarrow.org/index.htm) located in Phoenix, Arizona. The ACP Repository collection site at Barrow is led by principal investigator, Dr. Roberto Bompreszi and site study coordinator, Stacey Lent.

With their collaborative approach to providing care to people with MS and their focus on innovative research, it is no surprise that the staff at the MS clinic at Barrow play an eager and active role in the ACP Repository. One of our ten collection sites, the Barrow team, led by Dr. Roberto Bompreszi, has enrolled 187 people with MS, related demyelinating diseases and their family members into the ACP Repository, collecting samples and data that are vital to researchers studying these diseases.

Clinical research coordinator Stacey Lent joined the Barrow team in April of 2011 and took over the ACP study coordinator duties from Breanna Bullock. While new to MS research and excited to learn more every day, Stacey brings impressive clinical research experience to the project. Her expertise ranges from asthma studies to those involving drugs used to treat scorpion stings and snake bites. The topics may be diverse but the experience of engaging people in clinical research is universal and a particular love of Stacey's. "Helping individuals who are expressing curiosity about their disease and learning through their experiences" is Stacey's answer when asked about what she finds particularly meaningful about working on the Repository. "It's challenging but I love working with the study participants. They are so interested in being part of this research and doing whatever they can to find a cure." A New York native now residing in Arizona, Stacey is quick to praise the study participants who "come out in 120 degree heat to make a difference."

The MS clinic at Barrow was founded 10 years ago and provides care and support to more than 3,500 patients with MS, NMO and related diseases annually. Multidisciplinary teams work together to address the many ways that MS affects the individual and their families, from the initial diagnosis through the variety of issues that may present themselves. The MS clinical research department at Barrow focuses on understanding MS and the pursuit of new ways to treat it. Directly in line with ACP's goal of curing MS by accelerating research into its causes and mechanisms, there's no question that the collection site at Barrow represents a perfect fit.

To learn more about the ACP Repository, please contact Repository Director, Sara Loud, at 781-487-0032 or via email at acp-study-director0807@acceleratedcure.org.

Believe in the Power of the Bike

(continued from page 1)

Rule #1: The weather can turn on a dime.

Rule #2: It has LOTS of dimes in its pocket.

Shortly into our canoe excursion, a black cloud came charging in from the north end of the lake. We started paddling back furiously, got doused a bit by the rain, but were spared being out in the hail which began a few minutes after our arrival at the dock.

Tuesday – Into the Ice

There's an encouraging amount of blue sky visible above the mountain tops this morning. The forecast of a rain-free day with highs around 70 seems like it may actually be realistic. And certainly will be a welcome change after the soaking slog up from Banff yesterday.

Today's ride will be the first leg of a 2-day journey up the Icefields Parkway to the town of Jasper. The Parkway wends its way around glacial lakes, rocky ridges, and (of course) icefields. There is one point, I'm told, that the road comes within a short walk from the foot of a glacier. The terrain is sure to be spectacular today, and I'm very thankful for the favorable turn in the weather.

Tonight, we'll be staying in a place called Saskatchewan Crossing, which will be the most remote location we'll reach during the trip. There will be an early roll-out Wednesday for the longest day of the week—a 95-mile trek down to the town of Jasper.

Wednesday – The Crossing

The ride from Lake Louise up to Saskatchewan Crossing took us into some really majestic landscapes. The valley that the Icefields Parkway follows is quite wide with sharp rocky promontories springing up along its sides.

Five guys formed a vicious pace line for the last 30 miles of the ride to the Crossing. This section of the Parkway trended downhill and we simply flew. Unlike the others in our crew, I don't really have any racing experience and don't do many group rides these days. So at a sustained pace in the high 20s and low 30s mph, this was an eye opener for me. But fun! As I've said before, there are some extremely strong riders here.

Thursday – Road to Jasper

Today featured our 95-mile trek from Saskatchewan Crossing to the town of Jasper. Everything that the Crossing lacked in civilization, Jasper has in spades. It is a gentrified mountain town with a year-round tourism industry—probably not as ritzy as its Colorado cousins Aspen and Vail, but certainly nice in its own Canadian way.

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Taking Stock

by Sara Loud

The concept of “taking stock” of the ACP Repository certainly makes literal sense: counting the number of subjects enrolled, the number of samples collected, the amount of data amassed. Factored into this inventory assessment is the number of research teams supported, the quantity of samples distributed, and the data points returned.

What may be less clear, however, is the need to “take stock” in a figurative sense: the notion of stopping activity (or at least greatly slowing it down) and assessing the value of what we have created and how to best grow the Repository in the future. We have recently decided to do just that; to essentially halt enrollment at our collection sites and to use that time to evaluate the next phase of growth for the Repository in order to best meet the needs of the research community, give study coordinators a chance to complete their data entry, and also gather valuable clinical data to further characterize our subjects. While we've slowed the number of samples coming in, the distribution of samples to scientists all over the world continues at a rapid pace.

With samples collected from more than 2,700 people (including 300 who have participated in two enrollment visits), the support of our 10 collection sites, and samples and/or data distributed to more than 50 research teams, the value of the Repository is unquestioned. Taking an enrollment hiatus and working with our scientific advisors and members of the research community to refine the Repository to ensure that it meets the evolving needs of researchers working to cure MS and provide better tools and treatments is essential, and our goal.

Should you still get in touch at this time if you are interested in participating? Absolutely.

We continue to enroll selectively and if you aren't eligible at this time we'll put you on a waiting list to be contacted once enrollment resumes in the coming months. To learn more, please contact: Sara Loud, Repository Director at 781-487-0032, or via email at

acp-studydirector0807@acceleratedcure.org.

Mining for Genetic Riches

By Alla Katsnelson

Like gold prospectors who headed west in the mid-19th century, a cadre of researchers are stalking an elusive treasure. Instead of material wealth, these scientists seek genes that might reveal the secrets of various diseases. Some have struck gold. Most—including those studying multiple sclerosis—have succeeded in marking many sites of reward, but have only begun to unearth the bounty. Much work remains to dig out the full medical value of the discoveries.

MS researchers prospecting for genetic riches toiled for decades without much success. Just one gene, identified in the early 1970s, had been found to affect people's risk of developing the disease. Thirty years later, researchers were stumped. MS clearly ran in families: 15-20% of patients have a relative with the disease. But the one known MS-related gene accounted for less than half of the disease's heritability. These observations suggested that unidentified genes must contribute to the development of MS. Although a long list of genes had surfaced as possibilities, each one failed follow-up tests.

In the last five to seven years, however, this trend has reversed. By applying a relatively new technique to thousands of patient samples, collected over many years and shared among more than 20 laboratories around the world, researchers have begun to identify genes that they think underlie the disease. A 2007 report broke the dry spell, pinpointing two additional genes. After that, the trickle turned into a deluge. By 2010, 15 to 20 genes that influence a person's likelihood of developing the disease had been confirmed. A study published in August brought the number up to 57, with another 45 or so candidates.

"We are close to getting a pretty complete picture" of the most commonly involved genes, says Philip

De Jager of Harvard University, a participant in the effort. With this list in hand, however, he and other MS geneticists now face an even bigger challenge. Although researchers know that many of these genes shape immune activity, what they do and how different versions might help trigger MS remains mysterious.

The genes that MS researchers have identified probably will not benefit most patients soon. Unlike disorders that stem from glitches in a single gene—such as cystic fibrosis or Huntington's disease—MS arises from combinations of multiple genes, each of which exerts a small influence on whether someone develops the disease—plus environmental factors. In single-gene disorders, finding the DNA glitch typically lays the groundwork for simple screening tests that determine who will fall ill; in some cases, it also points toward effective therapies. "If the genetics had been different, there might have been an effect on clinical practice," says Jonathan Haines, a geneticist at Vanderbilt University in Nashville, Tennessee. Instead, he says, scientists hope that understanding the genetic architecture will uncover fundamental features of the disease, which will provide the basis for new treatments.

By the turn of the millennium, a new approach was emerging for probing genetically complex diseases. By sampling the genomes of many individuals, enterprises such as the Human Genome Project were identifying hundreds of thousands of SNPs—single-letter variations in the genetic code—common enough to be found in 1-5% of the population. Researchers could scan the genomes of a defined set of people—those with MS, for example—and compare their SNPs to those of healthy controls. In this way, scientists identified genetic variants that are consistently more common or less common in the former group compared with the latter.

Such genome-wide association studies (GWAS) promised to revolutionize how investigators study the genetics of complex diseases and traits. But early reports in the field of MS were a flop, and researchers quickly realized why: The sample sizes were too small to achieve statistical significance. "No one [research] group had the ability to gather together the requisite number of samples to make progress," says Alastair Compston, a clinical neuroscientist at Cambridge University. In 2003, Compston and a handful of other labs that had competed until then launched the International Multiple Sclerosis Genetics Consortium, a collaborative project whose members vowed to share resources and expertise.

The group's first GWAS, published in 2007, linked two genes—both of which previously had been associated with MS—to the risk of developing the disease, thus providing confirmation that the approach could expose relevant genes. Indeed, a therapy called daclizumab, currently in advanced trials for MS, targets the protein encoded by one of the genes.

Since that report, the consortium has expanded, and it now encompasses most researchers who study MS genetics. The group's latest paper, which utilized samples from the ACP Repository, was published in August and included 9,772 patients and 17,376 controls; a replication study to be completed next year will include an additional 11,000 MS patients. The work not only implicates a long list of genes, but begins to provide a broad biological picture of the disease, consortium members say. MS researchers have long debated whether MS is a neurodegenerative process that causes inflammation or an inflammatory process that targets the brain. Most of the genes identified have immune functions, De Jager says, which strongly favors the latter

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Mining for Genetic Riches

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explanation. Many of them help goad T cells, or lymphocytes, into action. The results “give us hints that lymphocyte activation and alterations in the behavior of these cells is important in the onset of MS,” De Jager says. Some of the genes also appear to be regulated by vitamin D, an observation that dovetails with evidence that sun exposure influences an individual’s risk of developing MS.

Beyond those general messages, no one yet knows what information researchers will glean from these gene variants, whose identification has cost \$25 million to date. The jobs of most of these genes in the body—and how exactly they contribute to MS—remains enigmatic. But with such a substantial list, researchers can begin to tackle such questions, notes Hanne Harbo, an MS geneticist at Norway’s Oslo University Hospital and one of the authors on the GWAS work. “We have many years of work ahead of us,” she says.

Still, the path is likely to be difficult, as it is in other complex diseases to which the GWAS approach is being applied. One stumbling block, for MS as well as other illnesses, is that even if researchers can uncover functions for the newly found genes, each one represents a miniscule portion of the disease’s heritability. The first-identified MS-associated gene—HLA DRB1*1501, which is involved in immunity—explains 40-50% of the inherited piece of MS, and the new batch in total explains only about 5% more. Therefore, approximately half of the familial component of the disease remains unaccounted for. “The experiment they embarked on was worth doing,” says George Ebers, a neurologist at Oxford University, but “if I was spending this amount of time and money on this and I came up with genes that explain 5% of the risk, I’d be disappointed.” Michael Demetriou, an MS researcher at the University of California, Irvine, notes that identifying numerous genes after such a long period of fruitless effort “was a definite achievement,” but

“there was an expectation that a lot more would be found.” Researchers involved in the GWAS work say that even genes with small effect sizes could reveal pathways that play a central role in the disease and might suggest druggable targets.

Although a simple explanation for the so-called missing heritability of the disease might not exist, filling in gaps from other angles could help resolve some of the mystery. GWAS scans cover only about 80% of the genome; additional common risk variants might lie undetected, although their collective effect is unlikely to be bigger than that of those already found. Furthermore, techniques that can fish out variants that occur infrequently are beginning to emerge. Such methods could identify rare variants that boost disease risk—some perhaps so uncommon that they crop up only within a single family. MS susceptibility could also be shaped by changes in gene activity that are not encoded in DNA, but rather, in heritable chemical markings on the genome; the search for such epigenetic risk factors has barely begun. Finally, genes might influence one another’s effects on the disease, and the GWAS approach misses such combinatorial phenomena. Similarly, the strategy does not identify risk-prone interactions between genes and environmental factors.

Meanwhile, the MS-related variants might have yet another use—predicting MS susceptibility not in the general population, but in people whose risk is already elevated because they have a close relative with the disease or because they have experienced an isolated episode or have MS-like lesions. What’s clear, says Yale University immunologist David Hafler, is that the hit list of MS-associated variants represents not an end but a beginning. Having those genes to work with provides a framework—previously nonexistent—for understanding the genetics of the disease. “If you’re an optimist, we have succeeded beyond expectations,” he says. “If you’re a pessimist, my response is, come on, we’re just starting.”

VOLUNTEERS

Our volunteers are a precious resource! These generous folks have been giving their time to Accelerated Cure Project in recent months:

ADMINISTRATION

Caressa Kislus
Claire Metcalfe
Kara Chmielewski
Karishma Thakrar
Melissa DelPrete
Pam Clasby
Richard Ho
Shilpi Vyas
Susan Norris
Susan Pantalone

BOSTON SHIMMER & SHINE EVENT

Ann Assarsson-Krentz
Caressa Kislus
Catherine Pisacane
Debra Robison LaRocca
Frank Favata
Janet Roche
Kristina Fanucci
Marie Rudzinsky
Melissa Delprete
Nancy Costello
Theresa Grenier
Tracey Cleversey
Tricia Cromwell
Wendy Campana

CALENDAR FOR A CAUSE 2011

Billie Jo Mendoza
Deborah Mann
Jane Harter
Kelly Basinger

MS GLOBAL 2011

Bill Hamilton

YOUNG PROFESSIONALS GROUP

Carson Lappetito
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Mohegan Sun
Not Your Average Joe’s
Ocean Edge Resort and Golf Club
Ogunquit Playhouse
Oye’s Restaurant
Rest The Back Store
Southwest Airlines
Warner Bros. Television

Upcoming Events

More information can be found at
www.acceleratedcure.org/events/calendar.php

October

October 1, 2011 until January 31, 2012

Calendar for a Cause: Cincinnati area volunteers have created a unique date book/calendar just in time for the holidays. Beautiful photographs of dogs are displayed on each calendar month and additional dog photos are on each and every page. There are almost 100 photographs in all. Several of the dog owners are diagnosed with MS and have shared their stories about their relationships with their calendar canine. Of course 100% of the proceeds are gladly donated to the ACP. The calendar measures 8 1/2 x 11, is wire-bound for easy use and is artfully executed in sepia tones. www.acpcalendar dogs.org

October 29, Boston, MA

2011 Opening Doors: This year's Recognition Dinner and Symposium will be held on October 29, 2011 at the Sheraton Boston. We hold this grand event to recognize and celebrate those who have supported our mission, both corporate and individual. Come and enjoy this fantastic night out, bid on live and silent auction prizes, and raise a glass to ACP's future progress. For more information regarding this event, please contact Karen at karen@acceleratedcure.org.

October 30, Washington, DC

Marine Corps Marathon: Our 2011 Running For A Cure team is training hard and raising funds through the People's Marathon. Please see their FirstGiving.com pages to hear their stories and to "adopt a runner."
www.firstgiving.com/acceleratedcure/marine-corps-marathon

October 30, Arlington, MA

Music To Cure MS: Classical singers and musicians donate their glorious talents for the enjoyment of ACP supporters! Local eateries will provide refreshments for intermission and gift certificates for a drawing. Visit the Music to Cure MS website, singtocurems.org

November and December

November 18, Boston, MA

December 1, Atlanta, GA

Shimmer and Shine: Stepping Out To Cure MS

This year's fashion and footwear fetes will be held at the trendy Liberty Hotel in Boston and the DeFoor Centre in Atlanta. An exciting evening that benefits the Accelerated Cure Project for Multiple Sclerosis, Shimmer and Shine gives footwear fanatics and fashionistas an opportunity to dress up and enjoy a glamorous night out on the town. Great sponsors such as Barefoot Wine and Bubbly, Lindt Chocolate, and SkinnyGirl Margarita are already on board. Our committee is always looking for new members to share their ideas and put their best foot forward to create a sensational event. For more information, please contact Kelly at 781-487-0013 or kelly@acceleratedcure.org to get involved.

New Employee Profile: Robert McBurney

Name: Robert McBurney

Occupation: Chief Executive Officer

Reason for joining ACP: This position offered me the opportunity to contribute my experience in neuroscience, drug discovery and development, and tools to optimize healthcare, to ACP's innovative approach to enabling a cure for multiple sclerosis and other demyelinating diseases.

Last Job/Occupation: Co-founder and Chief Executive Officer of Optimal Medicine Ltd.

Current Residence: Newton, Massachusetts

Hometown: Sydney, Australia

Hobbies: Any activities with family and friends; making things; golf; sailing

Ideal vacation spot: Anywhere near the sea. Cape Cod is great, especially in September.

Person (dead or alive) you would most want to have dinner with: Howard Florey, the Australian who made penicillin possible for the world. He did this by turning his Pathology Department at Oxford University into a factory to translate Alexander Fleming's scientific discovery—that a substance from a mold was able to destroy bacteria—into a revolutionary new medicine. The fellowship that brought me from Australia to Cambridge University in 1974 was instituted and named in his honor by England's Royal Society after his death in 1968.

Fuel Your Fundraiser



BJ's is Accelerating the Cure

Do you have a BJ's membership? Do you want a BJ's membership? For a limited time, if you buy or renew your BJ's membership through ACP, ACP will receive \$5 of your membership fee. For only \$40 (\$10 less than the normal fee), you will receive a second membership card for a family member, and an extra three months for free. For renewing BJ's members this means the expiration date of your existing membership will be extended by 15 months. The enrollment period is November 21 to December 9. What are you waiting for? To purchase a BJ's membership and show your support for ACP, please e-mail or call Heather at heather@acceleratedcure.org or (781) 487-0008.

Campaign Donor Recognition

Opening Doors to cure MS

Legacy Leadership Circle \$3,000,000+

Water Cove Charitable Foundation

Ambassadors Circle \$250,000+

Benificus Foundation
Return Path
Charles & Marilyn Stuckey

Directors Circle \$100,000+

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Andrew & Karen Hirschberg

The Kanner / Baker Family
Teva Neuroscience
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Diamond Circle \$10,000+

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Emerald Circle \$7,500+

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Frederic J. Marx
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Elizabeth Riley
John & Edith Sacco
Jane Shapiro
Skelmir, LLC
Vertex
Mike Westphal & Michele Sequeria

[Includes gifts pledged as of 8/31/2011](#)

Believe in the Power of the Bike (continued from page 3)

The first 20 miles of the day rolled gently along the Saskatchewan River, and the next 10 climbed through Sunwapta Pass. The climb was the biggest that we have had yet this week. It wasn't particularly steep at any point, but it was infuriatingly persistent. I was again (for a reason increasingly elusive to me) chosen to ride with the fast group, a circumstance which led to me plodding up the last few miles of Sunwapta alone, with half my group ahead and half behind.

After soaking in the vastness of this landscape, we continued down the Parkway on an amazing descent,

reaching around 55 mph. Ummm... one problem to note: We have to ride UP that descent on Friday to get back to Banff.

Saturday – Back to Banff

The weather, which began with the drenching, freezing rain on Monday, has gotten better with each day. And it couldn't possibly get much better than it was today for our final ride. We did a relatively short loop from Banff, allowing us to get back in time to disassemble the bikes and get them packed for their flights home tomorrow.

Although it was short, included in it was a tough 5 km climb to Mount Norquay, a ski area perched right

above Banff. At the top we re-grouped and snapped a few pictures of the trio of bighorn sheep eying us from the parking lot before flying down the descent back to Banff.

Great way to close out the week! We are now back at the hotel, bikes re-packed snug in their cases. It has been a fantastic week. Great riding, great people, great cause.

Jupiter Bridge

A special thank you to Jupiter for the blog. To read more please go to: jupiterbridge.blogspot.com

[To the sponsors and 30 participants of MS Global 2011 – Thank you! Together, you raised over \\$125,000 in support of ACP's mission!](#)



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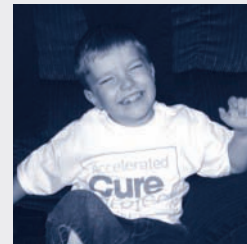
Accelerated Cure Project T-Shirt Pictures



Hannah LeBlanc,
daughter of ACP
staff member.



Robert Haynes, local
construction worker.



Sam Pantalone,
son of ACP volunteer.

ABOUT MULTIPLE SCLEROSIS

Multiple sclerosis is a chronic demyelinating disorder of the central nervous system that often results in severe disability including the inability to walk, blindness, cognitive dysfunction, extreme fatigue and other serious effects. MS affects over 400,000 people in the US and 2 million individuals worldwide. The disorder occurs twice as often in women as in men. The cause is not known and there is no known cure.

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