



Organic Acidemia Association
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Organic Acidemia Association Newsletter

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Coming Soon! July 2012 FOD/OAA Family Conference, Portland Oregon

We are pleased to announce that the OAA and FOD will hold our next joint conference in Portland Oregon, on July 20 and 21, 2012. The location chosen is the Red Lion on the River. Information is available on page 2 inside this newsletter and more will be posted online as it becomes available. The Oregon Health and Science University will be our Premier Sponsor. Thanks OHSU! I hope you all can plan ahead for this conference next year as it is a great way to meet others with the same disorder.

Photo Book New for 2012

Raymonde had so much fun designing the 2012 calendar that she volunteered to also make a 2012 PHOTO ALBUM showing all our "kids". So far the album is two dozen pages showing over 100 of our "kids". If you would like to have your child included, please send a photo by email (or snail mail) to Kathy Stagni (address at the left). Information for ordering the book will be available in the next newsletter and on our website when it's available. Deadline: January 1, 2012.

2012 OAA Calendar Available Now!!

Café Press has a large selection of items available with the 2012 OAA calendar cover printed on them. They carry long and short sleeve shirts, tees, sweat shirts, bags, ornaments, license plate holders, toys, mugs, magnets... and calendars galore. Be sure to check out the pictures on the inside, too.

Thanks to Raymonde for her efforts!
(See Calendar cover below)
<http://www.cafepress.com/organicacidemia>

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2012 Conference Information

The 2012 FOD/OAA Family Conference is scheduled for July 20 - 21, 2012 in Portland, Oregon. We will post information on our websites as it becomes available. There will be NO Registration fee for attendees for the 2012 Conference! In the past, it was \$50.00 per person.

Hotel & Conference: Red Lion Hotel on the River 909 N Hayden Island Drive Portland, OR 97217

Hotel Online Reservations: Attendees are responsible for making their own Hotel reservations. Prices will be in effect 2 days before and after the conference dates of July 20 and 21, 2012. If you have special needs (i.e., refrigerator, microwave, crib, etc) please call and ask about availability.

Hotel Phone Reservations: If you call 503.283.4466 be sure and state your reservation is for the FOD/OAA National Metabolic Conference so you will be given the reduced conference rate - starts at \$99 - \$114 depending on room size. If you have special needs (i.e., refrigerator, microwave, crib, etc) please call and ask about availability and/or extra cost.

Airport: Red Lion Hotel on the River is 15 minutes from the Portland International Airport and there is complimentary on-call airport transportation provided by the hotel, as well as other ground transportation services. Ask about the Hotel's airport service when you call for a reservation.

Travel to Conference: Attendees are responsible for making their own travel reservations. Speakers will work through Deb and Kathy for both Hotel and Travel arrangements.

Meals: We will be working with the Hotel chef to provide a wide variety of food offerings for **Friday and Saturday Breakfast and Lunch, and the Friday night Reception** for all registered attendees, as well as lowfat and low protein options to accommodate our Families' needs. **All other meals are your responsibility.** Once we have the Registration Form online you can state if special food restrictions are needed and the Hotel chef will try and accommodate as much as possible.

Child Activity Room: Once again, we hope to provide an activity room for children - however, each family will be responsible for providing someone to supervise their child (i.e.,

grandparent) and that person will also need to be registered. We will try and find local volunteers to help in the room to provide drawing activities, games, videos etc. Children will be allowed in the conference sessions IF they can do so quietly. Otherwise they will need to be removed from the session. Older children and teens are encouraged to attend sessions - **every child will also need to be registered** if they plan on attending the Friday and Saturday Breakfast and Lunch, and Friday night Reception.

Registration Form: Will be online soon - **Only Registrants** will have access to our Conference Breakfast and Lunch on Friday and Saturday, as well as the Friday night Reception for Families, Professionals, Exhibitors, and Speakers. If you choose to print the form, you can then mail it to Deb Gould at Deb Lee Gould/FOD Group, PO Box 54, Okemos, MI 48864

Check out OAA's New Revised Website!! Easier navigation and user friendly!

Family Conference 2012
PORTLAND, OREGON
JULY 20-21

Google Groups
Subscribe to Organic Acemia Association

Email:

Visit this group

Meet Our Families in the Photo Gallery

See the OAA/FOD Quilt.

baby's first Newborn Screening

Sienna's Story

Methylmalonic Acidemia, Cobalamin C, Age 13



I had a normal pregnancy except for only gaining 9 lbs and having morning sickness every day. The last 2 weeks the doctor noticed that Sienna had stopped growing so he induced my labor one week early. She was very floppy and not breathing for the first minute or so but then she seemed ok, although she only weighed 4 lbs 15oz. She was released after two days and we were excited to bring out little bundle of joy home. I immediately noticed that she was very fussy and only

slept 6 or 7 hours in a 24 hour period. She also was having trouble feeding and it took her a long time to finish a bottle.

After about a month and a half I took her back to the pediatrician to discuss the possibility of her having reflux, which she did. Before that diagnosis she was on 12 different formulas. The doctor also put her on medications for reflux which did not help.

When she was 2 1/2 months I knew something was seriously wrong. I immediately took her to the pediatrician and the nurse practitioner took one look at her and sent us to the lab to have her blood drawn as she was very pale. She called me one hour later to ask me to go back and have it drawn again because she thought the lab had made a mistake because her hemoglobin was only at a 6. It was redrawn with the same results. We were immediately hospitalized that night and did not leave the hospital for almost 3 months.

She had every test imaginable including, a sweat test, bone marrow extraction, tests for cancer, etc. The GI doctor who was seeing Sienna felt for sure that after all these tests it was some type of metabolic disorder but did not know which one.

Finally after two weeks we were given a tentative diagnosis of MMA with Homocystinuria, but by that time all her organs were failing. She was put on a vent and they were doing blood exchanges because her red blood cells were fragmenting. We were told to call our families as she was not going to make it thru the night. I prayed so hard that night asking God to please let her live and I would take her however he wanted to give her to me and I meant it.

She lived thru the night and started improving a little. At that time we were told that she would have to be transferred to San Antonio because there was not a genetic doctor in the Dallas Fort Worth area that could treat her so we were careflighted 5 hours away. She was still on the vent. Although she was improving she was still a very sick little girl.

The genetic doctor in San Antonio said there was very little information on the internet and what little there was, was very grim. At the time of diagnosis we were told there were only 19 children with this diagnosis and that several had died. We saw so

many doctors and she also had surgery for a central line, g-tube, and a fundoplication for reflux. Because she had not fed by bottle for so long she had to relearn how to feed. We were told that she would be protein restricted, be in and out of the hospital, and would probably have significant delays.

She was released almost 3 months later on special formula with 24 hrs feeds via the g-tube and several medications. She was immediately seen by genetic doctor Lewis Waber at Dallas Children's Hospital. He said he never received a call asking if he would see her as a new patient three months before. She only had her g-tube until she was 6 months old.

On the 28th of October, Sienna turned 13 and is such a blessing to our family. She has never been hospitalized since that time. She is also not protein restricted or on any special diet. She is slightly delayed academically but does very well. She has retinal degeneration and has very little vision. She cannot read text so she reads and writes Braille. She is a very smart little girl!

I feel so blessed to have her in my life but sometimes wonder what her life would have been like if Newborn Screening were available in 1998. Maybe she might not have suffered the crisis that almost ended her life.

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**Challenging the Paradigms:
Liver Transplantation for Metabolic Disease**
May 4-5, 2012 • Pittsburgh, PA

SCIENTIFIC SESSIONS: Friday, May 4, 2012

FAMILY PARTICIPATION DAY: Saturday, May 5, 2012

Children's Hospital of Pittsburgh of UPMC
John G. Rangos Sr. Conference Center
One Children's Hospital Drive
4401 Penn Ave.
Pittsburgh, PA 15224

For updates and online registration,
please visit www.chp.edu/metabolic2012

Riley

Methylmalonic Acidemia, Mut 0, Age 1

Riley has a very rare disease that only 1 in 50,000 to 100,000 people are afflicted with in the world. Riley has what is called Methylmalonic Acidemia Mut 0. What this means is that she does not have the ability to break down the proteins in food to the essential amino acids needed for normal growth. Instead, her body creates high levels of ammonia and acid, both of which are directly toxic to the brain and organs. To give you some insight on how severe her condition is, when Riley was admitted to the NICU at birth her ammonia levels were as high as 870 ppm. The normal range for a newborn is 30-50 ppm.



Baby Riley was born June 3, 2010 at 2:34 in the afternoon and weighed 6 pounds 11 ounces. She appeared perfectly healthy and was the most beautiful baby we had ever seen. We were sent home June 5th as two incredibly proud first time parents. The next day, Riley went to her grandma's. That evening, I came over to watch the Laker game and noticed that her breathing was a bit labored and heard she hadn't eat well the entire day. We decided to take her to a hospital in Pasadena as something didn't feel quite right. When Riley arrived, the neonatologist immediately said that she was very sick. They ran a few tests and before we knew it she was rushed to Cedars Sinai Hospital in Los Angeles.

That night was the worst night Katie and I hope to have for the rest of our lives. We arrived at Cedars around 12:30 AM and immediately spoke with one of the resident pediatricians in the neonatal high intensive care unit (NICU). She was supportive, though brutally honest. She said the next 48 hours would be the worst of our lives and that we would be bombarded with a team of specialists all trying to save our daughter's life. We saw 3 kidney specialists including a dialysis doctor, a neonatologist, 2 geneticists, 2 pediatricians and countless nurses. If it weren't for the neonatologist from the Pasadena hospital and the dialysis specialist, Riley would not be alive today. Katie and I are forever grateful for them. We watched as countless doctors huddled around our baby girl trying to save her life. After two rounds of dialysis treatments and countless Kleenex boxes later, she began to get better and we returned home from the hospital after 11 long days.

After we were released from the hospital, Riley, Katie, and I all settled in and got to know one another. For the first couple of months, aside from her specialized diet, Riley was just like any other baby. She slept quite a bit, loved her mom, and had a spark about her as though nothing could bring her down. It was in this spirit that Katie and I decided to take Riley on her first vacation in August of 2010. We were a bit nervous as we had been monitoring her so closely and we didn't want to be too far away from Cedars Sinai Hospital as we knew not every hospital could handle her disorder. Nonetheless, in an effort to give Riley as normal a life as possible, we decided to go.

Looking back, I'm not sure I'd make the same decision again but no use in complaining about it now. Riley didn't do too well on her first trip away from home for whatever reason; we still don't know. Her ketones were elevated and she was throwing up constantly. Ketones are substances that are made when the body breaks down protein for energy. Normally, your body gets the energy it needs from carbohydrates in your diet. Riley's ketone levels are one of the things we monitor constantly. Despite these setbacks however, we stayed in touch with our doctors and were able to maintain her levels at home through the use of her 'sick day diet'. This all changed in October when we had our first trip back to the hospital after being released 4 months earlier.

It was October 31, 2010, when Riley experienced her first metabolic episode. For the past few months, Riley was eating surprisingly well according to her doctors and wasn't having nearly as many 'episodes' as other cases they were familiar with. On Halloween night 2010 however, that all changed. Riley was refusing to eat, vomiting, her ketones were the highest we had seen them, and she seemed weak and lethargic. Without really questioning anything, Katie and I both decided that we needed to rush her to the hospital. Unfortunately though, as mentioned earlier, we couldn't just go to any hospital. We had to travel for an hour and fifteen minutes to Cedars Sinai in Los Angeles. Needless to say, that was a terrifying car ride for Katie and I, but more importantly Riley.

Our first hospital visit back was more terrifying still. When Riley gets sick, it's important that she is hooked up to IV's as soon as possible so that she can get the medicine and hydration in order to prevent her body from going into a deeper metabolic crisis. When we got to the ER, the nurse attempted to start an IV in Riley's wrist and was unsuccessful. After three more failed attempts, she called someone else in to try. This went on for 6 hours. All the while, Riley was screaming bloody murder looking at her mom and dad wondering why they are putting her through this terrible pain. It was heart wrenching. After 4 sleepless days in the hospital, countless needle pricks for Riley, we all got to go home.

The Halloween night visit to the hospital was the first of many in the months to come. Two weeks after this visit, we were admitted again for five days and then again two weeks after that for three. It was on the third visit to the hospital that Katie and I made our first difficult decision in regards to the treatment of our daughter. After having Riley suffer through countless hours of needle pricks and being held down by complete strangers, we decided to move forward with a portacath surgery for our daughter. This would eliminate ever needing to draw blood from her veins again.

A portacath is a small medical device that is inserted directly
(continued next page)

underneath the skin, typically near the clavicle, which has a catheter that extends near the heart. It is easily accessible and allows for the drawing of blood and insertion of medicine. Because of the frequency of our hospital visits and the agony Riley would go through while being held down, we felt we had no other choice than to go through with this surgery.

In addition to the portacath surgery, she also had a g-tube inserted. This allows us to feed Riley the formula she needs when she refuses it by mouth. By having this, we have since been able to avoid a few hospital visits as we are able to administer the medication and/or formula she needs at home through the use of a feeding pump. The two procedures were completed in about 2 hours and Riley was released a few days after. She did experience a few side effects from the anesthesia but overall she pulled through like the fighter she is.

While the hospital visits grew further apart after this surgery they certainly didn't stop by any means. A new problem arose with Riley about a month and a half after her portacath and g-tube surgery. She began to suffer from quite a few ear infections despite our best efforts to do everything we could to keep them dry. After about four back to back infections, a couple of which caused her to be hospitalized, we decided that, again, it was in Riley's best interest to move forward with yet another surgery. This time, Riley would have Ear Tubes placed inside her ear canals which would help drain the excess fluid the doctors were seeing. This surgery was scheduled to be an outpatient procedure but due to complications, we ended up having to stay at the hospital for another five nights.

When Riley's doctor started the surgery he attempted to access her portacath so that he could draw blood and give her the medicine she needed. However, when attempting to do so, he realized that the port was clogged and was essentially rendered useless. He went forward with the surgery by successfully placing an IV line in her jugular vein as he was unable to get access from any other location. Later that night, Riley was put under yet again so that her portacath could be replaced.

After this visit, we were able to stay out of the hospital till August of 2011. We got to enjoy some quality time together during these couple of months and did our best to live the life of a 'normal family', though I've come to learn that such a thing doesn't exist. Riley turned one in June of 2011 and had a blast doing so. She was able to stay healthy for a month prior to her birthday and began to hit some really big developmental milestones. She learned a few words, was really involved with her surroundings, and did her best to build her muscle tone. For her first birthday, our good family friend took it upon herself to bake a protein free Elmo birthday cake. Not only did it look like the real Elmo but surprisingly, even without protein, still tasted great. Riley loved it. It was her first taste of food that she appeared to actually enjoy.

From May to August of 2011 Riley learned how to say "mama", "dada", "papa" (Grandpa), and "nana" (Grandma). Through her therapy classes and the help of her mom, she has also learned to sign "I want", "Eat", "Me" as well as a few other expressive gestures that the therapists say are good. She also learned how to walk around the room while holding on to objects. Oddly enough, this came before her ability to crawl. During these few

months away from the hospital we truly got to enjoy each other and were able to share with Riley some of the lighter/happier things in life. She enjoyed a few trips to Disneyland, participated in play dates with her friends, experienced a preschool like atmosphere in her therapy classes, and so much more.

Our hospital hiatus was short lived however as we found ourselves there again in August of 2011. In late August and in early September of 2011 Riley was hospitalized two times and began to suffer from random vomiting spells. She seemed to appear more lethargic, uncomfortable, and not the typical Riley we had seen for the past few months. We spoke with her doctors, called in a gastroenterologist to take a look at her intestines, and attempted changing her feeding schedule in an effort to help her with whatever she was going through. Unfortunately however, nobody had an answer. Right or wrong, we simply attributed it to the MMA and did all we could to help alleviate the symptoms.

It was during this time that Katie joined a MMA support group and began asking more questions regarding what experimental treatments were being done on children with this disorder. Up until this point, we had been holding out hope for a drug in Europe which was in the testing phases that we were told could help with Riley's disorder, though it wasn't originally meant for this purpose. Unfortunately however, we found out that the testing phases had been cancelled. Disappointed, Katie reached out for advice from the support group she had joined and was pointed to Stanford University where they have been performing liver transplants on children with MMA.

A commonly known fact in the 'MMA world' is that children who suffer from this disorder will eventually need a liver and/or kidney transplant. Common practice, until now, has been to wait until these children suffer from a catastrophic metabolic crash or complete organ failure. However, new research suggest that by performing these transplant surgeries early the children may experience a dramatic improvement in both the quality and longevity of life. After countless hours of research and talking with all of our doctors, we have decided that it is in Riley's best interest to move forward with the surgery. She has been placed on the National Organ Donors Transplant List and we're told that we can expect to move forward with a liver transplantation within 2 months.

While speaking with the liver transplant team at Stanford and performing the required pre-operative testing the doctors found a duplication cyst which essentially is a benign growth in Riley's intestines. They believe it may be pushing against her stomach wall and preventing Riley's intestinal tract from functioning properly. What this means is that even if we decided not to go through with a liver transplant, Riley would still need surgery to remove this cyst. Riley will have this removed at the same time as she receives a new liver.

Only time will tell what Riley's future will hold. Needless to say, this is the hardest thing we have ever been faced with. That said, we have no doubt that we can get through it. Katie

(continued page 13)

Wedding of Bert and Stephanie

Methylmalonic Acidemia, Cobalamin B

Many parents know that having children is something really special. Parents whose children have a metabolic disease realize that these children may not lead a normal life.

That's what happened to us, Dirk and Lut. We had made us a family and in the early years everything seemed perfectly normal. Although there were these constant "little" problems: the children frequently had ear infections, they were bad eaters, they vomited a lot, were constantly tired. We were young, knocked on doctors doors, weren't heard, - and life goes on. Always on our guard and a little worried ... but we got marked as over-protective parents and thus we were silenced.

Later on, when Marc went into a coma, and after many, many tests and much searching, we got a diagnosis. Marc and Bert had a metabolic disease: MMA. Prognosis then, 1987, was that their life expectancy was limited, about 7 years and probably they would be severely handicapped, both physical and mental. Alright, that was hard to swallow (these days there was no psychological counseling available), but as a parent you've got a choice: either you go for it or you let go ... To make a long story short: we went through several critical, even very critical periods, but both surpassed the prognosis and we felt as if we were given "extra time". We didn't take this extra time for granted, we adjusted our idea of the future and both boys developed pretty normal, with the usual ups and downs of course. Today, the result is worth being seen ... we are the proud parents of two grown up boys each going his own way.

Why this long introduction ? Just to give you an idea of what went through our minds, as parents, on Bert's wedding day. An event we thought, nor he, would ever experience. Being allowed to experience this day, was the ultimate dream we cherished !!! On this day a dream came true. Our son found the love of his life and started his own family. Something so normal, something that is part of life for the average human being, but for us so very special, so extraordinary ... A milestone in the life of Bert, as well as in ours. A day full of emotions...

We are twice as happy and enjoying it to the maximum! Being so lucky to experience this, is the most beautiful gift ever. A moment to say: we, as parents, have accomplished our mission, a job well done... Now it is up to them, because a wedding is an event, but a marriage is an achievement. Yes, Bert and Stephanie, you both deserve this happiness. We truly hope that many more beautiful years lie ahead of you ... that your shared dreams may come true.

Lots of luck to both of you, lots of luck together as a couple !!!
Proud mum and dad, Dirk and Lut (from Belgium)

Our experience with the Ataluren clinical trial on MMA Cbl B and A

First of all, we would like to say that by looking and surfing on the internet, I accidentally discovered that a clinical trial would start for the metabolic disease both our sons are affected with. Our interest was aroused and we talked about it at home, especially with our sons, because it mostly concerned them! When they agreed upon getting in, I discussed our interest with their doctor, who eventually took the necessary steps to be recognized as a center where this clinical trial could take place, and our sons could get started and participate.

That's how both our sons ended up participating in this clinical trial. It's a bit funny and weird to actually experience what it means to participate in a clinical trial and to go through every step, to be able to follow it all from very nearby. We met with the "study nurse", who had to make sure everything went smoothly. After reading and signing the consent form, we were able to take a look at the guidelines for this study. Quite soon it became clear that patient organizations nor patients were heard before and while composing these guidelines. Doctors and pharmaceutical industry clearly are not aware of the daily concerns/do's and don'ts and so they didn't keep simple things in mind while composing the guidelines.

But at first sight, everything was in order ... This clinical trial had already been tested on people with Duchenne disease and Muco. Probably they just took the same papers and they only changed the name of the disorder. What can be read in the protocol? Amongst other things, that the medication had to be swallowed with some milk or water! That's weird! People suffering from MMA, aren't allowed to drink milk, so big hilarity ... A bit further we read that the medication had to be taken every 6 hours! Second problem ... our sons are used to every 4, max. 5 hours, in order to spread the daily intake of proteins and never to be sober. Well, how were we to solve this? A solution was found quite quickly: they had to eat every 3 hours, de main meals every 6 hours.

Also, it was recommended to take the meals and medication every day at the same time. Which isn't that simple when working in shifts as both our sons do. Marc works early, late and daytime shifts; Bert has shifts of 12 hours (either day or night). But this little hiccup was dealt with very quick... but iron discipline was a necessity.

We had to consider doing lots of administration as well. A diet diary had to be kept, on the two days before checkups (an average of every 2 weeks). In order to keep this job as limited as possible, we did our best to have the same meals/menu every time, these two days before checkups.

(continued next page)



The checkups themselves weren't big fun because it meant checking blood pressure every hour and so they had to stay in hospital where they could wonder about (but hospitals are dangerous places for patients with MMA due to the many infections they can get there). They were very lucky (or unlucky) to be chosen for two checkups from both lasting 2 days (with sleepover, but no real sleep).

Any result of this clinical trial during this short period of time, was not quite clear or noticeable, but yet could be seen in different parameters. It's a pity, that after the clinical trial, the medication is stopped. As a patient, this feels weird: my levels are better while taking this medication, so I'm doing better now ... but I can no longer take this medication, do I have to deteriorate and get worse again? It's a pity also, that not enough patients are willing to participate in this clinical trial, with the negative result that a possible Phase III can't get started because Phase II has to be concluded. Thus ... this medication will not be on the market in a couple of days ...

We are very glad we have participated and were able to contribute to optimizing the treatment on MMA. Thumbs up that other candidates will stand up and be found, that results on all participants are satisfying and Phase III can get started.

To be continued ...
Lut (in Belgium)

Want to know more on this trial? Info can be found on our website: [www. boks.be](http://www.boks.be), then clicking the title MMA Phase 2 Clinical Trial concerning Ataluren or by this link: <http://www.boks.be/site/index.php/content/view/331/1/lang,nl/>

OAA newsletter had an article about the trial in the May 2011 issue: http://www.oaanews.org/documents/may2011_newsletterPDFFinal_000.pdf

Baby's First Test



In honor of Newborn Screening Awareness Month, Genetic Alliance recently launched a Health Resources and Services Administration, HHS funded, newborn screening website, [www. BabysFirstTest.org](http://www.BabysFirstTest.org). The website is an objective resource for expecting and new parents to learn about newborn screening and is a place for families and health professionals to share their questions and experiences. Baby's First Test is a central site that brings together stakeholders and provides easy access to newborn screening resources from community groups, government agencies and public organizations. The site also features condition specific information, state information, family videos, and a Community Corner section, where visitors can learn about reliable sources of information pertaining to maternal and child health.

Lara's Award

Methylmalonic Acidemia, Mut 0, Age 11



It was an ordinary Monday morning when I received a call from our local radio station, to let me know that Lara had been shortlisted to win the Child of Sussex Award. Lara and her family had been invited to a red carpet event at the luxurious Grand Hotel in Brighton, for a gala evening, with meal and the awards ceremony, to be followed

by dancing until midnight!! I was asked to pop into the radio station to record a message about Lara and to provide some nice pictures of her, which I duly did! Lara was so excited and we spent an afternoon searching for the perfect dress for her to wear, with matching accessories, of course!!

On September 30th, Lara and I, her Dad and her Grandparents made our way by hired Limo to the hotel - well, its not often that you get treated to such a glamorous night out!! We felt very special walking in on the red carpet and enjoyed a glass (or two) of champagne before dinner. Lara was thrilled to receive a number of comments on how gorgeous she looked!!

After dinner the awards ceremony began and as soon as they began mentioning the Child in the Community award it became apparent that Lara had won. Following my voice recording and her photo montage Lara's name was announced by the compare of the evening and Lara was on the stage in a shot!! Her face was an absolute picture as she received her engraved glass trophy and she answered all of the questions that she was asked in a clear and confident voice! I cannot tell you exactly what it was that she said as by this time I was blubbing like a baby!!!

Lara won the award for her fund raising efforts for our local and for Great Ormond Street Hospital in London. In her short life she has to date endured approximately 40 hospital admissions, some of them very lengthy - and whenever she gets the opportunity she gets fund raising for these hospitals to try to pay them back for the wonderful treatment that she has received and also to help other unfortunate children that find themselves admitted too!! Funds have been raised via family and friends, school and her Brownie Guide pack and to date she has provided all of the cubicles on her local kids ward with a new colour TV, DVDs and last Christmas time a present from Santa for everyone!! Great Ormond Street have benefitted from portable DVD Players and Lara continues to help by being the face of West Sussex on the Great Ormond Street Charity website!! I always admire Lara for her strength of character during the tough times and for being the beautiful little girl that she is - but on this night I was the proudest Mummy on the planet!!

Written by Julie (in England)
Mum to Lara MMA Mut 0 Age 11 years

Austen

Glutaric Acidemia, Type II, Age 13



I share the same story with many of you. The normal pregnancy, the c-section birth, the sight of that precious, little face and the feeling that finally, all was right with the world. And then the shock.

My previous pregnancy, eight years back, was difficult. I had conceived triplets through the in-vitro process, after trying for years to get pregnant. I lost a baby after my first attempt so I was off my feet for this whole pregnancy and hospitalized four weeks before their

birth at thirty weeks. Although they were preemies and had to stay in the NICU for five weeks before coming home, they had few problems once they were home and were all good nursers after they got the sucking reflex which happens at about thirty two weeks of age. I nursed all three of them for the first six months and when they went onto solids my kids were great eaters!

I was surprised that Austen had no interest in breast feeding and although the nurses said it was not an uncommon thing for a baby not to eat for the first few days, I remember being very concerned about his crying. He wailed like only a hungry baby could. When he was taken from my room so I could get some rest, I could hear his cries in the little nursery down the hall, louder than all the others. The second day was like the first, now I was worried. The staff seemed indifferent. He still wouldn't eat, but he was clearly unhappy. That evening lying next to my bed in his little bassinet, his wailing forced me to get out of my bed to pick him up. The nurses were all busy and because it was a Friday there were lots of visitors and noise and rejoicing the birth of all the new babies.

Once I got Austen settled in my arms, I tried once again to nurse him. Nothing. His crying turned to a sound that a little kitten would make, the light was low and I held him and tried to soothe my sweet little man. I don't know if I fell asleep or we both became one again and my breaths were his and finally he was at peace. Suddenly my dream turned into a nightmare. I stroked his head and it was cold. I called his name and he didn't move. I screamed at the top of my lungs for help and my baby didn't flinch. I recall screaming forever until the room was full of people and lights and the hallway was silent. Austen was a

strange blue color. They took him away and I knew he was dead and I still kept screaming.

Austen was eventually revived. The nurses said he was without oxygen for twenty minutes. I think it was longer because no one came to my room to tell me anything and I was very hoarse from wailing. He was transported by ambulance to New England Medical Center where he was stabilized from the seizures, put under oxygen and once again I had a baby hooked up to wires and tubes, but there was no excitement this time.

He had suffered serious brain damage and on the third day of his stay in the NICU, I was asked to sit down with the doctors who had been following him. Dr. A, the metabolic doctor who had been spending a lot of time with him, told me that he had a serious genetic defect. She called it Glutaric Acidemia type II or otherwise known as Multiple Acyl Co-A dehydrogenises Deficiency (MADD). She told me that it was a fatal disease and explained that he could not metabolize fats or proteins. She said that no other child born with this disease had lived for longer than six to eight months. She was patient with me when I cried. She said that she wanted to send a muscle fibroblast to a doctor in Iowa who would confirm the disease. She said that he could be brought home once he was taken off the tube feeding him through his nose and suck on his own. He should be given the best life possible in the next few months. It was best "not to resuscitate" should he stop breathing again, because of all the damage that he had already sustained. He was not to drink breast milk, too much fat and protein, so he needed a special formula.

Up to this point, I was in shock and depressed and felt very alone and defeated. But as I spent days with him watching as he came out of his long sleep and when he finally looked up at me and took formula from a bottle, something changed in my attitude. On the day we were told we could go home I became an angry, assertive woman, a person I had never been in my whole life. I demanded an apnea monitor to have at home in case he stopped breathing, I insisted that I would breast feed him and I didn't want the formula, (after all if he was to be given the best life in six quick months, shouldn't he be allowed to breast feed?) He went home and I pumped and he learned how to nurse. I got in touch with the FOD (Fatty Oxidation Disorder) organization and got a home computer (one of my smarter purchases!).

Austen got bigger and gained weight and I became more determined not to let the diagnosis defeat us. We got the confirmation from the fibroblast that he had " 2% of controls...as low as enzymes get". It was a mitochondrial disease and there was no cure except to continue with the carnitine and B2 supplements that were supposed to sustain him. I read Dr. Andrew Weil's book, "Spontaneous Healing" and was particularly affected by the chapter that addressed malfunctions in DNA. He says that it can be reversed through diet especially by ingesting natural enzymes. I changed my diet radically after going to see a naturopathic doctor who put me on a meat-free, dairy-free diet which included mostly raw fruits and vegetables (both Austen and myself still follow this

(continued next page)

diet). I didn't stop there; I sought out a Native American shaman, a Catholic priest who was a faith healer, a Chiropractor...and a second opinion from another metabolic doctor. From the first time I met Dr. Korson, I knew that we would be in good hands. He believed in treating Austen the individual, not the disease. His approach was much more hopeful and that is what I needed to keep going, especially since I was a single parent at this point. He marveled at his weight gain and cognitive abilities, although he was delayed, he seemed to be progressing. The one concern was that his head circumference had come to a halt. Dr. Korson prescribed CoQ10 and in the next few months after starting it, his little head started growing again, although he is still considered to be microcephalic. When we started with solid foods each meal was traumatic, because he would throw it up from reflux. I had to clean up the mess and start all over again, because I knew if he didn't eat we would end up in the ER. He came to recognize that he had no choice in this food business, he had to keep it down!

I weaned him very gradually off of the barbiturates that he had to take for seizures and he has never had another one that I know of. Early on I recognized that Austen had a severe visual impairment and hooking up with Perkins School for the Blind got us involved with the infant toddler program, preschool, the 'Lower School' and this June will graduate to the 'Secondary Program'. Social skills, PT, OT, sensory integration, mobility, music therapy, gym, arts, swimming and of course academics are only part of the total program. We have a skilled health care clinic on the grounds and we have been very lucky to live so close to the school and be part of this wonderful community.

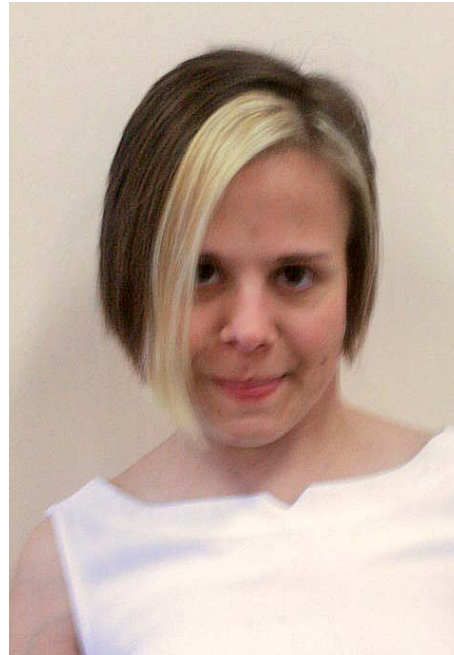
Today, fourteen plus years after his birth, he is of normal height and weight, a handsome devil who is devoted to his older siblings, Nathan, Sasha and Taylor, and his loving stepfather, Joe. It has not been an easy road. We have had many bumps and starts. He stopped sleeping, (night and day) at about age three. Several trips to the ER after a vomiting bouts, severe sinusitis (now controlled with Periactin), incontinence still to this day, it hasn't been easy. He has many food allergies which have been hard to decipher since he can't really tell us 'where it hurts' and displays his discomfort through tantrums or negative behavior, although once we got the wheat, eggs, peanuts, etc. out of his diet we have seen much less confusion and better spirits.

The change in diet and realizing that his behavior was on the autistic spectrum (and getting the diagnosis of Asperser's syndrome), has afforded me with much more knowledge of how to help my son deal with this world that he doesn't really understand, and help others to understand his world. I feel strongly that the choices I have made for my son have been the right ones, but I could not have done it without the help of all the wonderful people I have met along the way and who now share a part of Austen's world, and without them, I might not have made some of the connections that have made such a big difference in the quality of my son's life.

Gwen
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Update on Amber

Methylmalonic Acidemia, mut0, Age 27



I am 27 years old; I have been working at BB & T Bank as a wholesale check processor for the past five years. I have 27% kidney function and have been evaluated for a liver/ kidney transplant (LKT). I will be the first MMA patient to have this transplant at Johns Hopkins Hospital in Baltimore, Maryland.

I am currently in Dr. Venditti's research study at

NIH in Bethesda, MD. Out of 100 people in the study, my MMA levels are one of the three highest at 9,000 micromoles. About two months ago, I developed optic nerve atrophy. The vision in my left eye is 20/400, and my right eye is 20/50. The doctors at NIH and Hopkins think this is due to the high MMA levels.

I am on dialysis while waiting for placement on the waitlist for the LKT. Before dialysis, I was eating 37 grams of protein per day. I am now eating 60 grams per day. It is predicted that I will be off all MMA and kidney medications after the double transplant. I am very nervous about this because I have never had an operation. Luckily, two of my friends have had the double transplant successfully.

If any older patients, or any patients or parents would like to talk to me, feel free to call at 301-204-1786.

Best wishes,
Amber, MMA, Mut 0
Bowie, MD
Smrtyantz02 on FB



Kathy Stagni and Jana Monaco at the Genetic Alliance 25th Anniversary Gala in Washington DC. (September)

In Memory of Drew Kai

Nonclassic Homocystinuria with a Cobalamin Defect.



Our beautiful baby boy, Drew Kai, was born May 18, 2011 after an easy labor and delivery. He was 9 lbs. 5 oz., 21.5" long, and thriving. After a short, un-eventful stay at the hospital we arrived home to begin a

normal, rather mediocre life. I left my job to stay home with Drew and our 5 year old daughter Alexis. We had a regular summer. Drew had regular checkups at the doctor and had no apparent red flags to his disorder. He was an active and aware baby boy. He loved bath time and was a "talker." When his sister was close to him he would open his eyes and look around for her, waiting for the kiss and cuddle that was readily available. Drew continually gained weight and was always hungry. He nursed well and had no problems with his appetite. I couldn't have asked for more. Our home was filled with love and we felt peace at how our lives were.

After a day trip out of town, our lives turned upside down. After being misdiagnosed with acid reflux after his first seizure we were left with more questions than answers until we finally received his diagnosis; nonclassic homocystinuria with a cobalamin defect. The seizures affected his ability to breath and the toxicity in his body, along with a complete depletion of B12 in his body, caused severe cerebral atrophy.

After being placed on a ventilator Drew slowly recovered. However we were warned that the damage and trauma done to his brain could not be reversed and may be causing the breathing problems. We waited patiently for 2 weeks while his enzyme levels stabilized and his body adjusted to the seizure meds. We decided to give Drew a G-tube to aide in feedings and giving medications. The day arrived when they decided to take the breathing tube out. We were absolutely ecstatic.

They removed the breathing tube at 9:30am on August 26th, 2011. He breathed fine at first but after less than an hour; he began the same breathing pattern that originally caused him distress. Our worst fears had come true. The breathing problems were not only associated with seizures but the damage done to his cerebral tissue was so severe that he could not coordinate his muscles to breathe. We waited, hoped and prayed that he would be able to establish a healthier breathing pattern but the time came, late that night to make the hardest decision of our lives. The doctors told us that if we decided to intubate him again, they would, however he would most likely never be able to breathe on his own. It was now a question of when. When would we decide to let him go? We prayed and felt strongly that it was his time. It was apparent to both of us that he was no longer with us. We wrapped him in his favorite blanket that was green with a monkey, and we held him. We whispered our goodbyes, told him we loved him and within minutes he passed from this life to the next. As difficult as it was to watch our beautiful baby boy leave us, we knew it was the right decision. We didn't want him to live that kind of life, hooked up to a ventilator for our benefit. We miss him more every day and will never forget his beautiful smile.

Brittany britparke@yahoo.com

Brayden's Memorial

Methylmalonic Acidemia

Little we knew that morning
God was going to call your name,
In life we loved you dearly,
In death we do the same.

It broke our hearts to lose you,
you did not go alone,
For a part of us went with you,
The day God called you home.

You left us beautiful memories,
Your love is still our guide,
And though we cannot see you,
You are always by our side

Our family chain is broken,
And nothing seems the same,
But as God calls us one by one,
the chain will link again.

In Loving Memory of
Brayden Gene Rood
April 27, 2010 - July 31, 2010
Deeply loved and missed by
Mommy, Daddy, and Miya

I have attached a picture to use in Brayden's memorial. This is one of the pictures I treasure most because it was shortly before he passed away and he was just starting to get his personality and started smiling. I have written a little something and I found the poem I have included shortly after Brayden's passing and actually have passed it on to others who have suffered a loss because I think it has such meaning.



On April 27 2010, our precious son and brother, Brayden Gene Rood came into this world. Little did we know what the future held for us and how short of a time we would have with him. When Brayden was eight days old, it was confirmed through the Newborn Screening in the state of Michigan that Brayden had Methylmalonic Acidemia. Our minds raced as we knew absolutely nothing about this condition or what it meant for our son. The weeks after were a blur as we learned to care for Brayden. Brayden may have had a rare condition and specials needs, but he was perfect to us. On July 31, 2010, Brayden grew his Angel wings. Brayden is missed deeply everyday by his family that loved him unconditionally and not a day goes by we don't think and talk about our precious baby.

Update from Washington DC

By Jana Monaco, IVA parent

It has been 10 years since my husband and I came to realize the meaning of newborn screening and how important it really is—both to a child and a family. Our son Stephen was diagnosed with Isovaleric Acidemia at age three and a half, because this disorder was not routinely screened for at the time of his birth. If it had, his and our life would be extremely different. It would have been full of typical, wonderful and amazing milestones that we had hoped to experience with Stephen. Instead, it has been 10 years of continuous grieving of what we lost and continues to lose; learning and accepting the severe disabilities, seizures, surgeries and other complex health issues that are a direct result of the lack of expanded newborn screening for Stephen. Every year is another year of lost opportunities and memories taken away from us.

As we celebrate Stephen's 14th birthday on October 26th, I reflect on the past 10 years and its whole new meaning that is one that has helped to give some sort of solace, however small, to our personal experience and loss. A multitude of initiatives have taken place allowing us to use our tragic experience to help change newborn screening. The Secretary's Advisory Committee for Heritable Disorders in Newborns and Children commenced seven years ago to address the disparity of newborn screening across the nation. Laws are now in place across the country in all 50 states expanding newborn screening to include all 29 disorders recommended by the American College of Medical Genetics and endorsed by the advisory committee. With the addition of SCID to the ACMG panel a year ago as recommended by the Secretary's Advisory Committee, states are assessing their programs and gradually including it on their newborn screening panels. The most recent condition added to the recommended panel by the Secretary's Advisory Committee, just last month, is Critical Congenital Heart Disease. Screening for this group of disorders with pulse oximetry will now challenge states to further assess their programs as they must consider adding it to their newborn screening panels. I am proud to have served a four year term with the committee and participated in the vote for each of these disorders. Though my four year term ended in January 2011, I continue as a member of the committee's Education and Training Subcommittee. This subcommittee has been successful in influencing the decision of the American Academies of Pediatrics, Obstetrics and Gynecology and Family Practitioners to include education on newborn screening and inborn errors of metabolism for their physician training material and to find ways to incorporate it into their patient education material. The advisory committee was tasked to identify a newborn screening "clearinghouse" by the Newborn Screening Saves Lives Act. It would serve as a "go to place or one-stop shop" for in-depth educational information for professionals and the general public regarding newborn screening. The Genetic Alliance was chosen to fulfill that goal and it successfully launched the site, "Baby's First Test" last month. These are just a few recent accomplishments of the advisory committee in its efforts to fulfill its charter and mission for newborn screening. With the celebration of its 25th meeting last month, Dr. Rodney Howell, the chair of the advisory committee since its inception, completed his extended

term of this committee. His passion and commitment to children's health and newborn screening along with his years of knowledge and experience as a physician have guided him in leading this committee in a most reputable and distinguished manner in achieving its goals. Dr. Howell has been a prominent figure with the committee and will certainly be missed. At a recent dinner hosted by Dr. Howell in Washington to celebrate the 25th meeting of the committee, his time with the committee and its achievements, I had the honor of presenting Dr. Howell with a beautiful photo book full of kids with different organic acids, created by our own Raymonde DeGrace, and share a few words of our appreciation to him. Dr. Joe Bocchini, already a well respected and valued member of the committee, was selected as Dr. Howell's successor. Following day one of the committee meeting, many were in attendance at Genetic Alliance's 25th Anniversary Gala to celebrate 25 years of its hard work and achievements in the world of genetics. It was a privilege to be a part of its innovation theme this year and be included in its video collection of innovators viewable on YouTube.

Exciting and important work supporting the process and further progress in newborn screening continues and I am honored to represent the voice of the consumer and OAA in Washington. Most recently, I presented at the recent committee meeting on the consumer perspective and role with the committee and was able to raise the issue of reimbursement for medical formula and foods at the US Conference on Rare Diseases and Orphan Products in Washington, sponsored by NORD. The work never ceases, but progress is being made. Babies are being diagnosed at birth and receiving the necessary treatment for their disorder.

Children like my daughter Caroline, now nine, are living out their hopes and dreams despite their disorder, thanks to that early detection. Education and awareness of these disorders and newborn screening is greater than ever. More importantly, babies' lives are being saved! As my family and I continue to cherish each day with Stephen through bittersweet eyes, we rejoice with his and Caroline's life and the testimony to newborn screening that they represent. We celebrate each and every achievement to enhance newborn screening across the country.



Dr. Rodney Howell and Jana Monaco

A Witches Brew Of New Work From The NHGRI

Charles P. Venditti, on behalf the NIH MMA and cobalamin research team * (Nuria Carrillo-Carrasco, Randy J. Chandler, Irini Manoli, Julien Senac, and Jennifer Sloan) Organic Acid Research Section, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD
Email: venditti@mail.nih.gov

Since our last update, we are very fortunate to have led a series of clinical and laboratory research projects, each of which has generated important new observations. We continue to study the hereditary methylmalonic acidemias (MMA) and inborn errors of cobalamin metabolism, in the lab and the clinic, and are grateful to all the families that have taken the time to visit the NIH. This article will overview three new chapters of our recent work.

A NEW GENE THERAPY APPROACH TO TARGET THE LIVER AND KIDNEY IN MMA. We continue to study gene therapy for MUT MMA in the lab and hopefully, in the clinic. Several months ago, we wrote about the impressive results obtained when tiny MMA mice were injected in the liver with an AAV (adenoassociated viral) gene therapy vector immediately after birth. In the MMA mouse model, all affected and untreated MMA mice perish, with most dying immediately after birth in the first few days of life. However, when these mice receive gene therapy on the first day of life, the treated MMA mice lived to 1 year of age, thrived and appeared normal compared to non-MMA littermates. In our most recent paper (1), we have extended this work and examined the efficacy of an alternative adenoassociated viral (AAV) serotype to improve the effects of systemic AAV gene delivery in the MMA mice. The serotype of the AAV is akin to the covering of the virus and one unique feature of AAV is the ability to make different strains by changing the serotype or coating of the virus. We decided to use an AAV, specifically of serotype 9, which had been previously demonstrated to direct high-level expression of a reporter gene in almost all tissues when given to mice as a systemic injection by the tail vein. In our first set of studies, we were able to use 10-fold less AAV9 virus to rescue the MMA mice from lethality than in our previous work. What was surprising and important was that the AAV9 treated MMA mice, despite having very high levels of MMA in the blood, had normal kidney function. We then used the AAV9 treated mice to ask a question about the dose of virus needed to produce a biochemical response. When the treated MMA mice were re-injected at 1 year of age with a dose of the virus similar to that given to humans in other gene therapy trials (example: hemophilia), we were able to document biochemical improvements in the mice within 3 days. At one month after re-injection, we searched for evidence that the AAV9 could carry our MMA gene therapy virus to the kidney and liver and were pleased to find the expression of the Mut gene in both organs after a systemic injection. The practical implication of these results are that they show MMA can be treated by this novel type of AAV in a mouse model that replicates the most severe (mut) form of MMA and can direct expression of the viral transgene (Mut) throughout the body, including the kidney. We were also able to demonstrate a biochemical effect of gene therapy using a dose given to humans in other gene therapy

trials, a result with practical implications for human extension. If successful gene therapy for MMA can be developed, it may require multiple treatments throughout life and because humans can mount an immune response against any virus they are exposed to, including an AAV used for gene therapy, the ability to choose from different serotypes that are biologically efficacious will be important. The analogy to our AAV9 gene therapy studies in mice would be that a patient with MMA could receive a single IV infusion and experience the effects of gene therapy in the liver and kidney.

COBALAMIN C DISEASE: IS IT TIME TO REASSESS OUR APPROACHES TO TREATMENT? Cobalamin C (cblC) disease is stated to be the most common cobalamin metabolic disorder in humans yet there are widely varied approaches to management and fundamental aspects of the natural history of the disorder that are poorly defined. A few such examples might be: what is the dietary and nutritional approach to manage cblC patients and what is the evidence to support such practices; what are the growth, development, and neurological complications seen in cblC patients and are there any predictive clinical covariants; what are the expected ranges of metabolites seen in the patients and are there any correlations between metabolic control and clinical parameters; and what is the nature and progression of the eye disease for the patients? As the many unresolved and difficult to study issues in cblC are apparent, what was missing from the published literature was a set of comprehensive scholarly reviews that document what progress has been made and where future studies might help. We wrote two very long extensive reviews on cblC as a resource for the community (2,3). One article has a supplemental table that reviews all case and treatment reports for cblC since the 1970s – but please know before you click print, the table itself is 50 pages!

NEXT GENERATION SEQUENCING HELPS FIND THE CAUSE OF COMBINED MALONIC-METHYLMALONIC ACIDEMIA. When an infant, child or adult gets diagnosed with “increased methylmalonic acid” in the blood and/or urine, what happens next? Many parents and children have undertaken this diagnostic journey, which ends in most cases with a skin biopsy result proving the main MMA pathway in the cell (and by extension, the patients body) does not function properly. The exact type or cause of MMA is also pursued – letting a person know if they have mut, cblA, cblB, cblC, ... or other type. And finally, DNA analysis is performed to identify the exact change(s) in the underlying gene, and confirmed in the parents, who are each almost always obligate carriers of the DNA changes in the gene that causes the MMA. In the end, all this testing is required to precisely define the genetic form of MMA in each patient.

But what about those who have normal results of MMA testing yet convincingly have elevated metabolites and symptoms suggestive of a metabolic disorder? We have evaluated such a group of patients over the past few years in the NIH clinical research center. Despite extensive evaluations, including skin biopsies, enzyme measurements and genetic testing, these patients emerged as having significantly elevated MMA in the blood and urine for an unknown reason. On careful assessment of the organic acids they produced, it was noted that they all

had increased MMA as well as malonic acid (MA) in the urine, with MMA levels much higher than malonic acid levels. Some may know that there is, in fact, a recognized cause of combined malonic-methylmalonic aciduria; something called malonyl-CoA decarboxylase deficiency (MCDD). However, patients with MCDD have much more malonic acid than methylmalonic acid in the urine and also have decreased activity of the malonyl-CoA decarboxylase enzyme in fibroblasts. We were able to confirm that our “unknown” CMAMMA patients also had normal activity of this enzyme, this ruling out the possibility that they had a malonyl-CoA decarboxylase deficiency variant. Our patients therefore had a variant form of MMA featuring combined malonic methylmalonic aciduria (CMAMMA) and resembled a patient reported several years earlier.

Because extensive biochemical genetic testing results had not yielded the answer of what was causing this condition, we turned to a new genomic technique called exome sequencing to identify the genetic cause of their increased metabolites. Exome sequencing is a high throughput method that can be used to determine the DNA sequence from all the coding regions of the genome. This allowed us to sequence almost every gene in the genome concurrently and then ask the question – can we detect the gene that is mutated and the cause of this condition? This is truly akin to finding the needle in the haystack. In collaboration with Dr Leslie Biesecker’s group at NHGRI, the National Institutes of Health Intramural Sequencing Center performed exome sequencing of an affected CMAMMA patient and her parents. In less than one week, we were able to use a series of informatic filters to comb through >110,000 possible DNA changes to identify 12 possible genes that fit a recessive inheritance pattern and were inherited uniquely by the patient, meaning that her parents were each carriers of one change, but not both. One of the 12 genes stood out because it was predicted to localize inside the mitochondria and was further investigated. Indeed, in 8 other patients with CMAMMA, multiple mutations were detected in the same gene, AcylCoASynthaseFamily 3, *ACSF3*. This enzyme had been previously described as an orphan member of a large gene (enzyme) family whose products appear to catalyze an ancient and conserved reaction in metabolism - the activation of fatty acids and organic acids into their respective coenzyme A derivatives for intermediary metabolism. Based on this information, we hypothesized that ACSF3 was a malonyl- and methylmalonyl-CoA synthetase and next demonstrated that the purified enzyme did indeed catalyze the hypothesized reaction. We also were able to develop a cell culture assay to prove that the gene could restore aberrant organic acid metabolism to cells derived from patients with CMAMMA, and even discovered changes in the homologue of *ACSF3* in a dog that had previously been reported with CMAMMA. This body of work has established that a new form of MMA, specifically CMAMMA, is caused by mutations in ACSF3, a protein that is NOT involved in cobalamin metabolism or the function of the MUT enzyme (4). This enzyme appears to be critical in a newly discovered pathway of direct MMA (and malonic acid) metabolism inside the mitochondria, and is likely to be connected to other pathways of importance inside the mitochondria. Future studies will need to focus on the development of an animal model to further understanding the

importance of this enzyme in mammalian metabolism, and detailed characterization of patients with CMAMMA.

In closing, we would like to thank all the patients and families who have participated in our research. The importance of a partnership to help increase the knowledge of MMA and cobalamin disorders is paramount and will continue to advance the field.

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4. Sloan J.L., Johnston J.J., Manoli I., Chandler R.J., Krause K., Carrillo-Carrasco N., Chandrasekaran S.D., Sysol J.R., O’Brien K., Hauser N.S., Sapp J.C., Dorward H.M., Huizing M., NISC, Barshop B.A., Berry S.A., James P.M., Champaigne N.L., de Lonlay P., Valayannopoulos V., Geschwind M.D., Gavrilo D.K., Nyhan W.L., Biesecker L.G., and Venditti C.P. (2011) Exome sequencing identifies *ACSF3* as the cause of Combined Malonic and Methylmalonic Aciduria. *Nature Genetics.* Aug 14. [Epub ahead of print] PMID:21841779

Riley (continued from page 5)

and I have been a couple now for over 10 years (since we were 15) and have loved each other the whole way through. We will continue to love and support each other AND Riley as we all get through this difficult ordeal.

Please keep praying. Please keep her in your thoughts and hope for the best. This will obviously take time to accept and embrace but I know we will as we get to know her and learn what she has to contribute to the family. The first day at the hospital the nurses were all saying how pretty she is and how she was the sweetest baby they've seen in a long time. I hope her calming and kind nature and natural beauty remain with her throughout her whole life. I have only known her for a short time and am already jealous of these traits.

It also goes without saying that she is already one of the strongest people I know. She has endured so much in her short lifetime and has gone through it all with a huge smile on her face. I can only hope her persistence to live and thrive will only grow as she does.

Kyle and Katie
kyleomiller@ gmail.com

Section 504 Helps Kids with Metabolic Disorders

Beth-Ann Bloom, MS, CGC

Genetic Counselor

Beth-Ann is the parent of a young adult with a disability and has enjoyed over 30 years of working with families dealing with metabolic and other genetic disorders

With school starting again this is the perfect time to become familiar with how to help your child in school. Special education helps children whose metabolic disorders have caused serious complications, but many children who were diagnosed early and are doing well still need some extra help and protection in school. Federal law protects the rights of children with metabolic disorders. It guarantees reasonable accommodations and saves parents the need to go from teacher to teacher pleading for "favors" to keep their children healthy and in school.

Section 504 is a law that can help people with metabolic disorders. It protects them from discrimination. This US law gives people with disabilities the same chance as other people. The 504 law can help children in school.

Section 504 of the Rehabilitation Act of 1973 gives rights to people with disabilities. The law says that any group that gets money from the US government must be fair to people with metabolic disorders like OA and PKU. Public schools, cities, park programs, etc. must include people with disabilities.

504 says that public schools have to include all children. They have to make reasonable changes to make it possible for all children to join in and learn. These changes are called accommodations.

Children with health problems including metabolic disorders can get help from 504. Parents can ask for a 504 plan. It is a list of the accommodations the school will make. These changes will allow the child to be part of the school. These changes will make it easier for the child to learn. These changes are a civil right.

Parent Training Centers can help you learn about the law. In Minnesota, contact PACER www.pacer.org. For centers in other states check here <http://www.parentcenternetwork.org>.

To get a 504 plan the child must qualify. The rules are different in every school district. To start write a letter to the principal asking for a 504 plan. There is a sample letter at the end of this article.

Ask your child's doctor to write a letter. The letter needs to say why the child qualifies for a 504 plan. It needs to give the name of your child's disability. It needs to list which part of the body is affected. It needs to say which life function is changed. It can suggest accommodations. There is a sample doctor's letter at the end of this article to guide physicians who may not be familiar with 504 plans.

The law says your child can have a 504 even if he or she is doing well. If a special diet or treatment is working, the 504 can make sure it keeps working. School staff will tell you how they will decide if your child can have a 504 plan. You have rights. If they don't agree to write a 504 plan, you can appeal. A 504 plan is NOT special education. It gives help in regular classes. There are no special teachers or funding for 504.

Here are some of the kinds of accommodations children with metabolic disorders can get:

- Staff will send a note home daily about what was eaten at lunch
- Teachers will have training about the metabolic disorder
- Child's cafeteria lunch will meet special dietary requirements (Same cost as regular cafeteria meal)
- Can keep water bottle at desk all the time
- Can go to the bathroom at any time
- Can have indoor recess when it is too hot or too cold
- Grades not lowered if work is late when sick or at a clinic appointment.

All the teachers need a copy of the 504 plan. Other school staff like the nurse and the bus driver needs a copy of the plan.

Learn who is in charge of the plan. This person is often called the 504 Coordinator.

If the plan is not followed, tell the 504 Coordinator. If the problem continues, advocate for your child. Write to the coordinator. Ask for a meeting. Ask for help from a friend or another parent. Contact a parent center.

If your child needs more help, ask the teacher or the 504 coordinator. Review the plan at the start and end of every school year.

Children with metabolic disorders can do well in school. Section 504 helps them do their best.

Sample Letter Asking for 504 Plan

Date _____
Dear Principal _____,

My child, _____, Date of Birth _____ is/will be a student in grade _____ at _____ School. My child has a medical diagnosis of _____. This condition can have serious impact on major life functions including learning.

I am requesting that a 504 Accommodations Plan be written for my child. I will ask my child's clinic to send a letter explaining the condition. Please contact me this week with information about the process used at the school for writing an implementing a 504 plan.

I can be reached in the following ways:
Home phone: _____
Cell phone _____
Email _____
Other: _____

I look forward to working with the school staff in writing this accommodation plan that will allow my child to be a fully included member of the school community.

Sincerely,

Sample Letter Asking for Doctor's Help to Get 504 Plan

Date _____
Dear Dr _____,

I need your help so that my child _____ Date of Birth _____ can be considered for a 504 accommodation plan at school. A doctor's letter is usually the first step in getting the plan. It would be very helpful if your letter includes the following information. Can you please send a copy straight to the principal and another copy to me? Thank you again for all you do to keep my child healthy. I appreciate your help in making sure things work well at school too.

Sincerely,

GlutarAde GA-1

Applied Nutrition is happy to announce the release of the GlutarAde GA-1 product line which includes GlutarAde Junior and GlutarAde Amino Acid Blend. GlutarAde Junior was developed during a five year clinical trial conducted with the Clinic for Special Children in Strasburg, PA. The study is entitled "Safety, efficacy and physiological actions of a lysine-free, arginine-rich formula to treat glutaryl-CoA dehydrogenase deficiency: Focus on cerebral amino acid influx" Strauss, KA, et al. *Mol Genet Metab* 2011;104(1-2):93-106.

Between 2006 and 2011, 12 children diagnosed with GA-1 were placed on a lysine free study formula within the first week of life. The original design of the study formula was based upon a known competition between lysine and arginine for entrance into the brain. This means that when arginine levels are high enough in the blood compared to lysine, the arginine can block some of the lysine from entering the brain. Therefore, it was hypothesized that increasing dietary arginine along with a low lysine diet, could help block brain lysine uptake and reduce risk of brain injury while providing enough lysine for normal brain development. Over the course of the study, each amino acid was studied and adjusted to provide the optimal formula.


At the time of publishing, the study patients were ages 6-59 months. All 12 patients were physically and neurologically healthy. There were no acute or insidious motor injuries detected and all children sat independently before 7.5 months

and walked by 15 months. This represents a 36% reduction of neurological risk compared to 25 children with a protein restricted diet treated from 1995-2005. A treatment protocol was established from the results of this study that provides metabolic professionals a guideline for how to treat and monitor the GA1 patient. The protocol is a very important part of the management of GA1; it contains recommendations for outpatient well-day management, outpatient sick-day management and emergency treatment, which all contributed to the success of the trial. This study demonstrates that newborn screening; frequent follow up with a metabolic clinic, an emergency management plan and an appropriate diet that monitors lysine to arginine ratios can be a useful strategy for treating GA1. Please consult your metabolic professional for additional information.

Applied Nutrition is excited to add GlutarAde GA-1 to our extensive line of medical foods and join the OAA community. As a global leader in metabolic support we hold ourselves to a higher standard. Our products are developed with formulation experts and backed by science. Our success comes not only from offering great tasting medical foods for GA-1, PKU and MSUD, but by providing outstanding customer service. We truly understand the importance of our products and have a team of experts to help you with any questions regarding GlutarAde GA-1 medical food. Learn more about Applied Nutrition at www.medicalfood.com.

Alana Duffy, MS, RD
Director of Nutrition at Applied Nutrition


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Please make the following changes to my address, phone number, or email address. Remember the newsletter does not get forwarded when you move!

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Organic Acidemia Association
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The Organic Acidemia Association (OAA) provides information and support to parents and professionals dealing with a set of inborn errors of metabolism collectively called organic acidemias. The OAA is a volunteer organization registered with the IRS as a 501(c)(3) non-profit corporation. Donations to the OAA are tax deductible. OAA publishes a newsletter 3 times a year, hosts a Google Group for information exchange and maintains a website. Services are funded by corporation & individual membership donations. Annual membership donation of \$25 (US) and \$35 (international) plus \$5 for the family roster is requested, but not required. Our 501(c)(3) non-profit status qualifies OAA for United Way donations through their write-in option. If there is a write-in option, just write "Organic Acidemia Association" in the blank line on your pledge card. Donations can also be made at OAA's website through the "PayPal" and the "Network for Good" option.

OAA Internet Google Group

OAA's main mission is to empower families with knowledge about organic acidemias. If you would like to connect with other families who share the same or similar diagnoses, please join our OAA Group. Visit the OAAnews.org web site to sign up. This is a private list not open to the general public (but you never know who may be "lurking").

- * The information contained herein does not necessarily represent the opinions of our Board of Medical Advisors or Board of Directors
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Facebook

OAA is on Facebook -- donations can be send through our "Cause" Page, connection with other parents can be found through our "OAA Group" and "Fan" Page.



Wanted

* Articles are ALWAYS needed for the newsletter.



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