Winter 2013—2014

HELPING HANDS

FOR FRIENDS, FAMILY, AND SUPPORTERS OF THE CHILDREN'S GAUCHER RESEARCH FUND


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Three Legs of the Stool

… *A reminder*

By Greg and Deborah Macres

In our last newsletter we discussed that the Children's Gaucher Research Fund established and is close to accomplishing three strategic goals – to fund the following

1. **Basic Scientific Research …** create the foundation for understanding the disease
2. **Animal Model …** create a viable animal model for use in research laboratories
3. **FDA/EMA Approval …** create a road map for drug approval in the US and Europe

Because of your generous support we are close to accomplishing these goals, and collectively we are making a significant contribution in the path to find a cure. We remind you of these three strategic goals for two reasons. First, our efforts and funding of science could provide for accomplishments beyond the "Three Legs of the Stool" … we will not get ahead of ourselves but there may be more on this in future newsletters. Second, as you read the articles in this newsletter you will see how the "Three Legs of the Stool" contribute to current global scientific efforts.

Preface - Why Study Rare Disorders - The Gaucher Parkinson Story - by Ellen Sidransky, M.D

In this newsletter Dr. Ellen Sidransky tells us about the link between Gaucher and Parkinson's – giving us the history – the significance – and the future possibilities. It is an honor to have Dr. Sidransky share her thoughts. For years, Dr. Ellen Sidransky was the lone voice in the scientific community claiming there was a link, when many were dismissing her thesis. In 2006 the CGRF hosted a Lysosomal Diseases and the Brain conference with over 130 scientists in attendance. To "spice up the conference" we set up a debate of sorts between Dr. Sidransky and scientists from the Michael J. Fox Foundation. It was a Saturday night – the debate was lively – passions ran high – and although bruised, Dr. Sidransky stuck to her guns. It is clear now in 2013, she has been vindicated. With the link between Gaucher and Parkinson's firmly established, the accomplishment of the "Three Legs of the Stool" become important not only for Gaucher disease, but for Parkinson's as well.

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Deborah Macres R.N.
Founder

Gregory Macres
Chairman/Founder

Inside

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Preface - From Parent to Professional – a mothers story

It was sometime in the late 1990's when the CGRF was contacted by a mother whose beautiful daughter Madeline had been diagnosed with neuronopathic Gaucher disease. She begins her article on Page 3 by saying "Early January 1996, just a day after New Year, my life changed forever." Read this story written by a mother, Tanya Collin-Histed – think about how she responded to that devastating news in 1996. Think about the love, the courage, and the persistence that she has displayed over the past 19 years, and how her response has positively affected so many families around the world. Tanya is working closely with the CGRF as we pursue the third leg of the stool – an effort to pave the road to drug therapy approval with the European Medicines Agency (EMA).

Why Study Rare Disorders - The Gaucher Parkinson story.

By Ellen Sidransky, M.D

As a physician and a scientist, I study a rare disorder, Gaucher disease. I have been motivated to continue to study Gaucher disease for the past 25 years because I feel that our understanding of basic aspects of this disorder are still lacking, and that my patients with Gaucher disease, whom I have grown to know and love, will benefit from these discoveries.

Unexpected Association - However during the past 10 years, a discovery made in the Gaucher clinic has shown that studying a rare disorder can also have far broader implications. We noted that a few of our patients with Gaucher disease developed symptoms of Parkinson disease. This was a relatively rare occurrence, and initially we thought that it could be a coincidence- after all, having a rare disorder does not make you immune from other common diseases. But the finding persisted, and in 1994, I published an article describing 18 patients with Gaucher disease who had developed a seemingly unrelated movement disorder, Parkinson disease.

Parkinson disease is a common disorder that is known to have a complex inheritance. This means that unlike Gaucher disease, which results from mutations in one specific gene, Parkinson disease can have many causes and many genes likely contribute to how the disease presents. Patients with Parkinson disease develop a resting tremor that often begins on one side, but they can also have slowed movements, unstable posture and gait, and at times, dementia. It affects about 1.5% of the population over age 65, and the risk increases with advancing age. There are disorders associated with Parkinson disease called the Lewy body dementias that have similar manifestations, but more progressive dementia.

Shortly after we discovered an association between Gaucher disease and Parkinson disease, we noted that when we carefully asked about each patient's family history, there seemed to be many instances of Parkinson disease among relatives of patients with Gaucher disease. About 25 % of patients surveyed had a parent, sibling or grandparent with Parkinson disease or a related dementia. This caused us to speculate whether Gaucher carriers might also be at risk for Parkinson's disease.

The Link is Confirmed - The first evidence of this came from brain bank samples. When we evaluated DNA samples from patients who died of Parkinson disease, we found that 14% carried mutations in the Gaucher gene. This was so unexpected that at first no one would believe it. Journals would not publish our initial results. But the finding persisted. There were studies in the USA, Israel, Japan, and Europe that confirmed our results, that a relatively high number of patients with Parkinson disease were carriers for Gaucher disease. In 2008, sixteen Parkinson centers came together and screened over 5000 patients with Parkinson disease, and an equal number of matched controls without Parkinson disease, for mutations in the Gaucher gene, glucocerebrosidase. The combined results definitively showed that patients with Parkinson disease were over 5 times more likely to carry a glucocerebrosidase mutation, and the study was finally published in the New England Journal of Medicine. This past year, we again came together to look at mutations in glucocerebrosidase in patients with the related disorder dementia with Lewy bodies. Here, the risk for having a mutation was even higher- over 8 times that found in controls.

Now this is a widely accepted finding. Glucocerebrosidase (deficient enzyme in Gaucher disease) mutations are considered to be the most frequent known genetic risk factor for Parkinson disease and for dementia with Lewy bodies. However this does not mean that everyone with Gaucher disease, or that all Gaucher carriers will develop Parkinson disease. After all, in order to develop Parkinson disease many different factors likely come into play. Glucocerebrosidase may merely be one of these risk factors.

So why is this important? Well for one thing, insights that we gain from the study of Gaucher disease may have a far reaching impact. As we better understand all of the effects related to the deficiency of glucocerebrosidase, we will better understand Gaucher disease, but in addition, we can learn about basic pathways that may be impaired in Parkinson disease. For example, glucocerebrosidase works to break down lipids in the lysosome, an organelle that handles the breakdown products of the cell. The discovery of this association has now focused a great deal of Parkinson research on the lysosome, and it likely plays a role in the development of Parkinson pathology.

> "…a discovery made in the Gaucher clinic has shown that studying a rare disorder can also have far broader implications."

Most Exciting - But perhaps most exciting is the concept that a therapy that can impact Gaucher disease may also prove beneficial for Parkinson disease. There are many companies and centers highly invested in discovering new therapies for Parkinson disease. It is very likely that these approaches may lead to new treatments that could be used for Gaucher disease. Since Parkinson disease is a disorder that affects the brain, these discoveries could make a difference for the neuronopathic forms of Gaucher disease, which have been so hard to treat.

Research on Rare Disorders is Important - So don't ever let people discount why research into rare disorders is so important. Discoveries related to one group of diseases are likely to have benefit not only for the small patient population so needing the research, but advances and treatments can have important implications for others with far more common disorders.

Ellen Sidransky M.D.
Head – Molecular Neurogenetics Section
National Institutes of Health
Bethesda, Maryland, USA

From Parent to Professional – *a mothers story*

Early January 1996, just a day after New Year, my life changed forever. At the time, the bottom literally fell out of my world, finding out my daughter Maddie aged 16 months old had a rare neurological disease was a period of three or four months where my days were long, spent in a strange place, miles away from home, sleeping in a parents room (in bunk beds), with a small cupboard to store my clothes and having to queue up in the morning with other mothers to wash. Not to mention the regular interruptions of nurses in the middle of the night in search of someone's mum because they were needed on the ward urgently.

Seventeen years later Maddie is now 19 years old, an inspiration, a tough cookie, having survived many roller coaster rides of pain, bouts of depression, endless tests, hundreds and hundreds of needles, delivery of bad news, medicines galore and countless people intruding in her life.

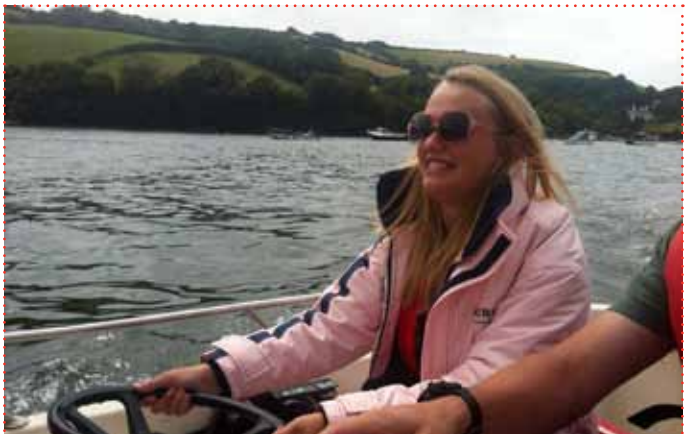
It took me a year to really get my life back to some sort of normality, by that I mean juggling work with having a sick child, the guilt, a broken marriage, being able to pay the bills now that I was a single parent and having to attend regular hospital appointments, arrange fortnightly infusions and supporting community nurses that cried every time they came to help me give Maddie her infusion as she had a needle phobia and had to be restrained.

In 1997 the feeling felt through the loss of control to protect my daughter, to take away her pain, the pain inside me caused by knowing this was caused by me and Maddie's dad passing on our defected genes caused a fire so strong inside me that I knew that I had to find a way to feel like I was doing something.

I felt so alone, the literature was woolly, frightening, my friends were wonderful but they didn't really know how I was feeling. I knew that there were other parents out there that were in the same position as me so I started to attend meetings of the UK Gauchers Association, I asked questions and in late 1997 I was asked to join the board of trustees to be a representative for neuronopathic Gaucher disease (the children's form that affects the brain).

You could say the rest is history really; I always said that as long as Maddie was well I would do whatever I could to support other patients and their families with Gaucher disease. Despite a tough road, Maddie has remained stable and this has allowed me to travel around the UK and the World supporting parents and patients to access charitable treatment in countries where there isn't any reimbursement programs through their Ministry of Health; assist in setting up new patient groups i.e. in Pakistan and supporting emerging patient groups; educating and supporting doctors to improve their knowledge of Gaucher disease and how best to treat Gaucher patients and pushing scientists and pharmaceutical companies to advance the boundaries of research into

"Early January 1996, just a day after New Year, my life changed forever."



"… Maddie is now 19 years old, an inspiration, a tough cookie, having survived many roller coaster rides of pain, bouts of depression … and countless people intruding in her life."

nGD which has proved to be hugely challenging and a very slow road. In 1996 when Maddie was diagnosed, gene therapy was 10 years away, 17 years later it is still 10 years away.

My heart however has always laid with the patients and their families, whether its travelling 200 miles to hold a mother's hand whilst she cries on my shoulder in pain as she watches her daughter disappear in front of her eyes, or spend the afternoon with a young women with Type III Gaucher disease who feels that life isn't worth living. Patient support is where I feel I have been able to help others the most. We are a small UK community and throughout the world I have discovered many more small communities of nGD patients, some with treatment, many without, but knowing that you are not alone is a comfort in what is often a very lonely and uncertain life.

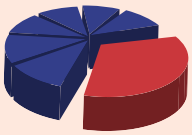
"… the pain inside me … caused a fire so strong … that I knew that I had to find a way to feel like I was doing something."

As many treated nGD patients get older and too many untreated nGD patients lose their battle with Gaucher disease, the need for a cure has never been more critical. We live in a world where we now have four drugs for Gaucher disease, however none of them cross the blood brain barrier and the neurological aspects of the disease continues to burden these patients and their families lives, often taken too soon from this world. For those whom treatment has given them a life and a future, the disease continues to throw up many new challenges not seen before as these patients would have lost their lives many years ago, these include; seizures, mental health issues; challenges with education, employment, relationships and independence to name a few. Sadly despite the increase in the number of drugs available for Gaucher Disease, the access for patients who live in countries without reimbursement has reached a critical point. The competition has diluted the market for the companies involved and they have had to limit the amount of charitable access they can contribute, therefore despite a huge amount of drug being produced patients are not being treated and doctors need support and guidance on how best to treat the ever growing number of patients who because of where they live in the world are not treated with ERT or SRT but who need to be supported clinically … sadly many of these are very young children who sadly pass away.

So I wear three hats; I am first and foremost Maddie's mum; secondly I am the Chief Executive of the UK Gauchers Association and thirdly the Executive Director of the European Gaucher Alliance (representing 40 member countries). This means that I help make up Maddie's treatment; I sit in clinic and hold her hand; I meet with NHS England to ensure access to good clinical care and treatment for patients in the UK; I meet regularly with patients and their families in their homes especially newly diagnosed patients or patients in crisis; I stand by the graveside to say goodbye to friends and see our group get smaller and smaller and I travel to India, Russia, Bulgaria, the Middle East, Ukraine, Macedonia to meet with clinicians and Government officials to advise on how to develop their infrastructure to support patients. So, Gaucher is my life, embedded in my soul, every day I think about all the people that I have been fortunate to meet, the amazing families, the dedicated doctors, the far thinking pharmaceutical companies, colleagues who work tirelessly in other countries in Gaucher disease and other lysosomal storage disorders who have been a tremendous support to me.

I believe it's good to smile, things are changing, patients are better supported, but sometimes it's hard, sometimes behind the smile is sadness that so many people are still suffering. We wish there was a cure – there is not – but the foundation of research has been built and there are many dedicated researchers and clinicians in the US, Europe and globally who are working collaboratively to find a cure. This is new and ever growing over recent years – and this provides hope for the future.

Tanya Collin-Histed
Chief Executive
The Gauchers Association
United Kingdom



2012 Financial Audit

The CGRF receives a Clean Bill of Health

The Children's Gaucher Research Fund just completed a Financial Audit for the 2012 calendar year and for the fifth year in a row received a clean bill of health. In May of each year the CGRF files our 990 Tax Return to the IRS - we then enter the summer season accumulating financial documentation to satisfy the requests of the Certified Public Accountants that review our books. This financial audit combined with a global audit of our efficiencies and program effectiveness has resulted in the CGRF receiving the …

Best In America Seal

"The Independent Charities Seal of Excellence is awarded to the members of Independent Charities of America and Local Independent Charities of America that have, upon rigorous independent review, been able to certify, document, and demonstrate on an annual basis that they meet the highest standards of public accountability, program effectiveness, and cost effectiveness. These standards include those required by the US Government for inclusion in the Combined Federal Campaign, probably the most exclusive fund drive in the world. Of the 1,000,000 charities operating in the United States today, it is estimated that fewer than 50,000, or 5 percent, meet or exceed these standards, and, of those, fewer than 2,000 have been awarded this Seal."

> "Of the 1,000,000 charities operating in the United States today … of those, fewer than 2,000 have been awarded this Seal."

Awake-A-Thon

$10,480 Raised

"Awake-a-thon 2013 was a tremendous success with 375+ attendees and $10,480 funds raised in 12 hours! Awake-a-thon is hosted annually by high school students at Pleasant Grove High School's Key Club. Students from Sacramento, Stockton, and Rocklin are invited to stay awake for 12 hours and raise money for local charities. From attending an exciting rally with ice breakers and educational speakers, to dancing the night away at midnight, to participating in various basketball, dodge ball, and volleyball tournaments until dawn, Pleasant Grove Key Club promises a memorable experience to reward and thank all attendees for their generosity and continual efforts to support the Kiwanis Family House and the Children's Gaucher Research Fund."

Megan Su
President - Key Club
Pleasant Grove High School
Elk Grove, California

ONLINE DONATIONS

can be made by visiting
www.childrensgaucher.org
OR
www.cgrf.org
All family stories can be read on the web site.

100% TO RESEARCH

You need to know:

1. The CCRF is a *legitimate* IRS approved 501 c3 non-profit organization.
2. *100% of every donation* goes to medical research.
3. We *do not* hire professional fundraising companies who keep 50% of donated funds.
4. We have talented volunteers who *donate* their time and talent for a variety of our needs.
5. All administrative costs are paid for by the *founders.*

Simply put: if you send your hard earned dollars - *It ALL goes to medical research.*

Visit our web site at:
www.childrensgaucher.org
All family stories can be
read on the website.

Contributions Payable To:
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