Winter 2003 - 2004

HELPING HANDS

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

Valerie Yannias | Victoria Villar | Gregory Austin Macres | Noah Jerome Shaffer | Baby Kyle | Jared Patrick Ashley | Joseph DeFacci | Andrew Dennis Doran Jr. | James Tyler Cooper | Lauren Marsh | Ryan James Conklin | Cameron Robert Watson | Kristina C. | Madeline Collin | Grant & Garrett Geyer | Hannah Colwell

A short time ago we were asked, "How close are you to a cure?" We responded, "We don't know, and it does not matter. What matters is that we know the final outcome – and it will be a cure!" We should pay no attention to the score at halftime. The reality with medical research is that a cure could be ten days away, or ten years away. We will not let the enormity of the task deter us. The score at halftime does not matter, because with people like you, we will find a cure.

The Children's Gaucher Research Fund believes that anything is possible. We believe this because we have found through this effort that people do care. It is your support that will lead us to a cure for this rare children's disease.

The effort to find a cure for Children's Gaucher disease is making great progress. You need to know that your support for this effort goes far beyond Gaucher disease. Our Scientific Advisory Board believes that the research you are funding will likely help in finding a cure for other Lysosomal Storage diseases that affect the brains in young children. We have included in this newsletter, "A Layman's Overview", that will help you appreciate the future potential of the research you are funding.

We can only begin to wonder what affects our efforts today will have upon thousands in the future. One day a doctor will meet with a concerned mother and father and say the words, "Do not worry, we have a cure". There will not be tears of sadness, but tears of joy. Parents will be spared the agony and children will be given a chance at life. That day will come. We will find a cure. Each of you will own a small piece of that cure. Each of you will own a small piece of those tears of joy. We believe in our hearts that the day will come, that parents will thank God, and God will thank you.

"Anything Is Possible, If Enough People Care."

Lou Holtz, *Head Coach, Notre Dame Football*

Gregory Macres
Chairman/Founder

Deborah Macres R.N.
Founder

The Only Thing Incurable Is Our Passion

Emma C. Pozzobon

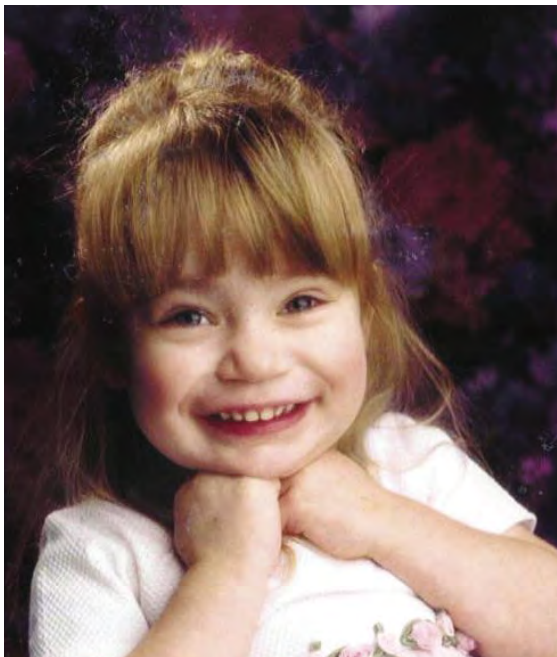
An Angel From The Beginning

Emma was an angel from the very beginning. When I was pregnant with her I knew she was special and was going to touch many people's lives, but I really didn't realize how right I was.

On December 18, 1996, Emma was born, and this day was when she made her first visit to the N.I.C.U. (Neonatal Intensive Care Unit). She was not able to remove all of the fluid from her lungs and needed to be watched closely. She recovered and Scare # 1 was over. I took her home 27 hours later - she was a good baby. She loved to be snuggled and this is how she got her nickname "Buggy". Emma progressed normally, and in some cases above normal in her developmental skills like rolling over and crawling. She never ate very much. She would eat often but only drink an ounce or two at a time. Emma seemed smaller than other children her age and this was confirmed, as she was not keeping pace with the growth charts. At the time we attributed this to her simply being a tiny baby, as this seemed to run in our family.

At 10 months old Emma tried to walk. She was doing very well and then one day she just stopped trying. We then noticed her eyes were doing a funny thing. When Emma turned her head to look at some-

see *ANGEL* page 2



Angel

continued from page 1

thing it was like she moved her eyes sideways then her head would follow. Like a sprinkler, only side-to-side never up and down. I later learned that this was Supra Nuclear Gaze Palsy, a common symptom of Neuronopathic Gaucher disease. We then received Scare #2. Emma had a cold and developed little red bumps all over her body, especially around her socks and diaper area. This was called petechia. The Doctors immediately tested her for Leukemia. We thanked God when the tests came back negative. It was decided that the petechia was a result of her cold and low platelets.

We discovered we were pregnant again right after Emma's first birthday. Shortly thereafter Emma got very sick with a virus. She had diarrhea for nine days. Each night I would rub her tummy for comfort. Once night, I noticed there was one side that was hard as a rock, while the other side of her tummy was soft. I took her in the next day for her follow-up appointment for the virus and the doctor sent us for an immediate ultrasound. When I returned to her office the ultrasound results showed her spleen was 30 times larger than normal and her liver was 5 times larger than normal. We were immediately sent to Children's Hospital. At Children's Hospital Emma endured endless testing, and it was concluded that she had Gaucher disease. Emma began enzyme replacement therapy a month or so later and she improved tremendously. Her liver and spleen reduced in size. Within 18 months her spleen was normal size, something her physicians never thought would happen. When our second daughter was born it was recommended that we keep her stem cells. We did so, and as it turned out Emma and Maddi were a perfect match.

At this time Emma became more unsteady as she walked. In addition , her unusual eye movements seemed to be getting worse, so we scheduled an appointment with a Neurologist. After observing both her walking and her eye movements, he concluded that she had the classic neurological symptoms of Gaucher disease. It was at this time that we decided to do a Bone Marrow Transplant. This was one of the most difficult decisions I have ever had to make. With the stem cells being a perfect match everything seemed to be "in her favor", so we decided to move ahead with a Bone Marrow Transplant. On May 15, 2000, at 3 years old, Emma underwent a Bone Marrow Transplant. We almost lost her 4 weeks into the BMT due to seizures and other complications. At one point she had complete kidney failure, but eventually she returned to full function. She also had severe Graft Versus Host disease. Emma's determination amazed the doctors and nurses. She tried so hard, but was unable to walk after the transplant. One year after transplant she lost her ability to talk, and began communicating by pointing and using inaudible sounds.

It became clear in the last nine months of Emma's life that she was losing the battle. Her seizures became uncontrollable. Emma was now on 6 different seizure medications. Despite this, she would still have 100-150 seizures a day. She was eventually on oxygen, an oxygen saturation monitor and a feeding tube. As her mother, watching her go through this was heart wrenching! I simply wanted to be her Mother, not her nurse.

The last couple of weeks she did not want to watch her movies that she had enjoyed so much. She was frustrated, and just wanted to sleep and be held. Emma then went into "status" seizures. She was now in a "medical coma", where she continued to have seizures. She had a breathing tube, her blood pressure was low, and her heart rate was high. On November 6, 2002, with our second child on the same floor of the hospital with gall bladder surgery, we made the decision to let her go. This was the hardest and most difficult decision of my life. One I will struggle with, for the rest of my life. Emma left us peacefully, just prior to her 6th birthday. I miss her so much - I was the luckiest person in the world - I was truly blessed to be Emma's MOMMY~!!

Caring for Emma was exhausting. Looking back I don't know how I did it day after day. I had the help of her Grandma's, a wonderful neighbor and Emma's Father. Despite the hardship, I would do it all over again. I would take her back in a minute – to care for her – to take away her pain – to tell her how much I love her. The Children's Gaucher Research Fund has brought support, and has allowed for the opportunity to talk with other families. There is comfort in knowing that you are not alone. I have chosen to join this effort to find a cure, and I will do what I can to help this come to pass. When the day comes that we find a cure, I know that Emma will be smiling down upon us.

Jeanice St.George
Auburn, Washington

"When the day comes that we find a cure, I know that Emma will be smiling down upon us."

Gaucher Disease

"A LAYMAN'S OVERVIEW"

In past newsletters we have included many articles written by members of our Scientific Advisory Board and by researchers whom your generous donations are currently funding. If you are not involved in the medical field, Gaucher disease can be overwhelmingly complex when discussing metabolic defects, the pathogenesis of the disease, or clinical symptoms such as splenomegaly. Here we go again, using these Big Words! So we have decided to explain Gaucher disease in its simplest terms – "A Layman's Overview". We will explain the disease in a logical progression, from the basic genetics (how a child gets the disease) through the potential outlook for a cure.

FIRST THE GENETICS

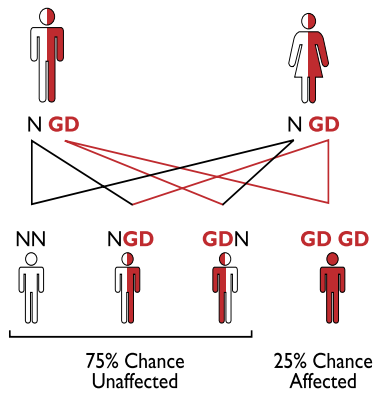
Let's begin by understanding that genes within the body provide certain functions necessary for good health. In other words, every gene has a job to do. Second, every gene in the body comes as a "pair", meaning that there are two that provide the same function. Think of a pilot and a co-pilot who fly a plane. Collectively, they have a job to do – fly the plane. Every person's body is composed of thousands of pilots and co-pilots (i.e. genes) each with their own instructions on where to fly the plane. Of the thousands of genes that we have, each of us has approximately 10 genes that have a co-pilot that does not know how to fly (defective). This is referred to as carrier status. It does not cause health problems because a person who is a carrier still has the pilot (the healthy side of the pair) who knows how to fly a plane and provides the necessary function for the body. In summation, everyone reading this newsletter is a carrier of some genetic defect because we all have approximately 10 co-pilots on various genes that do not know how to fly. Again, carriers carry the gene (defective co-pilot) for the disease, but do not have the disease because the pilot is healthy.

HOW IS THE DISEASE PASSED ON TO CHILDREN?

Let's take Gaucher disease as an example. There are those of us who are carriers of a defective "Gaucher" gene – i.e. the co-pilot on the Gaucher gene cannot fly. As stated above, we are healthy. We choose to marry and have children. Because each of us has hundreds of thousands of genes the odds are remote that we choose a spouse who also has a Gaucher co-pilot that cannot fly. Therefore, the odds are highly remote of finding a spouse who of their 10 recessive genetic defects happen to also have one on the Gaucher gene.

We then marry and have children. For every gene in the body our child receives one half of the pair from the mother, and one half of the pair from the father. In the situation where both the mother and father carry the defective Gaucher gene, there is a 25% chance that the child inherits the defective gene from both parents. Here is what can happen: A) If the child receives the pilot from the mother and co-pilot from the father, the child is healthy (remember, the pilot can fly), but is also a carrier for Gaucher disease. If the child receives the co-pilot from both the mother and father, we now have two co-pilots for the Gaucher gene who are unable to provide the necessary bodily function. In this situation the child has the

Gaucher Disease Inheritance Pedigree



N = normal gene **GD = Gaucher disease gene**

disease - Gaucher disease. Therefore, similar to many other diseases (Tay-Sachs - Niemann Pick – Batten's – Krabbe – Mannosidosis –Fucosidosis – Sialidosis - Mucolipidosis etc.) Gaucher disease is an inherited genetic disease.

WHAT IS THE BODILY FUNCTION?

The Gaucher gene instructions (of the pilot and co-pilot) are to deliver to the body an enzyme called glucocerebrosidase ("gloo-ko-sere-bro-si-dase). This enzyme is responsible for digesting and removing from the body a portion of old worn-out cells. It is part of the recycling process – to grow new cells – and remove old cells. Because the individual inherited the two co-pilots (two defective Gaucher genes), the body does not produce the appropriate enzyme necessary for this cleansing process. Without the enzyme the older worn-out cells are not removed from the body. They begin to accumulate. We call these cells Gaucher cells.

WHAT HAPPENS WHEN GAUCHER CELLS ACCUMULATE?

Gaucher cells most often accumulate in the spleen, liver, and bone marrow. They may also collect in other tissues, including the lymphatic system, lungs, skin, eyes, kidney, and heart. Frequently, an organ that contains Gaucher cells becomes enlarged and does not function properly, resulting in clinical symptoms associated with the disease. The symptoms we have addressed here are the systemic symptoms – meaning everywhere in the body excluding the central nervous system (brain). We will address brain related symptoms later.

ARE THERE THREE TYPES OF GAUCHER DISEASE?

Yes, and we are glad you asked! This is where you will begin to appreciate the progress that has been made with your generous donations. There are three types of Gaucher disease – Type 1 – Type 2 – Type 3. Type 1 Gaucher disease affects the systemic system only – the entire body excluding the central nervous system (brain). These patients do not have any neurological affects from the disease. However, Gaucher Type 2 and Type 3 patients have neurological (brain) involvement.

IS THERE ANY TREATMENT?

Yes. In 1991 the FDA approved a new drug that is referred to as Enzyme Replacement Therapy. This genetically manufactured enzyme is infused into the body and supplements the deficient enzyme the Gaucher gene did not produce enough of. Enzyme replacement therapy, although not a cure, has helped to control the systemic symptoms (i.e. enlarged liver, enlarged spleen). This drug is one of the most expensive drugs in the world, and for most patients, it has to be infused bi-monthly. Despite the cost and inconvenience, it has greatly improved the quality of life for those patients with Type 1 Gaucher disease. However, the drug is ineffective for Type 2 patients, and is only effective for the non-neurological symptoms of Type 3 patients.

GAUCHER TYPE 2 AND TYPE 3 (THE BRAIN IS AFFECTED)

With Gaucher Disease Type 2 and Type 3 symptoms generally appear in infancy or early childhood. Children with Type 2 and Type 3 Gaucher disease have all of the systemic symptoms mentioned earlier (enlarged liver, enlarged spleen, etc.) that Type 1 patients have. However, unlike Type 1, the central nervous system (brain) is also affected.

NEUROLOGICAL SYMPTOMS: Abnormal Eye Movements - Inappropriate Balance - Swallowing Problems – Myclonus (twitching) - Seizures, Etc.

TYPE 2: Gaucher disease Type 2 is the most severe form of the disease with symptoms that become apparent from birth to one year of age. Generally, the child displays multiple neurological symptoms. These children generally pass away from 1 to 3 years old.

"We continue to maintain our commitment – If you send your hard earned dollars – It ALL goes to medical research."

TYPE 3: Gaucher disease Type 3 is less severe than Type 2, and often times displays only one initial neurological symptom. These children generally display neurological symptoms from one to seven years old. Often one neurological symptom will present itself, and then over time the disease will progress to multiple neurological symptoms. It is important to note that:

1. *No child is the same.*
2. *There is a range of neurological problems – from minimal to severe.*
3. *Neurological problems can present all at once, or slowly over a period of many years.*
4. *Some Type 3 children display only one neurological symptom and do not progress.*
5. *Brain symptoms are significantly more serious, and in many cases, cause death.*

WHY DOESN'T THE ENZYME REPLACEMENT WORK FOR THESE CHILDREN?

Enzyme replacement therapy does have a positive affect on the systemic symptoms (liver – spleen – etc.), except in the more severe cases when children die prior to any visible improvement. The problem is that the replacement enzyme does not help the brain. The reason is that there is a filter of sorts referred to as the Blood-Brain Barrier that protects the brain. The replacement enzyme is not able to cross the blood-brain barrier. In 1991, when enzyme replacement therapy was approved it was viewed as a "turning point" for Gaucher disease. It certainly was a turning point for the vast majority of Gaucher patients, mostly adults, who have Type 1 disease.

RESEARCH SLOWED

In 1991, after the discovery of the replacement enzyme serious research on Gaucher disease slowed significantly. As a parent of a Type 3 child, I became very discouraged when I learned there was little, if any research being conducted on how the brain is affected in Type 2 and Type 3 children. This is where you, the readers of this newsletter, have made a tremendous difference. Because of you there is now research, and thus, new hope for these children.

IS THERE NOW RESEARCH THAT MATTERS?

Absolutely! Let me break it down into four areas:

1. BRAIN NEURONS

Just two years ago researchers did not know how the neurons in the brains of these children were impaired, and in some cases destroyed. Because of the research you have funded, we now are in the process of understanding the exact molecular mechanism that causes brain problems.

2. BRAIN LOCATIONS

Research that you have funded for 2003 is now determining the exact locations in the brain that are affected, and correlating these locations with clinical symptoms displayed by children. Thus, we are well on our way in determining HOW, and WHERE.

3. THREE DIMENSIONAL STRUCTURE

Dr. Tony Futerman at the Weizmann Institute of Science in Israel has determined the 3 Dimensional Structure of the glucocerebrosidase enzyme. With this, it may be possible to create an enzyme replacement therapy with smaller molecules, one that may be able to pass through the Blood-Brain Barrier. We should not let our excitement get too far ahead of the realities we face. The Blood-Brain barrier has been a vexing problem for researchers for many years. However, this discovery does pose some interesting possibilities.

4. PARKINSON'S DISEASE Researchers at the National Institutes of Heath have found similarities in the brain between some forms of Parkinson's disease and Gaucher disease Type 2 and Type 3. We have always believed that our research would have overlapping, positive benefits, for other diseases that affect the brain. We are certainly not saying that is the case today with Parkinson's disease. However, stranger things have happened.

Let me summarize this section by saying that there are those in the medical community that have said that brain research for Gaucher disease had reduced to a snails pace, until you came along. The "you", is all of you who have supported this effort with your generous donations.

YES - THERE IS MORE EXCITING NEWS (LYSOSOMAL STORAGE DISEASES)

Remember those other inherited genetic diseases mentioned earlier? (Tay-Sachs - Niemann Pick – Batten's – Krabbe – Mannosidosis –Fucosidosis – Sialidosis - Mucolipidosis etc.) Like Gaucher disease, these are all in a category of diseases referred to as Lysosomal Storage Diseases (LSD's). Each of these LSD's has a neurological component. Meaning, that in each of these diseases not only are there systemic symptoms (affecting the body), but the brain is also affected. The impact on the brain is what makes these diseases terminal for the children who are afflicted. The impact on the brain in these diseases is also the most difficult part of the disease to understand. Researchers believe that a better understanding of one of these diseases will lend itself to a greater understanding of the others. Further, and more exciting, researchers believe that a cure for one of these diseases may lead to a cure for the others. Thus, your support will go far beyond helping to find a cure for children with Gaucher disease!

SHOULDN'T WE GET THEM TOGETHER?

Good idea. And that is exactly what we are going to do. On May 14, 2004, the Children's Gaucher Research Fund will host a Scientific Conference in Washington DC. At this conference Dr. Tony Futerman will be presenting cutting-edge research – the research you have funded. In addition, we are inviting researchers who are conducting cutting-edge research on these other Lysosomal Storage Diseases. There will be two full days of research presentations, all focusing on how these LSD's impact the brain. The initial response from the medical community has been overwhelming. They view this as an opportunity to cross-pollinate ideas and theories. After all, a cure for one may very well lead to a cure for the others.

100% TO RESEARCH

Yes. 100% of donations to the Children's Gaucher Research Fund go directly to medical research. All administrative needs are provided free of charge by our talented volunteers, or paid for by the founders. Your donations do not pay for any part of the Scientific Conference. Corporate sponsors who have an interest in brain research will pay for the conference planned for the Spring of 2004. We continue to maintain our commitment – If you send your hard earned dollars – It ALL goes to medical research.

Greg Macres
President/Founder
Children's Gaucher Research Fund

Jazz In The Garden Fundraiser

Country Moms and Kids is an organization that serves moms in the Northern California communities of Roseville, Rocklin and Granite Bay. Country Moms and Kids provides support, education and friendship, along with opportunities to become involved in the community. They became aware of our efforts and offered to join hands in our search for a cure. This past summer, on a beautiful Saturday afternoon a "Jazz In The Garden Fundraiser" was organized to benefit the Children's Gaucher Research Fund. Initiated by Sherri Goode, Jessica Swan and Vilma Stoberlein, the event provided food and entertainment in the beautiful California sunshine. We thank Country Moms And Kids, and assure them that the funds they have raised will go directly to medical research.

Anything Is Possible, If Enough People Care

John Carmen, manager of the Coldwell Banker office in Palo Alto, California, chose to golf at the Gregory Austin Macres Memorial Golf Tournament. He then made another choice - to ride his bike 50 miles from his office to Cinnabar Hills Golf Club, prior to playing 18 holes of golf. John asked around for a few individual sponsors, and things took off from there! No one asked John to do this - he simply had an idea, acted upon it, and raised over $7,500. He created his own charity event within the framework of the Golf Tournament. It is true! Anything is possible, if enough people care.

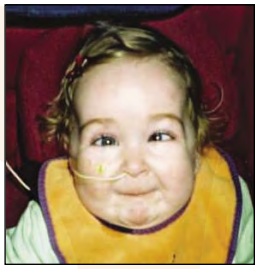
Pizza Hut Fundraiser

On September 17, 2003 Michele, Russell, Erin and Kelly Marsh, in concert with Pizza Hut of Maryland, sponsored a fundraiser for the Children's Gaucher Research Fund. Pizza Hut kindly donated 20% of all sales from the Perry Hall, Md. restaurant that evening to the CGRF. The event, in addition to donations that evening raised over $420. The Marshes would like to thank Pizza Hut of Maryland, St. Joseph (Fullerton) School families and others for a successful evening! Michele and Russell Marsh lost their daughter Lauren to Gaucher disease on March 28, 1992. Despite their loss, the Marsh's continue to fight the battle to find a cure.

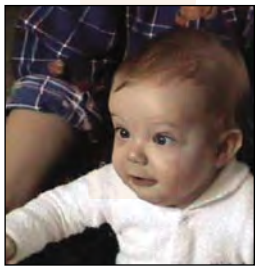
Charity Golf Tournament

The 7th Annual Gregory Austin Macres Memorial Golf Tournament to benefit the Children's Gaucher Research Fund was held on September 25, 2003, at Cinnabar Hills Golf Club in San Jose, California. Sponsored by Coldwell Banker, the full-field shotgun tournament was enjoyed by 226 golfers. We thank the tee sponsors that included local title, mortgage and pest control companies. After 18 holes of golf, the golfers enjoyed a cocktail hour, a silent auction, dinner, and raffle awards. The golf tournament raised over $50,000 for the Children's Gaucher Research Fund. We extend our gratitude to the members of the golf tournament committee who spent untold hours of planning and execution.

Top Row from Left to Right: Melissa Huntsman, Eric Peterson, Kim Sousa, Kara Strand, Janis Money, Maria Rodriquez, Lisa LoPresti, Theresa Ludwig, Cynthia Kent, Anne Treacy
Bottom Row from Left to Right: Jamie Schlicher, Heidi Bonnel, Sierra Stewart, Kacie Ricker



In Loving Memory of
Elsie Pearl Woods Douglas.
"At Home in Our Hearts"
September 18, 2001 to December 12, 2002.
Wellington
New Zealand.



In Loving Memory of
Brannon Gregory
"Our Precious Little Man"
September18, 2002 to September, 26, 2003
Bulli
Australia.

CONFERENCE NOTICE

"LYSOSOMAL DISEASES AND THE BRAIN"

Experts from around the world (USA - Japan - W. Europe - Isreal) will share cutting-edge research on the effects of lysosomal diseases on the brain. Conference focus: "Pathogenesis - Blood-Brain Barrier - Treatment."

May 14th and 15th, 2004
Washington D.C.

Sponsored By The Children's Gaucher Research Fund
Email: research@childrensgaucher.org for details.

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.

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

Contributions Payable To:

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