

January 1999 OAA Newsletter

OAA News from the Editor

Happy New Year 1999

Welcome to the Winter issue of the OAA Newsletter. I hope that each of you had a safe and happy holiday season. It was a wonderful time in the Stagni household. As you can see, this is the largest newsletter we've ever produced and I want to thank each of you for providing me with your stories.

We're Moving!

With the new year comes a new address. After ten years, we're moving to a new home in January. Its only a mile from our current house, but the neighborhood offers many more school age children for Melissa. And it's a little bigger too, which will just keep me even busier. While our street address is changing, our phone number and all of our electronic addresses (email, web site, etc.) are remaining the same. Its listed in the masthead above, so please make a note of it.

Webb-Beyer Update

I recently heard from Elizabeth Webb-Beyer and she wanted me to update those of you who know her that she's retiring from her law practice in Nevada and returning to school. As a result, she is relinquishing her status as "resident agent" for the OAA in Nevada, which means that we will have to move our registration. I am presently working on establishing the OAA in the state of Minnesota and want to thank the Larson family for their assistance in helping us make this transition.

Newborn Screening Survey

As we are all painfully aware, our children's medical care is quite expensive. And we believe that early detection of these disorders can minimize the long-term cost of their medical support. To facilitate early detection requires newborn screening, something that we have been promoting for some time.

In order to implement widespread newborn screening programs, we must have the support of healthcare providers. As with any business, the healthcare provider needs information from which they can make financial decisions. The question is ... can screening newborns for inborn errors of metabolism REDUCE the lifetime medical costs for those found afflicted with the disorder. We believe it can, but that must be proven.

To facilitate an analysis, we have joined with the Fatty Oxidation Disorder Family Support Group to conduct a survey of healthcare costs associated with our respective members. In this issue we explain the program, survey and ask for your participation. Please give it some thought and we sincerely hope that you decide to participate.

Andrew Crook

OAA wishes to express our sympathies to the Crook Family for the loss of their son, Andrew, MMA, who passed away on August 10, 1998.

Its Renewal Time Again

With the new year comes renewal of your membership in OAA. We appreciate the many contributions that we received during 1998 and hope that you can find it in your means to repeat your kindness for 1999. Once again, you have the commitment of the OAA board of directors and our parent advisory council to provide you with the most up-to-date information and with the most sincere support possible.

Luca, Davide and Simone Carbone

Pontelambro, Italy

Writes Daddy (Massimo Carbone):

This is the story of a mommy and her three little children. We wish we could write for a long time on, and also write a fourth story in the future. I don't know if we succeed, but we want to do all our best, and we'll do any sacrifice needed, because the joy that we had in our life, beneath all the pain and sorrow, is and will always be priceless and gave sense to our life and to our marriage.



Baby Luca, October, 1992

Writes Mommy (Paola):

When Luca was born, October the 23rd 1992, everything was ready: a nice room, nice clothes, chosen for months before and most of all love and will of embrace him. He kept us waiting for ten days after the end of pregnancy and had a hard time while coming out, and the doctors took the cupping-glass to help him. All this pain was quickly forgotten. Luca was really a nice baby boy weighing 3.7 kg (8 lbs., 2 oz). We spent the first day at hospital adoring him and I was keeping him tight - it was my first child and I couldn't believe keeping and embrace him. I was really an happy mom.

All this last only one day and then the hard life and the pain came. Luca and I were carried quickly to the Neonatal division of a bigger hospital. Everybody wanted to assure me that it was something that was going to solve soon, but no-one really knew what was happening to Luca. It took one and a half days to find out that it was probably a metabolic disease - Propionic Acidemia. It was only three days since his birth day, but these three day without a cure were too much. I understood by myself what no-one had the heart to say "Luca was in coma." His nice room and clothes were useless now, the only thing I could give him was love, because we really knew almost nothing of the disease. It took a few days before Massimo, the grandparents and I accepted this disease, and it wasn't that easy. Luca was in the incubator, full of wires and tubes and tube fed. In the next days I learned to put the tube through the nose and throat, because this tube, as the doctors taught me, was the only thing that could save him with an ipoproteic (low protein) diet. He didn't like eating from the bottle and he was vomiting very frequently, and each day tube-feeding was needed. Unfortunately Luca couldn't stand it. The first days suffering, plus a couple of days with the pump not working (and no alarm sounded and no-one looking at the bottle!), were too much for my baby boy. After 46 days he died at the hospital of an acute episode of organic acidosis. Nobody, even the doctors, could explain a sudden death like that. Luca was coming home in a few days, it was already planned.

I was really desperate, but when one year after Davide was born, I understood that the great sacrifice of Luca was not useless. This genetic, autosomic recessive disease could arise every time.

It was November the 24th of 1993 when Davide was born, he weighed 3.9 kg (8 lbs., 9 oz.), looks really like Luca and was the picture of health, but after one and a half day started with the first symptoms of Propionic Acidemia. Needless to say our fear for the future.

Davide should not die and, from that day on, we are still fighting for that and to give him an happy and serene life. Thanks to the prompt medical care Davide had no crisis and with the help of night tube feeding and day bottle feeding, he was growing regularly. He took my milk (he was not breast fed,) and at the beginning he was really a great eater. When after one and a half months came home from the hospital, things were going well. We had our weekly hospital visit with blood and urine tests. This for Davide became soon unbearable (being fatty the blood test was made from the neck vein and he was kept tight by two people). We are still working now to get rid of the fear and mistrust he has for the other people (for example - we cut his hair with the machine, because he doesn't like to enter the barber shop!).

At the fifth month things got worse. After a visit in Paris, to the best European center for metabolic disease, we stopped with the night tube feeding. Davide gradually stopped eating by mouth. After 15 days at

hospital trying to make him eat different food from my milk, we came home full of sadness, tubes and syringes, ready to start this new experience, that life reserved for us.

With pain and uncertainty, Davide was growing, this life full of tubes, syringes and night pump. It was very difficult as he vomited. We have to thank grandparents that were with us and helped us practically and morally.

With all this Davide was always happy and smiling. I thank God for this. His little angel was helping him and gave him a really good character. He made physiotherapy to diminish the hypotony and when he was two years old started walking. The language came a little later too, but he was very smart and intelligent and this was encouraging. Time was passing, but eating by mouth was still a dream. At two and a half years he started to drink water (still now it is the only liquid drink accepted) and at 3 we started logopedy and other playing activities in a children specialized center near home. We always kept Davide with attention and care, limiting winter contacts with the others to avoid flu and fevers, and also the way he was eating, limited the social aspects with the others. Now it was time to open the real world to him. He was a little boy like all the others with the right to live and have fun. At the beginning it was difficult for him to accept teachers, even if the only try to make him play, he was still afraid of doctors and strange rooms. As usual, time and patience solved a lot of problems, moreover taught by a good psychologist, we learned to be open with him, and to talk with him, and to tell him his story, and to explain to him the way we took him there. This worked well and he accepted this in a positive way. His resistance was less and was less defensive with the other people. With time he started speaking better and now is only a few below the level with the fine motor skill, while gross motor skill and language are ok. We learned the importance of telling the truth always to children, even if when it sounds difficult. They know how to take it and their easy way to accept it is really helping us to accept it better.

On January 3rd 1998, as promised, Davide make the bigger step: as my birthday present, he started to eat by mouth. The joy was immense and now after almost one year, he makes four meals per day, without the tube (it's used only when he has fever or flu). His meals are still liquid (milk, fruit juice and caloric formula), but for now it's ok (by the way for my next birthday he promised to start solid foods, like rice and pasta). He's going to pre-school morning and afternoon, coming home for lunch. Obviously contact with the other children raise the chance to get flu and fevers and this means that he's going to school one week and is home next week. We know that many difficulties will come again, but we are full of hope and we really trust our little boy, little but so big to accept all the rules of a difficult life, full of time schedule and food schedule. We are really proud of him and love him so much.

But hand in hand with Davide, watching over him, besides Luca, there's one more little Angel. Simone was born on July the 15th 1996, when Davide was almost 3 years old; he weighed a little more than 4 kg (8 lbs., 13 oz.) all precautions were taken and when the doctor gave us the usual diagnosis, I took it well, with no more despair. Davide was growing, and Simone would have grown too - at least two little brother with the same problem could help each other in the future.

But one thing worried me a lot - Simone had a little cleft in his soft palate. A very little problem, doctor said, a simple operation at one year, and everything would be ok. But this little thing once more gave us sorrow, pain and sadness. This "little hole", as we called it to make Davide understand it, prevent normal suction, moreover putting into direct connection nose and throat, made it easy to get flu, ear's and throat's ache. At one year it was planned the surgery, and after a lot of checks, full of doubts and fears, we decided to take him to Paris since it was the best for metabolic diseases.



Simone & Davide Carbone

I was really frightened for this travel and in my heart I felt that I had to enjoy my baby throughout this first year and so in my mind I kept freezing every moment spent with him, every progress and every pain. With his birth he gave a big present to all of us - a big help to Davide who, responsible for the fact of being the bigger one, made a lot of progress (even from before Simone was born); a big joy to daddy who, with two males, was thinking of future tennis matches with them; big happiness to grandparents who, proved by sacrifices and pains saw in this new boy the start of a new hope - and to me he made his best

present - his two lively and happy eyes, framed by a lot of curly brown hair, always followed me with love, making me feel protected and his quick legs make his go-cart run throughout home remind me his presence in every moment.

Simone was really "special", as I always said to grandma. He didn't look that much hypotonic, and while depending from the tube, he was always moving, making him look stronger than Davide. The Doctor was optimist and used to say that, after the cleft problem was solved, he'd have started eating by mouth.

I left to Paris with death in my heart. Davide and two grandparents came with us, and it was not easy to organize that travel.

All that Simone underwent in those two weeks was indescribable and I remember his sad and frightened eyes imploring to take him back home; I couldn't do anything to him, but loving and holding him tight. Last time that me and Massimo saw him happy was before entering the surgery room, sit on the bed in his yellow jacket, he was still smiling and giving us strength, instead of asking our help. Surgery apparently went good, but when we came home from Paris he had cleft ache and his arms were blocked by two piece of woods to prevent him putting his hands in the mouth. The next two months were hallucinating. Simone didn't recover completely, he couldn't eat from the bottle anymore (only spoon was allowed, but swallowing was a great pain for his cleft), his blood and urine test were almost fine, but every day he was vomiting (we made him vaccination, too, because doctors said that this wouldn't have hurt him). On the night of September 28th 1997 Simone suddenly died, his heart stop, in my arms, and I'm still thanking him for giving me even this last moment of his life. The emptiness that he left is still and will always be unfilled, but I'm sure that he and Luca are always here with us. I always tell Davide, who was really shocked by the missing of his adored little brother, that he's a very lucky boy: it is so rare to have two Guardian Angels and that he has to be happy for that: he's very comfortable with the presence of his two brothers and often, I find him playing with them and telling them stories and it touch my heart.

I'm really happy with my three children and I won't change them with any other.

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Gene Therapy Update

The following article was published in the MSUD Newsletter and we have re-printed it with their permission

by R. Michael Blaese, M.D., Chief Clinical

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We have all heard about the possibility that gene therapy could be developed to treat MSUD and other serious diseases that are caused by a defective or misspelled gene. So far that possibly has seemed to be just out of reach. Traditional methods of gene therapy try to take a "normal copy" of the gene that is causing the disease, and deliver it to the cells in the patient's body that are crippled by the defect with the hope that this new "normal" gene will reverse the disease. This treatment has worked in some very special cases where the diseased cells from a patient can be removed from the body and the corrective gene inserted while the diseased cells are growing in a test tube.

Unfortunately, for MSUD and the majority of other serious genetic diseases, the "diseased cells" cannot be removed for treatment in a test tube, and therefore the corrective gene needs to be delivered to the cells where they ordinarily live inside the body - for example, the liver or brain. Most of the traditional ideas for gene therapy have run into this "delivery" brick wall and their development has been stopped in this stage.

Many genetic defects can be thought of as a "typo" that causes the code contained in the gene to be misspelled. Such typos in the spelling of the gene, called mutations, can occur while a gene is being duplicated during cell division or as a result of external factors such as radiation exposure, etc. Since genes are inherited, once a misspelled gene develops for any reason, it has the potential to be transmitted from generation to generation, just as the normally spelled genes are passed on. For many genetic diseases, a misspelling involving only a single letter in a gene that is made up of thousands of letters (or bases) can cause disease. As an "ideal treatment", physicians would like to have tools to correct the typo in the spelling of the gene in those cells in the body where the genetic defect is causing a problem.

Recent research at Kimeragen, a biotechnology company, has led to the discovery of a way to correct, or mutate, the spelling of a gene directly in the cell of the body. Now, rather than needing to replace an entire gene that does not work, because just one letter out of the thousands in the gene is misspelled, it will be possible to treat genetic disorders with a much simpler idea - gene repair. This new gene repair technology is very different from the usual pharmaceutical product, because it uses a smaller molecule that is custom designed and produced for each individual or family in order to correct the unique gene defect that is found in that family. The molecule, called a chimeraplast, is a combination of both DNA and RNA sequences that direct the body's own molecular tools used to repair genes in order to change the defective gene sequence to a normal sequence.

To test the feasibility of this idea, rats with inherited genetic defects affecting the liver have been treated using a simple intravenous infusion of a chimeraplast which was specifically designed to correct their mutations. Because early results in two different genetic disorders in rats have shown such promising results, active plans are now underway to begin treating an inherited human disease of the liver, called Crigler-Najjar syndrome, beginning next summer.

Is this a treatment that could be used in MSUD, and when might it be available? Theoretically, many (but probably not all) of the mutations leading to MSUD should be correctable using this new technology, but no work has been done yet to actually test mutations from different MSUD families.

Kimeragen plans to develop this new treatment for patients with many kinds of genetic defects involving the liver including MSUD, PKU, OTC deficiency, hyperhlosterolemia, hemophilia, etc., etc. When treatment will become available for each of these diseases will depend on the success of early human clinical trials in Crigler-Najjar patients, as well as cooperation from the FDA in helping move this treatment from the experimental trials to general availability.

Also, Kimeragen is a small company with limited resources. We are working to establish partnerships with larger pharmaceutical companies in order to fund more rapid development of this treatment for a broader

range of diseases. If the early clinical trials show promise, clinical trials testing this treatment in MSUD could begin sometime in 2000 or 2001.

Editor's Note: This is the first article I have seen that addresses the subject of gene therapy for inborn errors of metabolism. These advancements can be beneficial for organic acidemias as well.

Vincent John Sanchez

MMA, mut-⁰, Age 19 months

After 19 hours of labor on February 19, 1997, we were blessed with Vincent John Sanchez. Our beautiful baby boy came into this world weighing 8 lbs. 4 oz., 19 1/2 inches long. I remember looking into his big beautiful eyes and thinking that I finally understood this "instant love" thing that mother's always talk about.

The pediatrician came to us the next day and told us that Vince was a very healthy baby boy, and we would be released from the hospital the following day. The next day came and I dressed Vince in an outfit it took me months to pick out, and I was ready to go home and start this mother thing that I had no idea about. As we were waiting for my husband Aaron to come take us home, an angel walked into our room, a nurse named Faith. Faith looked down at my baby boy and noticed that he was breathing a little heavy. She said she was going to take him to the nursery to clear his nasal passages and she would be right back. Little did I know this was the beginning of our worst nightmare.



Aaron arrived and we packed all of our belongings thinking that we would just leave the minute Faith brought back Vince. The few minutes turned into an hour and finally Aaron went out to see what the hold up was. The nurses just told him to go back to the room and they would send information when they got it. Finally after quite a while a doctor came into the room, but he didn't have Vince with him, nor did he have many answers for us. All he could tell us was that Vince was in the NICU very acidotic, but what the heck did that mean? We went to the NICU praying that this was all just a big mistake. As we arrived, we saw our baby boy struggling to breathe, it was then that I realized how serious this really was. The Metabolic team from Children's Hospital had already arrived suspecting that it was a metabolic disorder and the doctor tried to answer any questions for us. You'll have to excuse my memory on this, much of it is blank and I don't recall much detail. I do remember that the doctor told us that it could be a metabolic disorder or it could just be dehydration. We prayed for it to be dehydration. Unfortunately it was not. At this time they stopped feeding Vince formula altogether and had him hooked up to only an IV. They did continuous tests on him. The next morning we went back to the NICU and had Vince baptized in fear of losing him, everyone thought this was a good idea, I don't think many people thought he was going to pull through.

The Metabolic doctor called the next day and asked his nurse if he was in a coma yet, the nurse responded "absolutely not! This kid is hungry, we need to feed him!". The doctors were amazed; they decided that it was then time to feed him. That day we met our new lifelong friends, Nutritionist Laurie Bernstein and her asst. Richard Sheif, and Pediatrician Mark DeMarie. They taught us how to mix the Propimex/Similac formula and we all held our breath as we watched Vince drink his "special drink" for the first time, and he loved it. At this time we were still not positive on a diagnosis. The elevated acid in his blood was rapidly decreasing. It was a miracle. Vince started getting better day by day. He was taking about 2-3 ounces every three hours and was receiving B-12 injections. They were constantly poking him for various tests and performed a skin biopsy. Two weeks later the results from the urine came back positive for MMA. We were devastated but never gave up hope for misdiagnosis. The good news was that Vince was progressing nicely and after three weeks we were finally able to take our baby home.

At home a nurse was coming to give him B-12 injections that didn't seem to help. We saw our Pediatrician once a week and the Metabolic team once a week also. Finally we got the results from the skin biopsy. Vince was B-12 non-responsive, mut-0, the most severe type of MMA. Again we were devastated. We went into a state of depression and denial. Every time I took Vince to the doctor I remember thinking this was all just a big mistake and I hated everyone for doing this to us. It took me about eight months before things finally set in, when Vince got sick from a cold and had to spend four nights in the hospital. The doctors had suggested that we put a gastrostomy tube in Vince and we (still in denial) rejected it for a year.

Thank God we didn't put it off any longer. The G-tube is heaven sent, since we got it we have not spent any more nights in the hospital.

Vince is now 19 months old. He is about 25 pounds. He recently hit a growth spurt and went from the 5th to the 15th percentile for height! He started crawling at eight months and walking at 16 months. There is no known neurological damage at this time. He says about 20 words and salutes every time the Denver Bronco's score a touchdown. We have just started a new therapy of antibiotics. He is receiving 12 cc's of Neomycin 3x a day. We are praying that this will lower his methylmalonic acid levels which are currently at 55,000. He also receives carnitine and an iron supplement daily. His formula consists of Propimex-2, Similac, and Pro-Free for extra calories. He also receives 80 mgs of isoleucine from food, which mainly consists of low protein pasta with cream of mushroom soup, fruits and vegetables. He also enjoys candy, candy corn is his favorite.

My mom and I have also been experimenting with the Low Protein Cookbook, this has been a very fun and challenging task. Vince is seen every 3 months by his Pediatrician and about every other week for a blood draw at the Metabolic Clinic at Children's Hospital. We are still trying to regulate his MMA levels through diet which fluctuate between 24,000-74,000. So far we haven't had any luck with this.

On August 8th 1998 we were blessed with another baby boy, Evan Joseph. He is thankfully very healthy. We had an amniocentesis performed at 3 months to test him for MMA, the results were negative. We weren't expecting this pregnancy but we look at it as a true blessing. Vince was not planned either, it goes to show that sometimes the best things in life are unplanned. Vince loves Evan and is quickly fitting into the big brother role, pulling his ears and biting his hands when we turn our backs. We were very nervous when we left the hospital with Evan, the nurses laughed when I asked what to feed him, how much and how often. They said just feed him when he's hungry. WOW! That's a new concept for us.

We are very fortunate to have the love and support from my mom, dad, brother and soon to be sister-in-law. They have been so good to us and they are always wanting to learn more about this disease. We are so lucky to have them. We also have many other family members and friends who are always there when we need them. We are also very fortunate to be seen at the Metabolic Team at Children's Hospital in Denver Colorado. We are very confident in our medical staff, Dr. Carol Green, Dr. Janet Thomas and Dr. Dave Koehler.

Vince has changed our lives so much. He has touched the hearts of many. We have learned never to take things for granted and each milestone is greeted with sheer excitement. We've also learned that life is a day by day experience for everyone not just us, we are just fortunate enough to face it. God has blessed us with special children, I think that goes to show what he must think of us. Makes me happy to think that he chose me out of the millions he could have chosen. Our road may be a little bumpier than expected, but I have to believe that the gates to eternity will be wide open for us. We pray for you and your children. We'd love to hear from you!

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Lucy Harding

Propionic Acidemia (PA), Age 1

Hello to everyone and Happy Holidays! I really wanted to share our story as a tribute to our survival of the first year. For me it has been the first year of a second marriage, the first year as a stepmother of two teenagers, the first year basically unemployed since I was 16, the first year in a new home, and most importantly the first year as a mother. Please give me a break if I begin repeating myself at times, brain cells are limited these days. (Ha Ha).

Life with Lucy began on December 22, 1997. Actually it began long before that. I am 32 years old and ever since I can remember I have prepared to be a mommy. This is a second marriage for both of us and he is no spring chicken (43 and two teenagers). Anyway we wanted to complete our family as soon as possible and as luck would have it I got pregnant first try. We have friends in the medical profession and this child had more pictures before she was born than she does now. We wanted to know what she was, cause you see, no matter what we said we really wanted a little girl. At 25 weeks we were able to get a good ultrasound picture. So Lucy became "Lucy" about Sept '97. The pregnancy was uneventful up until the end. The last few days I showed signs of pre-eclampsia and if I had not gone into labor I think we would have had to discuss a c-section, but my Little Lucy came as I asked her to, before Christmas so she could be that special gift for all of us. (She wasn't actually due until December 31). The delivery went well, just like we were living all of our fantasies.



We came home from the hospital on Christmas Eve. Lucy was a poor breastfeeder, but I was sure she would catch on, everyone said new babies were sleepy and it took a couple of days. When I look back I see lots of signs of problems. Lucy vomited that evening and choked on it, we picked her up and she cleared it, but that was just the beginning. We watched her all night. Enoch slept most of the night with her on his chest so he could warm her and feel her breathe. I was concerned. She wouldn't eat, not even from a bottle and she wasn't having wet diapers. By morning she had a nice wet diaper but still would not eat. I kept thinking, "ok, calm down, things are ok" she just needs to wake up more. Wrong. Throughout the day she still would not eat, and started becoming more lethargic. She wouldn't even lick sugar water drops off her lips. She began this weird hiccup like breathing pattern that I later realized was her body trying to blow off extra carbon dioxide because she was acidotic. That afternoon it was Enoch, who said, "Things just are not right" and we took her back to the Hospital Emergency room the Christmas afternoon.

From here on out the story is fairly familiar to many of you I think. Lucy's temp was low, her blood sugar was low, and they did a spinal tap, started an IV of glucose solution, and did labs. I must give the doctors we have here a lot of credit. They don't see this often, most of them ever, but they all did good things when it comes down to it. The neonatologist knew as soon as he saw the initial labs that Lucy had an organic acidemia and she was transferred to the University of Kentucky Medical center here in Lexington. She rebounded quickly from this acidosis with the glucose solution and some bicarb in her IV and did not need ventilator support for her breathing like we anticipated she would. Further labs showed an ammonia level in the 900's and we were left with "let's stabilize her and see what tomorrow brings". The next few days were a blur. Lucy got a little better, and then her status hit rock bottom on Dec 28. Her ammonia level was climbing again, she was basically unresponsive and her breathing was becoming irregular. This was the most critical day I can remember and I really thought she was going to die that night. We decided to dialyze Lucy which in itself held lots of risks for a child so young, but for Lucy it appeared to work well. The ammonia and other toxins were filtered out of her system quickly and her breathing became normal again. Now we just had to wait and see how she responded.

One of the attending Peds ICU doctors at UK med center consulted with his colleagues at Duke and sent Lucy's blood and urine there for testing. We had an exact diagnosis when Lucy awoke on Dec 30 and began taking a little formula from a bottle. We started her on a Propimex 1 recipe. We spent the next 2 weeks at UK waiting to see how Lucy would respond and doing lots of tests. Because no one here had ever treated a child with this illness everyone agreed we needed some specialized help and we were off to Atlanta for a consult. We were there for a week while Lucy had more tests, a few diet adjustments and grew stronger all the time. By the time we left Atlanta almost a month after Lucy was born, she was taking her bottle, no more NG (nasogastric) tube, she was smiling, and gaining weight well. Now the challenges of taking care of her at home.... That was really scary.

All my ideas about being a Mom were gone now. I was terrified. I remember the pressure knowing I had to get a certain amount of formula in her and I worried so much about her throwing up. At first we fed her every 3 hours and held her up for about an hour after to help prevent reflux and decrease the vomiting. It was amazing how hungry she would get. For the first three months she had a great appetite and took her bottle well. Her scrawny little body starting filling out in no time. We held our breath watching for each little developmental milestone. Would she hold her head up, would she turn over, sit up, etc. and when would the next crisis hit.

One of the things that helped me monitor Lucy and give me peace of mind was checking ketones in her urine. This provided me a little security and still does. If Lucy's ketones are ok, I don't worry as much about how much she spit up or if she is sleeping too much.

We had our first setback when Lucy was about 3 months old. Even with all the hand washing and all the meticulous evaluation of everyone who was near her, she got a cold. She had trouble with all the drainage and even though she would still take her bottle, she coughed so hard she would gag and throw up. We still do a lot of that, but Mom is getting much better at anticipating and catching it. (Yes I said catching it; I am tired of cleaning up the carpet.) Anyway, I was determined to keep her in control so we used a NG tube for about a week during that cold to just dribble it in so she would maintain. I was so scared. We had her in the doctor's office 3 times in 5 days. (It does get better, the last cold we weathered on our own, and no doctors visit at all. Yea!!!) Lucy recovered from her first cold and began eating well again. At about 4 and a half months of age she started wanting to sleep all night and would not eat well, so I used a NG for night feedings and she continued to take her bottle during the day. At this time and throughout the next 6 months Lucy seemed to be real sensitive to acid changes in her body and had several periods of a week or two at a time with lots of vomiting. This even occurred before she was showing ketones in her urine. We would increase calories a little, increase water to flush her system more and do lots of continuous feedings to combat the gut dysmotility.

Using a NG for Lucy became rapidly more difficult. Lucy is very active and quite a fighter. It often took 3 or more tries to place the tube and then she would cough it up or pull it out. I was worried about the long-term effects this could have on her eating since feeding issues and oral aversions are common with PA kids. We gathered information on alternatives and pursued peg placement when Lucy was 5 months old. (Peg is a type of gastrostomy tube). At about 6 months of age Lucy lost interest in the bottle altogether and the tube became our sanity.

Lots of Lucy's care routines have arisen through trial and error and good advice received from other PA moms. We have always been pretty aggressive with Lucy starting with early dialysis, early intervention evaluation, and use of the NG and early placement of the peg. At 6 months of age she qualified for speech therapy and receives that in our home two times a week. We do continuous feeds at night with small bolus feeds during the day and time to work with real foods. I do two or three therapy sessions on my own with her each day. We have frequently run continuous feeds all day for up to a week at home during periods of vomiting. We always try to keep her well hydrated. We have always tried to key in on what would help keep her in control and early intervention for the future.

We work with the genetics division in Atlanta and the most fantastic dietitian Dr. Rani Singh. We run Lucy's Carnitine levels at about 175 mg per kg and we have decreased her calories to about 73 cal per kg. We use Isoleucine and calories as our markers and our goal is about 70 mg per kg of isoleucine per day. She won't have any meats or cheeses to try to keep her from developing a taste for them. She appears to have a sweet tooth. (gets it from her dad). Lucy also takes Biotin, Thiamine, Zantac, Propulsid, and Iron daily. Here in Lexington Lucy sees Dr. Charleton Mabry (a pediatric endocrinologist) and her regular pediatrician. Dr. Mabry has been excellent at administering the lab work and communicating with our insurance. He is quick to help with whatever we need and has a knowledge base that goes on forever. Our

communication with Atlanta has been frequent, and we have developed confidence in the care Lucy receives here at home when necessary.

Currently as we approach her first birthday life with Lucy is still stressful but we don't live quite so close to the control her weight some. She is 30 pounds and 30.5 inches tall. She appears to be tolerating this well. It is as if her body is used to the ketones a little now because the vomiting is a whole lot less. (She usually only vomits now if her gag is stimulated by a cough or new texture, etc). She is probably a little delayed, but it is difficult to see. Our speech therapist says she falls into all the normals. Lucy has, so far, hit all the developmental milestones: She rolls, sits, crawls, walks as long as she has something to hold onto, cruises furniture and cabinets, stands alone for a few seconds, waves hi and bye, plays patty cake, peekaboo and so big, has a vocabulary of understanding of about 20 words, says lots of sounds and is trying hard to make some sense of words. She actually says "Hi "on her own appropriately, can say dada, rara for rattle and boc for block, ba for ball, da for doll, etc. Anyway it would be difficult to find problems yet. Her eating is improving. She takes about 2.5 - 3 jars of baby food (stage 2) each day fairly consistently. What she doesn't eat we thin and put through her tube. She is learning how to use the sippy cup but really prefers to get some water in her mouth and then blow it all over mom. Lucy is very social and lots of fun. She has a great disposition and sure has a knack for getting people to smile.

This has been a hard year and I have received the most help from other Moms in OAA. Lots of good advice and always an ear to bend, shoulder to cry on. We try to maintain some normalcy in life for us all. Lucy won't go to day care (I quit my job as a nurse to take care of her at home) but she does have a playmate that is 2 weeks older than she (and he doesn't do the day care thing either). I have been fortunate to have nurse friends who will babysit a little and we are still pursuing respite nursing provided by the state. Lots of paperwork and waiting for these programs. We travel a little with Lucy, just take all our junk with us. I take her most anywhere during the day, bolus set and syringe in hand. I don't think we had any idea what was in store for us emotionally and physically when the year started, but somehow we have survived and Lucy has thrived. I am thankful for everyone's consistent thoughts and prayers, without which I am sure I would have folded. Our goals for the future: Be patient, try to let go of some of the stressors (especially with the teenagers), keep knowing and loving each other no matter how much effort it takes (especially Enoch and I), and enjoy Lucy. She does something-new everyday and it reminds me how fun and simple life should really be and what is really important. She is now and always will be quite the Christmas gift.

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Jennifer Mabbott

MMA, mut⁰, Age 2

Hi there, my name is Shelley Mabbott and I live in Edmonton, Alberta, Canada. My daughter, Jennifer was born November 10, 1996. The pregnancy was uneventful and the delivery went well. She weighed 6 lbs., 6 oz. and was 20" long and of course she was just beautiful! Jennifer was a quiet and content baby and by 3 weeks old was sleeping through the night. The only disappointment was that she wouldn't nurse, but I put her on Similac Advance she seemed to take quite well to it. Jennifer was never a big eater, generally 14-16 oz. of formula a day, but she seemed happy, so I didn't give it a second thought. Her pediatrician at her monthly visits would express little concern at the fact that she wasn't on the growth chart and there had been no big growth spurts to get her on there. She kept telling me to get more formula into her, which I would try, but to no avail. And now, looking back, I would see baby's at 3 & 4 months old, the same age as Jennifer at the time, holding their heads up and doing different things that Jen was not doing yet, but I just thought that she was tiny and would eventually do it.



Then at her 6 months check, her doctor suggested sending her for blood work and a head ultrasound, to see if there maybe was a reason she was so pale and no growing that fast. Well, the only thing the tests showed was that she was anemic, so all we did was start her on an iron supplement.

Well, 3 days later, Jennifer had stopped drinking. She became very lethargic and starting vomiting everything up that I would get into her. Finally, after 2 days of struggling to get some formula into her that she would keep down, I conceded and took her to the Emergency Ward. To make a long story short, they sent us home that night with some Pedialite, only to return 2 nights later, because she was getting progressively worse and would still not drink. They said she was severely dehydrated and asked to keep her overnight on I.V. After 1-1/2 hours they finally got some blood out of her for blood work and discovered her metabolic system to be all out of whack. They transferred her to the University of Alberta Hospital where look after metabolics and after a week of seeing dozens of different specialists and doctors, and going through countless tests, they finally came with the MMA, (Mut 0) diagnosis. Ironically enough, the day they told us about this was also Jennifer's "crash" night. She spent the night in PICU and that was the start of our next 4 weeks off hell.

A week after her diagnosis, it was decided to put in a G-tube and a Broviac (a central line I.V. in the chest). While they were doing the surgery for that, the surgeon noticed that she had an enlarged pancreas. Apparently, pancreatitis is common with MMA kids, but we did not know that at the time. So, she was put on a TPN for the next 10 days, to starve the gut, till we gradually worked her back onto her special formula. Also, while in the hospital, she got a blood clot in her leg from a central line I.V. in her groin, so that required heparin shots twice a day for the next 3 months. And she got a 3rd degree burn on her ankle from an I.V. that went interstitial, and that required a skin debridement and skin grafting. Then, finally, after 5 weeks in the hospital, we got to go home.

We have only had 2 more hospital stays since then, one in August and another in October. But both were from infections in her Broviac. So finally, after the second hospitalization, we decided that the Broviac was proving to be an infection trap and it wasn't worth it, so we had it removed. Since we did that she has been doing wonderful. She finally started gaining weight like crazy and is now at the 25th percentile on the growth chart, yahoo! Her doctors figure that there was probably always an underlying infection in the Broviac and she was using up all her calories fighting off the infection. Yes, now it is back to poking her for blood work, but I would rather that, than having to be in the hospital every 2 months the other way. We have resorted to sedating her for her blood work though, as Jennifer is not an easy poke and she was just

getting too worked up when they had to take blood, which in turn, was not giving us a real accurate readings of her levels.

Jennifer is behind developmentally, which I know is a symptom of MMA. At 23 months, she is still not walking by herself yet. She will go hanging on with one hand, but just doesn't have the confidence to go it on her own. She motors around the furniture quite easily as has mastered the stairs VERY well. She also has only 3 words she says, with MOM being the first and most important one! She has her own sounds for certain things and has no trouble with letting me know what she wants. She really watches my mouth when I try to get her to says words, but just can't catch on to it. We are on the list for getting her into rehab to try and see if we can get her caught up on her motor and muscle development and to work on her social skills. I don't know it is from all the trauma she went through in the hospital, but Jennifer is a very sober kid around strangers. But she is even improving with that. You might not be able to get a smile out of Jennifer, but she will give anyone a kiss Bye Bye!

So that is our story. Jennifer is the first and only known case of MMA in Edmonton. I'm not sure if that is good or bad though. It gives us alot of added attention and some very "preferential" treatment, but we are kind of the black sheep, as there are not too many doctors that have even heard of MMA. I like saying Methylmalonic Acidemia in front of them just to confuse them!

We have an extraordinary metabolic team with Dr. P. Ferrare, Dr. S. Bamforth, and Barb Marriage and Stefanie Conrad as our nutritionists (and sounding boards)! And Dr. C. Kyriakides is our great pediatrician, who is quite willing to learn about this right along with us. They have all been fabulous though out our whole ordeal as both a friend and a professional. They have made things a whole lot easier for me.

I think this OAA newsletter is both reassuring and refreshing. It helps just knowing there are others out there that have gone and are going through most of the same things we have. It has been great corresponding with Wendy Patterson. Everytime I hear from her, I am just amazed at how much alike my Jennifer is and her Zane. I sometimes feel a little isolated up here, as there are not too many known cases of MMA in Alberta, or as far as that goes, Canada, so it is kind of nice to have someone to share experiences with. I have learned a lot about MMA and have a lot more yet to learn. I am very interested in hearing from anyone who has information on this disease or who would like to chat. My address is:

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Heather

Glutaric Acidemia, Type 1, Age 2

Heather was born on January 16, 1997. She came into the world with good Apgar scores despite the hard induced labor. And except for a few minor problems, she was a "normal" baby. She had a very poor suck reflex and would not breast feed despite all our attempts for four days. She went from 9 lbs., 3 oz to 7 lbs., 9 oz, so we began to bottle feed her formula. She continued to be a slow eater and would take an hour to finish two ounces, she eventually got quicker at feeding and gained weight slowly. She would always stare at lights and never look at people's faces. She had an excellent Pediatrician who told us that was a self-stimulating behavior. However, our pediatrician was concerned about her weak neck muscles and one protruded out more than the other. She sent us to a Ophthalmologist and physical therapy for the torticollis of the neck at about 6 months of age. (Torticollis is a pulling of the neck muscles on one side, tightened so that the head tilts down and to the side.) She did extremely well with PT and her torticollis resolved by her first birthday. The



ophthalmologist was very worried that her right eye protosis was due to craniosynostosis (bone sutures of the head closing early, not allowing the brain to grow). This was in our family already and I knew she was in for an extensive surgery. He sent us to get a CT scan of her head. She was heavily sedated with chloral hydrate and as she lie under the CT scanner, I knew that something was devastatingly wrong with my baby girl. The Pediatrician wanted to review the CT scan herself and I had to beg to see a pediatric neurosurgeon. The pediatric neurosurgeon examined Heather, at that time 8 months old, and review the CT and decided that she did not have craniosynostosis, but she did have "some fluid around the brain" which he said was normal in some children. He wanted to see Heather back in a few months. We went back and he examined her again and said she was developing nicely. And in fact, she did reach all her milestones within normal limits, was just a little late with crawling and walking, but ahead of her age with talking. She was just about to take off and walk independently at 15 months of age, again, I didn't worry, after all, I didn't walk until I was 15 months old too.

Our world came crashing down around us on April 10, 1998. She was just getting over roseolla when she had a bad case of gastroenteritis. She wasn't able to keep down any fluids at all despite a phenegan suppository (prescription medicine to stop vomiting) she got at the pediatrician's office, so we went to a local emergency room. She was screaming her head off and was trying to bite me which was very untypical behavior, she seemed so mad. The ER pediatrician even asked me what she was so mad about. I was extremely worried. He said that she wasn't dehydrated, but he gave her about 200cc of intravenous fluid anyway. The next morning, Heather was very irritable and tired. I thought it was just the late night in the ER, so I put her back to bed. She woke a couple of hours later and was very weak and kept falling over to the right side when she tried to crawl. I tried to get her to smile and only the left side of her mouth turned upward. I called the pediatrician and he told me to call 911. At which point I began to panic. Heather started having focal seizures with the right side of her body in ambulance and a tonic clonic seizure in the catscan. (Tonic clonic seizure is same as grand-mal seizure.) As a registered nurse, I knew febrile seizures were very common and nothing to panic about. But Heather did not have a fever and a dreadful feeling washed over me. For the first time in my life I felt totally helpless.

The head CT showed temporal lobe "atrophy". Basically her brain doesn't occupy the entire space of the skull. The doctor decided to send her to Johns Hopkins Hospital. While we were waiting for the transport ambulance to arrive, Heather was given a loading dose of intravenous dilantin to control her seizures. The dilantin was effective, she no longer had any more seizures. When she arrived at JHH pediatric ER, she was very lethargic and wasn't moving the right side of her body at all. She underwent a lumbar puncture to rule out meningitis. Several hours later she was admitted to the infant floor where they told us we couldn't sleep at her side. She looked at me with this questioning look probably wondering what was happening to

her. I wish I would have known. I stayed by her side for 4 days, only leaving to sleep in a room a few yards away. She was never left alone, someone was always at her side watching over her and keeping her calm if she would awaken. I am so thankful to our family for staying with her at night. She slept a lot and was lethargic. She wouldn't laugh or smile and even had a hard time sucking and swallowing her bottle. Over the next couple of days, she made slight improvements. It put her in the highchair and she would just fall forward. I fed her some soft table foods, she used to love to eat. It would take her a long time to eat a few bites, but never choked on the food, thank goodness. She began to hate her crib and cry when she was put down even for a diaper change. My mother brought in a tape that Heather used to laugh to and we played it for her. We were so excited when she gave us a very weak smile and sound. Every night the doctors would give her dilantin to prevent further seizures. At first they speculated that her lethargy was from the seizures, then they said it is probably the dilantin. On the third night, I stopped the doctor and told him I didn't want her to have any more dilantin, because I wanted her to be more alert. He told me that her lethargy was not from the drug, but the disease process itself. Exactly what disease, they didn't know. This was another horrible shock, and as a nurse, I knew that what he was telling me was awful and probably not reversible. They said her diagnosis was one of three things: a traumatic event where her brain didn't get enough oxygen, an autoimmune disorder where the immune system attacks the brain, or a metabolic disorder. On the fourth day we had an answer at last: Type 1 - Glutaric Acidemia. A rare autosomal recessive inborn error of metabolism involving the inability to breakdown protein, specifically the amino acids lysine and tryptophan. A disorder that is very easy to control with diet, medicine and prevention or quick correction of dehydration or fasting. We were extremely relieved and ready to go home, even though they could not tell us whether she would be able to sit, crawl or walk ever again. They had hopes for her development to progress, but they couldn't give us specifics.

We were very fortunate to have one of the top physicians experienced with GA1 children. Dr. Kelly answered all of our questions and gave us an emergency protocol letter for times when Heather was sick. But he could do nothing to quell the fear of bringing home a "fragile" severely developmentally delayed child. Before we left the hospital, they had arranged for in-home physical and occupational therapy for Heather. Over the next couple of days, I pulled out all the infant toys: gymini, bath seat, boppy pillow, exersaucer and everything that she had outgrown as a toddler. But thank God, we didn't have them for long. Over the next months, she made an incredibly quick recovery and was able to sit, crawl, stand, and cruise. She also regained most of her fine motor skills and started babbling again. The therapy continued and she also received some speech therapy too. We were so excited about her progress. It was incredibly quick in the beginning, but began to slow up some. She was walking at 19 months, but not independently. She has a very wobbly gait and often topples over. For balance control, she likes to sit in the W position, instead of with her legs straight out or crossed. Her expressive speech has been progressing at a turtle pace and she is so quiet that she doesn't babble enough to practice her speech. Her receptive language is excellent, she understands everything we say. The special education teacher has taught her 5 signs so that she can communicate with us. She is now in the infant and toddlers early intervention program with excellent professionals. She receives P.T. once a week, O.T. once a month and special education bi-weekly. At this point, I am filled with joy that she can do so much! She is incredibly good child. She is sweet and nice. She is always well behaved in restaurants and around adults, I can take her anywhere with me. She is a happy child, always laughing and smiling. I thank God for her.

It's so hard to put this whole experience into words, this article is just a tiny piece of the pain and joy that Heather has brought me. But I know that somehow, somewhere, God has planned this for some purpose. And I hope that purpose is to help others. Even if only helping by sharing Heather's story. I would really like to become active in expanding newborn screening in Maryland. I know that no excuse is good enough not to start trying, but I also know that having a child with special needs is exhausting, physically and emotionally.

Steve and Shantel
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