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

Helping Hands

Summer 2003

www.childrensgaucher.org

Gregory Macres
Chairman/Founder

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Founder

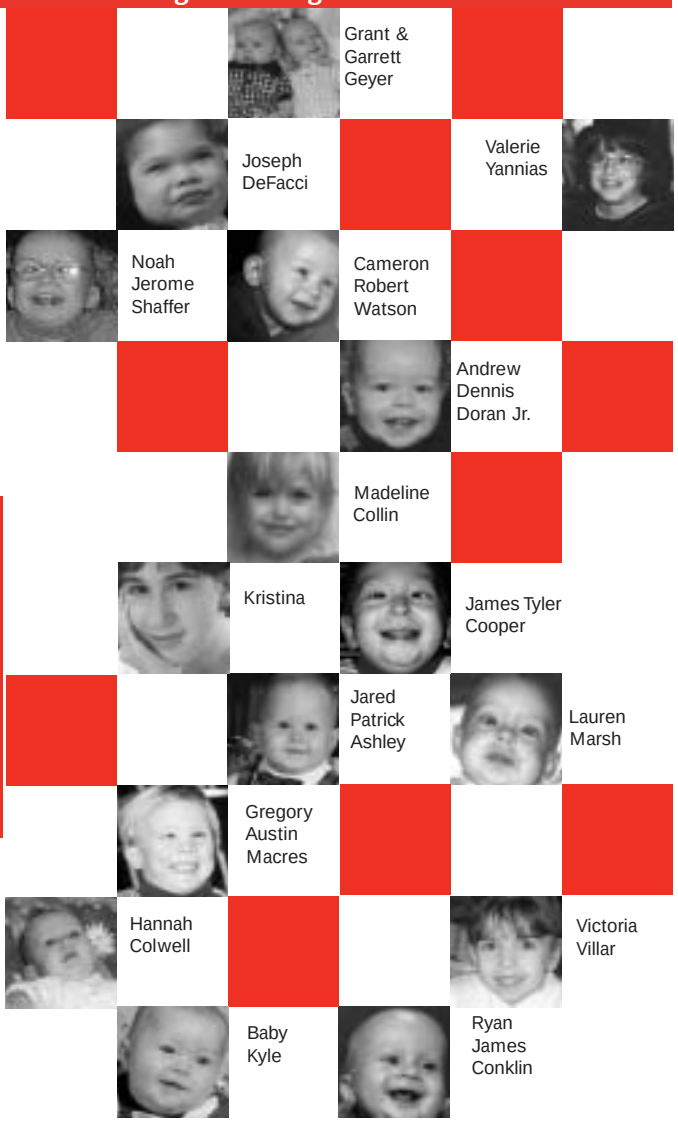
In this newsletter you will read about two families, and two children, who faced the challenge of Gaucher disease. Challenges in life cannot be predicted, yet we find that adversity often brings forth lessons we carry with us for a lifetime. Faced with adversity, a sick child displays a graceful innocence and a courage we cannot explain. We find children whose lives have been curtailed by a caprice of nature, yet whose smiles give us hope for the future. Faced with adversity, we find parents whose grief is transformed to hope. A Mother who says her daughter "was given to me to teach me the true meaning of love, faith and devotion … I learned to believe and have faith … I learned to be stronger than I already thought I was." Parents, who after losing their child to Gaucher disease, choose to join this effort to find a cure. In the midst of grief, adversity can bring forth life's finest moments.

We have learned the true meaning of devotion, and we have transformed it into a commitment, a commitment to find a cure. With your donations, in May of 2003, the Children's Gaucher Research Fund funded a second year of research with Dr. Tony Futerman of the Weizmann Institute of Science, in Rehovot, Israel. Dr. Futerman is blazing a new trail of research, searching for the exact cause of neuronal degradation in children affected by this most devastating disease. In this newsletter, Dr. Futerman will detail his research in the coming year.

"Do not go where the path may lead, go instead where there is no path and leave a trail."
-Ralph Waldo Emerson

You are helping us clear the path. You are creating a trail of understanding that we hope will lead to a cure for Gaucher disease Type 2 & 3. Many believe that the trail you are blazing may also create a better understanding of other neurological diseases that affect the brain. We appreciate your commitment and we thank you for your continued support.

The Only Thing Incurable Is Our Passion



See Family Stories Page 3 & 4

The Calcium Connection *A Continuing Story*

It is now 2 years since I wrote my first article for the Children's Gaucher Research Fund. Much has happened in this period, including significant progress in our research effort to understand the biochemical mechanisms that cause neuron degradation in Gaucher Disease. But before getting down to the nuts and bolts of what we have been doing in the laboratory, I would like at the outset to express my enormous and heartfelt appreciation to the fund for generously supporting my research over the past year, and for agreeing to fund our work for another year. Funds for scientific research normally come from national funding agencies, or from commercial companies interested in the 'bottom dollar', or from philanthropic organizations with huge bank accounts. The Children's Gaucher Research Fund is different. Originally established in 1999, by parents who lost a child to this devastating disease, hard-earned dollars have been donated by ordinary folk whose common passion is to find a cure for this disease. I find it quite remarkable to see how the balance of the fund has crept up year-by-year and month-by-month, due to a large number of relatively small

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donations rather than by mega-donations from one or two individuals or companies – of course, I am sure that the fund would nevertheless appreciate the latter! However, as someone whose research has directly benefited from this fund, I raise my hat in admiration to those who have so selflessly and generously given over the past few years, and to others who have given their time and energy to running the fund. I can only trust that my research team, along with others who will hopefully become involved in the research effort in the future, will be able to provide some answers as to why the brain is affected in those children who suffer from this disease. Although the road may be long, I genuinely believe that we have begun to travel in the right direction.

Now for the science. By way of reminder, the story so far is that in 1999, my research team made a finding that suggested that calcium, a key player in the normal functioning of nerve cells (neurons) in the brain, was altered when nerve cells from rat brains were cultured in a petri dish in such a way that they acted as a model of neuronopathic Gaucher Disease. This finding formed the basis of the work that we have been doing over the past couple of years, and specifically, during the first year of funding from the CGRF. Our goal in this period was to find out how the lipid that accumulates in Gaucher Disease, which is called 'glucosylceramide' or 'glucocerebroside', causes these unexpected changes in calcium functioning in nerve cells. To test this, we examined the effect of the lipid in biochemical experiments in a test tube, and showed quite clearly that glucosylceramide has a very specific effect on a protein, the 'ryanodine channel', that is partially responsible for regulating calcium levels in neurons. The remarkable thing about this finding is the specificity of the effect, inasmuch as only glucosylceramide, and no other similar lipid, affects the 'ryanodine channel'. This finding was recently published in a peer-reviewed scientific journal, the Journal of Biological Chemistry, and is, I believe, a significant milestone in our research. We also showed that this research is relevant for Gaucher Disease as we saw a similar effect in human brain tissue obtained from an autopsy of a Child with Gaucher disease, and are currently continuing these studies with the remaining autopsy tissue that is available. Although I realize that this is a sensitive and emotional issue, this is perhaps the place to stress that this research will proceed rapidly if such tissue continues to be available to us in the future, but more slowly if such tissue is difficult or impossible to obtain. Finally, another milestone in our research was the development of a new biochemical technique to measure accurately how much glucosylceramide accumulates in small amounts of brain tissue, which will allow us to determine if specific brain regions are affected in the disease, and hence may explain why specific neuronal functions are impaired in patients.

Those of you who attended the CGRF conference in Washington DC last fall will realize that there is a lot more detail about the science that I cannot explain in such a short article, and if you really want to get into the nitty-gritty of the research, then you are welcome to read the three scientific papers that have so far been published as a result of the fund's support. But I warn readers without a medical or scientific background that this is far from light reading before you turn in for the night! To be serious, it is clear that a cure for the disease is only going to be found if we understand, at a very detailed level, the biochemical mechanisms affected when the offending lipid accumulates in brain tissue. By way of example, now that we know that 'glucosylceramide somehow interacts with the ryanodine channel', one therapeutic avenue might be to block this interaction with a new drug, or with a drug that already exists, such as a calcium blocker. This is an approach that we are currently exploring, and will be part of our research effort during the second year of the CGRF research grant. As mentioned above, our major goal in the coming year is to determine whether there is any biochemical specificity in the brain regions affected in Gaucher Disease with a view to providing clues to explain specific neurological abnormalities.

None of the research described above would have happened without the help of an outstanding team of dedicated colleagues in my research laboratory in the Weizmann Institute in Israel. Amongst these are my research technician, Mrs. Rivi Zisling, who has been working with me for over a decade, a visiting student from the UK, Emyr Lloyd-Evans, who together with an Israeli student, Dori Pelled, and a German postdoctoral fellow, Dr. Christian Riebeling, spent more hours in the laboratory than at home and were the real movers behind the day-to-day aspects of running this project. In addition, it has been a privilege to work with Dr. Raffi Schiffmann from the National Institutes of Health in Bethesda, Maryland, who not only made his autopsy collection freely available to us, but also helped us integrate our biochemical findings with the clinical features of neuronopathic forms of Gaucher Disease. Indeed, one of the areas that has given me the most pleasure over the past couple of years has been seeing the relevance of our basic research to understanding a human disease. Although the nature of scientific research precludes guarantees or making false promises about whether we will eventually succeed in finding a cure for these children, or in suggesting novel therapies, I can assure you that we will leave no stone unturned in our efforts to provide a glimmer of hope for patients and parents alike.

I find it quite remarkable to see how the balance of the fund has crept up year-by-year and month-by-month, due to a large number of relatively small donations rather than by mega-donations from one or two individuals or companies – of course, I am sure that the fund would nevertheless appreciate the latter.

Victoria Villar - 8 yrs. (left) and Valerie Yannias - 6 yrs.- (right) meet and share at the CGRF Conference on October 24, 2002.

Excitedly, the girls said, “This is the first time we have met someone else with the same disease.”

A Vistor from Heaven

Hannah E. Colwell

Hannah Elizabeth Colwell was born on June 2, 2000. Just a few months prior to her birth, we received the devastating news that her 18-month-old sister, Sarah, was profoundly deaf. That was just the beginning of a traumatic year. Soon after Hannah was born, her father and I separated. But still, I believed that everything would be all right. I had three beautiful daughters, Emily, Sarah, and Hannah. We would face what was to come, together.

Hannah was a happy, healthy baby. She had the most precious smile with those silly crossed eyes. I would call her my little cross-eyed baby. I thought the problem would resolve itself, but it never got better. Around the age of 3 & 1/2 months, I noticed a change in Hannah. Something was not right. And one day, I began to make loud noises around her as she slept. Hannah's hearing was gone. But, I still believed, eventually, everything would be all right.

Then came double the trips to Children's Hospital of Cincinnati for audiology appointments, cardiology appointments, ear nose and throat, and ophthalmology appointments. At the beginning of her sixth month, she became very ill which brought us to the emergency room at Children's Hospital. At the end of our two-week stay in December 2000, the pediatrician discovered her enlarged liver and spleen. They took her to surgery for a liver and muscle biopsy and sent us home on tube feedings. Being a nurse, I felt confident that I could take care of her. As a Mother, I was scared to death.

We anxiously awaited the results of Hannah's test as we struggled to make it through the holidays. After the first of the year, we received a preliminary diagnosis of Gaucher Disease. We were referred to one of the top genetics specialists of Gaucher disease, Dr. Greg Grabowski and his genetics counselor, Laurie Bailey. I will never forget the day of January 8, 2001. My life and the lives of my children were changed forever. My little cross-eyed baby, who always smiled, seemed to be getting sicker, weaker and more sad. I am not sure that I actually heard much of anything that Dr Grabowski said to me except for those words that I just knew he was not going to say; "This disease is fatal." I felt like someone just ripped my heart from my body! Not my baby, not Hannah! There are no words that can describe the feelings that a mother experiences when she learns her baby is going to die.

I struggled most of my life with believing in God. Well, this did it for me. No God would take away my baby. No God would make her suffer this way. Why was this happening?

That day was the beginning of endless trips to the hospital. Just prior to her surgery for a mediport, Hannah was baptized in the hospital. We began to find ourselves in the mist of a whirlwind of Hospice, social workers, doctors, nurses, home healthcare personnel, therapists and so on. The support that my children and I received from our friends, the staff at Children's Hospital and Westside pediatrics, was incredible. They became our family. Emily, 7.5 years old at the time, was a very strong and loving older sister. Sarah, 2.5 years old, was affected so terribly by the separation of her father and I, by learning to cope with her hearing loss, and most devastatingly, she knew she was losing her baby sister, who she held in her arms everyday. The image of Sarah walking up to Hannah's crib, rubbing her hand across the mattress and asking, "Mommy, where Hannah," will never leave my thoughts.

The days and nights were continuous, never ending cycles of trauma and turmoil. Hannah rapidly moved through the stages of Type II Gaucher like a text- book story. Soon we would meet our angel of mercy, Julie. She was our home hospice nurse who loved my little Hannah as if she were her own. Questions arose; should we let her die at home? Should we be at the hospital? Should we make her a DNR (Do Not Resuscitate)? Little did I know at the time, but Hannah let me know the answers every step of the way. I began to plan her funeral, not knowing that it was only about a week away.

We lived day-by-day, then hour-by-hour, then minute-by-minute. She had continuous spasms that would keep her from breathing and she would turn blue. The fluid would build in her lungs and require continuous suctioning. Why would God make my baby suffer this way? No child should ever experience this kind of pain.

The day before she died was the calm before the storm. We only gave her medicines to make her comfortable. And, we just waited. She held on so tight and so did I. Finally, Julie explained to me that I needed to tell Hannah that it was ok with me for her to let go now. It really was not! But, I knew I had to do it. I knelt down beside her lying on the couch and told her that I loved her and would love her forever. I told her that it was ok to let go now. She passed that day on March 7, 2001 at 4:30 in the afternoon. She was only 9 months and 5 days old. She took a part of me with her. But she also left so much of herself behind in me.

My heart was broken and I thought I would never recover. Although my struggle with Hannah's illness was over, my struggle with understanding her life had just begun. I began to believe that here is a God and he is holding my baby in His arms everyday. He gave her to me because He knew I could love her like no one else could. And, He gave her to me to help me learn a lesson about life. I just could not figure out what that lesson was until over a year later when I read Joseph DeFacci's story (a little boy who lost his battle with Gaucher disease). Hannah was given to me to teach me the true meaning of love, faith and devotion. I learned that no one can control life or the people around them. I learned to believe and have faith. And, I learned to be stronger than I already thought I was. Thank you, Hannah, for touching my life and so many others. Thank you, God, for giving me an angel. Now, everything is all right.

I am happy to support the Children's Gaucher Research Fund and help in any way possible to find a cure for this devastating disease. This foundation is a family like no other that helps others through a never-ending cycle of grief. Their prayers and support showed me that I am not alone. Hannah has devoted her part to helping with the research of Gaucher Type II Disease. With this and the help of so many others, one day we will find a cure.

Susan Novinger
Cincinnati, Ohio

"Hannah was given to me to teach me the true meaning of love, faith and devotion … I learned to believe and have faith … I learned to be stronger than I already thought I was."

Baby Kyle

Kyle was born on June 22, 1993 weighing 11 lbs 1 oz. Kyle was the picture of health. We came home from the hospital 2 days after Kyle was born. July and August were uneventful. Kyle was your typical 2-month-old little boy. In September of 1993 we noticed some congestion in Kyle's chest but put it off as just a summer cold. Kyle had a choking spell in September and we were able to clear him. Again, we put it off as the formula going down the wrong pipe. The congestion was not getting better so our doctor referred us to an allergist. Kyle was tested negative for all of the normal allergies. Meanwhile, the congestion was continuing so the doctor thought Kyle was allergic to his formula. Again Kyle had another choking spell which was harder to clear. In November of 1993 Kyle went for a well baby check and the doctor told me that Kyle was very stiff for a 5-month-old and his head was slightly back. The doctor suggested that Kyle might have Cerebral Palsy. Kyle's congestion was only getting worse and in December of 1993 Kyle was hospitalized for the RSV virus. He spent about 4 days in the hospital and was sent home. We had an HMO and they were not really enthusiastic about sending us to real doctors. They kept us with their own team of doctors that only frustrated us, and it was not helping our son.

In January of 1994 we were at a restaurant in Syracuse and Kyle had a choking spell. This was the worst choking spell he had had, and he was rushed to Syracuse University Hospital for Children. Since this was a teaching hospital we went over and over Kyle's symptoms a million times with every intern. He was admitted to the hospital and the doctors told us he would not be released until they found out what was wrong with him. Kyle went through so many tests. A spinal tap, an acid reflux test and blood work that was sent to the Mayo Clinic. The neurologist finally diagnosed Kyle with Gaucher II but to be exact they had to wait for the blood work to come back. We prayed they had made a mistake and the blood work would be negative. Kyle was diagnosed in January of 1994. The doctors handed us a sheet of paper with one paragraph about Gaucher II. They told us there was no cure and he would not live past the age of two. I felt dead. They told us they only knew of one other case, in Cincinnati, Ohio, where Dr. Gregory Grabowski would prove to be the most informed.

Meanwhile Kyle's choking spells were getting worse. They put a GT-tube in Kyle's stomach before we took him home. While at home, Kyle choked again and was rushed to the hospital. The doctors told us that Kyle would not live much longer. Our only hope was a tracheotomy. Kyle's Father was against it but I could not bear to lose him so soon. Kyle was trached and he came home again from the hospital. The trach did give him some quality of life, nothing compared to a normal life, but more than he had. We had nurses 8 to 16 hours per day. Kyle was watched continuously. He was never alone. Kyle never sat up after he came home from the hospital. He never walked. Gaucher disease made him very stiff, which made it very uncomfortable for him to be picked up. Kyle did smile a lot. From the beginning of his sickness, Kyle remained such a pleasant baby.

> Through the efforts of the Children's Gaucher Research Fund parents not only have support, but they now have something even more important - Hope.

In April of 1994 I heard about a drug, an enzyme replacement called Ceredase. I spoke with Dr. Grabowski and he said he would prescribe the medicine for Kyle. I wanted it for the relief of his enlarged liver and spleen. I realized this would do nothing for the neurological damage that had already occurred. Kyle received his first dose in the hospital in case of a reaction. After the first dose, we had a Hickman catheter placed in Kyle's chest so he could receive the Ceredase infusions. A Registered Nurse gave the medicine at home.

Kyle's stomach reduced in size and we felt he was more comfortable. Kyle's day was spent lying in front of the TV or with someone reading or talking to him. Towards the end of 1994, Kyle was getting worse. Kyle was back in the hospital in November of 1994. When we returned home we were trained on how to administer morphine to keep him comfortable. In 1995 Kyle continued to get worse. He weighed only 11lbs. The same weight he was when he was born. Through the months we spent as much time with Kyle as we could. He celebrated his 2nd birthday on June 22, 1995.

It was July 30, 1995, at 4:00 am in the morning when I woke up to check on Kyle. He was resting peacefully. I gave him a kiss and told the nurse if he felt good to start his feeding at 6:00 am. That was the last time I saw Kyle alive. He passed away that morning. He was at peace, his face was so peaceful and he looked so calm and rested.

As Kyle's mother, I will never get over his loss. I move forward but I am not whole. I compare it to losing an arm, you go on the best you can, but everyday you look down and know a piece of you is missing. Knowing that doctors are now looking for a cure gives me peace. Through the efforts of the Children's Gaucher Research Fund parents not only have support, but they now have something even more important - Hope. One day, when a child is diagnosed, doctors will tell the parents, "It will be okay. We have a cure".

Adrienne and Phillip Herrell
Suwanee, Georgia

MATCHING GRANT NEEDED

In May of 2003 the Children's Gaucher Research Fund funded Year 2 of Research with Dr. Tony Futerman at the Weizmann Institute of Science in Rehovot, Israel. We are currently looking for a matching grant in the amount of $58,000 (Total Grant amount = $116,000). If you are aware of an individual, company or foundation that would be interested in partnering with this research please contact us at research@childrensgaucher.org.

100% Of Donations Go To Medical Research

Charity Golf Tournament

The Second Annual Coldwell Banker Sacramento/ Tahoe Charity Golf Tournament to benefit the Children's Gaucher Research Fund (www.childrens-gaucher.org) was held on June 9 at Whitney Oaks Golf Club in Rocklin, CA. The full-field shot gun began at 12:30 p.m. with 156 golfers participating in 18 holes on a mild summer day. Tee sponsors such as local title and pest control companies held exciting contests at their holes including a spa retreat, spiked lemonade, fishing for prizes, a marshmallow drive and Coldwell Banker Mortgage's "Beat the Pro" hole which raised an additional $680 charity donation!

Over 200 people enjoyed the cocktail hour, dinner and awards held after the tournament. Although the final donation for charity is still being tallied, an early estimate is about $30,000 with more than half of it raised from a prize raffle, 50/50 money raffle and live auction.

A special thank you goes out to all who participated in this fun-filled event, especially the tournament committee and volunteers: Les Boomer, Bob Bronswick, Jeff Culbertson, Robert Culbertson, Maxine Feil, Sher Granata, Lois Harding, Nanette Miner, Gregory L. Parker, Sandi Burden-Bradley, Heidi Bonnell, Jenifer Culbertson, Daunielle Cutting, Kris Davis, Michelle Harris, Jennifer Hobbs, Melissa Huntsman, Theresa Johnson, Malka Khan, Ashley Macres, Deborah Macres, Katie Minor, Barbara Navarrete, Susan Pierce, Kenneth Prescott, Jamie Schlicher and Jason Waggoner.

"It seems to happen. You might think it was someone who has lost a child to Gaucher disease. You then realize that this is someone who has never heard of Gaucher disease. They raise their hand; they agree to captain the ship. Instead of doing a good job - they immerse themselves – they do a great job. This is Carol Black, the Captain of the Coldwell Banker Charity Golf Tournament Committee. We thank you Carol for your tireless efforts.

In Loving Memory Of

Haley Elizabeth Young

2/15/02 to 4/14/03

Villas, New Jersey

In Loving Memory Of

Emma E. Pozzobon

12/18/96 to 11/06/02

Auburn, Washington

Helping Hands

Visit our web site at:

www.childrensgaucher.org

All family stories can be read on the web site.

"The similarities between Neuronopathic Gaucher Disease and the Lewy body dementias are so great, that therapy for Neuronopathic Gaucher Disease may impact Diffuse Lewy body disease, the second most common cause of dementia in the world. Thus, the monies spent on one disease may have an even greater impact upon a more prevalent scourge of mankind."

-Koni Wong M.D. Lt Col. USAF MC
Armed Forces Insitute of Pathology

Contributions Payable To:
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