

Editorial

by Kathy Stagni

It's been a very cold winter this year and I've heard from many families that had to visit the hospital this season...including our family! I used to "brag" that it has been over 5 years since Melissa has visited the hospital – but the stomach flu hit and she was in the hospital for about a week. It's amazing how I forgot what it's like to be in the hospital. I want to remind parents to bring their protocol letters with them to the hospital, even if it's their "home" hospital. Hopefully your family will survive the remainder of the winter hospital-free!

Thank you to all of the families that wrote their stories for this issue of the newsletter. I know sometimes it is not easy to re-visit the past and write these articles, but I think it's definitely therapeutic! Please consider writing for our next issue, which is due out in June. It's interesting how a couple of our articles this time were families diagnosed through newborn screening and the other two – well they probably should have been! We are making great progress in the states with newborn screening. I'm proud to announce that the state of Minnesota will begin expanded testing for all 30 metabolic disorders this coming March!

This issue of the newsletter will include information on our two upcoming family conferences. There is a preliminary registration form for the conference in Columbus in May, and information about the June conference in Houston. We are excited to be able to offer you these two options and hope that you'll be able to make at least one of them. I'm happy to announce that Dr. Pinar Ozand, a noted metabolic physician from Saudi Arabia will attend the conference in Columbus. Also in this issue, Dr. Ozand was kind enough to share his protocol for treating Propionic Acidemia patients in Saudi Arabia. Please remember that every child is different and to discuss any treatment changes with your physician!

This past October I attended the World Congress on Disabilities conference in Atlanta, Georgia. Cay Welch, International Glutaric Acidemia Association and I attended several interesting sessions relating to a wide variety of disability subjects. Dr. Larry Sweetman, Institute for Metabolic Disease, and Tera Mize from Tyler For Life spoke at the Newborn Screening session. OAA's sponsor, Sigma Tau Pharmaceuticals was a major sponsor for this conference.

I also want to mention that we are working to re-vamp our OAA website. It was suggested to me that we put older issues of the newsletter up on the website. Thanks to Dana Dozier for helping me get this accomplished. As you may know, the website has helped many families research OAA disorders and locate others dealing with the same issues. I feel very fortunate and rewarded to be able to offer this to our families & and future families.

Amber Nicole Dozier

MMA, cbl A, 20 months

Morgan, age 4 with sister, Amber, MMA



Amber Nichole Dozier was born on May 4, 1999. I had a healthy pregnancy other than a lot of nausea and vomiting. The delivery went as expected. She is our second daughter. Our first, Morgan, born in 1996 is unaffected by MMA.

During the first four months of Amber's life we saw none of the symptoms that we now associate with MMA. Her four-month checkup results were a healthy baby, able to roll in both directions, meeting all milestones. She was exclusively breastfed and was starting baby cereals. Five days after that checkup Amber began vomiting. She would push away from me while breastfeeding and vomit. I took her in to the pediatrician and was told that it was a bug. My instructions were to discontinue solids and only nurse

until she was over the virus. The vomiting only lasted two days and we restarted the diet of cereals and fruits.

But the next week she vomited again. We then began a series of calls to the doctor, which resulted in keeping a food diary of everything she, and I ate to try to track a food allergy. We could find no correlation between the vomiting and the foods she ate. She also slept a lot, but we just thought that we were fortunate to have such a good sleeper.

At 5½ months she experienced a day of vomiting, followed by a fever in the late afternoon. I had noticed after being called by the daycare to pick her up that she had an unusual color that reminded me of the slight jaundice that she had experienced as a newborn. I dosed with Tylenol, nursed and she went to bed early for the night. She woke me early in the morning, which was unusual because she was such a good sleeper. She refused to nurse and would push away. She was gagging and vomiting although her stomach was empty. I waited for the doctor's office to open and took the first available appointment, not knowing how serious her condition was. By now, she had unusual breathing. Nothing alarming to me, but different, like she did not feel well. In hindsight, I should have insisted on bringing her right in. Our pediatrician saw Amber and said she was dehydrated and would have to get fluids at the hospital. I began crying and felt horrible that she was dehydrated and I didn't even know it. The pediatrician told me that it wasn't unusual and she should be okay after receiving fluids and possible spending the night. That was the beginning of our three-week hospital stay. They did routine blood work and came back into the room to ask me if any of my children had ever died. It was the scariest moment of my life. By then my husband had been paged to the hospital and I had called my parents home from the beach. We were asked if we had dosed with aspirin, had anyone at the daycare given her aspirin? Had she been in our garage? Could our four-year-old have given her something? She was transferred a few hours later to Brenner's Children's Hospital and two weeks later to University of Chapel Hill Hospital. Her final diagnosis was MMA.

The next six months were a blur of physical therapy, early intervention, and doctor's visits. The worst was the persistent vomiting and gagging when she even saw her bottle. I had assumed that the vomiting would stop on the new diet, but it never did! We did give her B12 injections for one week and the doctors determined that she was NOT responsive. They had determined this by the amount of MMA in her urine. It remained a huge amount more

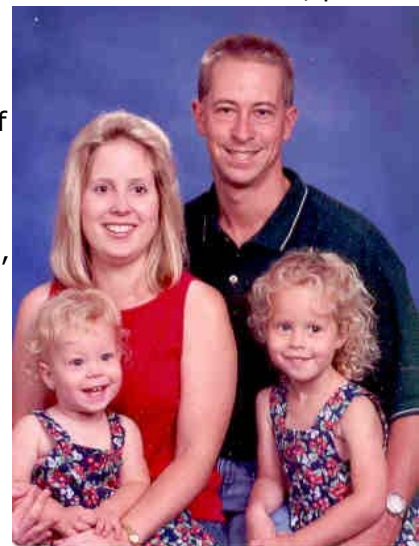
than normal. When she turned one year old, the skin fibroblast studies returned and we found out that she had type CBL A. I had done enough reading by this point to know that 90% of CBL A children respond to B12. We decided to determine her responsiveness via blood. Her initial serum methylmalonic acid level was 43.7 mmols/L. A normal person should be < 0.4. After seven days of injections her level was 17.3 mmols/L. I was so happy. She had begun eating with an appetite and no longer vomited or gagged. I was hopeful that her levels would continue to fall but they remained steady between 19.1 and 16.3. We eventually tried oral B12 daily and her levels remained in the new range. What a blessing.

North Carolina does screen for Methylmalonic Acidemia. Amber's test results when first run were above the cutoff. The state NEVER contacted our pediatrician or me; instead using the same blood spot punched out another fragment to run through. It was barely under the cutoff and they sent a newborn screening result of normal to our pediatrician. It makes me angry to know that they could have warned us that she was very close to the cutoff number and saved her a three-week hospital stay. I remember being told at the Children's hospital that she had been about 3 hours away from organ failure! In fact, if they had averaged the two results she would have still been above the cutoff. Instead they chose to ignore the first result and keep the second. I never knew these results until I requested a copy of the full report from the state. At the bottom of the report it reads: Methylmalonic Acidemia and her values of MMA are circled. It was not an oversight. They decided not to let us know about the previous failure. As any parent, if a doctor said to you that your child failed the first test for a disorder but passed the second wouldn't you take the time to research what exactly the disorder was. I would have. No doubt in my mind, I would have researched MMA even if she had passed on the second run. The first time she vomited I would have freaked out and made a big deal out of it. I would have known that her sleeping habits were a sign of MMA. I wouldn't have been keeping a food diary looking for a food allergy!

Amber walked at 15 months and is meeting all her milestones. Our metabolic specialist, Dr. Shawn McCandless strongly encouraged us to remove her from daycare. We wanted to avoid her catching anything that would harm her metabolic balance. She stays with my mom three days a week while I go into the office. The other two days I work from home and care for her. We will attempt to place her back into daycare when she turns two, part-time at first.

She receives 3 ml of Carnitine, 3 times per day. 70g Propimex-1 with water to make 14 oz. To that we add 6 oz. of whole milk and 4cc isoleucine. She gets 200 mg of valine per day. She eats bananas, applesauce, pears, peaches, broccoli, carrots, green beans, tomato soup, vegetable soup, very limited rice, low protein pasta, Cheerios, Cheetos, french fries, sweet potatoes, cabbage, crackers, sugar wafers and occasionally low protein bread. I keep a daily diary of everything she eats, which medications she consumes, how she feels, etc. This has helped me tremendously.

I love to correspond with other families. I have spent a lot of time looking for families that have children who are type CBL A, but have only found three other families. I know that there must be more. Please feel free to contact me!



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Gabrielle Millett

Propionic Acidemia (PA), 11 months



Gabrielle Irene Millett was born on February 11, 2000 with bright blue eyes and a full head of dark brown hair. We took our beautiful baby girl home – ready to start life with two children under the age of three. (Gabrielle also has a big brother, Alexander). For the next two weeks we went back and forth to the pediatrician's office trying to figure out why Gabrielle was so sleepy and unable to nurse. She was finally admitted to our local hospital and treated for an infection. Alex & I were very scared – little did we know that things would get much worse. Within 24 hours, Gabrielle slipped into a coma, had seizures and was having trouble breathing. She was rushed to Maine Medical Center and diagnosed with

propionic acidemia. The doctors told us that she had suffered severe brain damage and had little hope of survival. Her breathing was getting worse every hour and we were given the option of letting her die at home instead of in the hospital. After much soul searching, Alex and I decided to let her die at home. We were unsure that she would survive the 20-minute ride home so, Alex drove very quickly. (It was the only time I didn't complain about his driving) We held Gabrielle all night long and I prayed that she would open her beautiful blue eyes one more time. Early the next morning, Gabrielle stirred and started to cry. We couldn't believe it- she was waking up from her coma! Her eyes opened and she began to eat! Needless to say, Gabrielle survived and we began the long road of raising a child with a metabolic disorder. Gabrielle ate and developed normally until she was 7 months old. In September, with little warning, Gabrielle suffered a metabolic stroke that left damage to her basal ganglia area. She lost her ability to hold her head up, sit up, and developed a movement disorder. It has been a very difficult few months but Gabrielle is beginning to improve her motor skills. She has occupational, physical, and speech therapy 7 times a week. Her g-tube and port-a-cath were placed in November. This has made life much easier. We have a nurse come to our house to draw blood through the port-a-cath. No more holding Gabrielle down while they poke her repeatedly. She has actually slept through her last two blood draws! Gabrielle is starting to eat some foods. Her favorites are mashed potatoes and applesauce.



Currently she is on Propimex 1, Similac, 80056, and breast milk. For medications she takes Carnitor, Dexamethorphan, Coenzyme Q10, Neomycin, Metronidazole and Phenobarbitol. We hope to wean her from the Phenobarbitol by next month. Gabrielle sees Dr. Mark Korson and his wonderful medical team at the New England Medical Center in Boston. We could not have made it through this year without their help. Being part of OAA and getting information from this group has also been invaluable. Gabrielle's story has sparked many

news articles on Expanded Newborn Screening. We pray for the day that a child will not have to experience such trauma before being diagnosed. Gabrielle has grown into a beautiful, happy baby. She has a calm disposition and smiles at everyone. Seeing her play and laugh brings us such joy. She is our angel. Our family looks forward to meeting many of you at the conference in May. Here's to a happy and healthy Year 2001. God Bless!

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Kristine & John, Jr. Sabalauskas

3-Methylcrotonyl-CoA Carboxylase Deficiency (3-MCC), 5 & 4 months



Hello Everyone:

Our names are Kerri and John Sabalauskas; we live in Philadelphia, PA. We are the proud parents of Kristine-Lee, age 5 years and John Jr. age 4 months. Five years ago, when our daughter Kristie was born, they did not do the advanced newborn screening tests, so 4 months ago when our son Johnny was born they told us he had a metabolic disorder known as "3 Methylcrotonyl CoA Carboxylase Deficiency," we were devastated. We had no idea what this was or how it was going to affect our son.

We were told to make an appointment with a specialist at a Metabolic Clinic as soon as possible. We met with Dr. Kaplan at Children's Hospital of Philadelphia on Oct. 1, 2000. After 4 hours of testing and consultation, our son's diagnosis was confirmed. We were told how fortunate we were that because of the advanced newborn screening tests this disorder was diagnosed early and if we followed a diet consisting of little or no protein, he could probably lead a normal life without any major complications. We were also asked to bring in our daughter, Kristie, to be tested to see if she was a carrier. On Oct. 23, we received the results of Kristie's tests, she also tested positive for 3-MCC. This was quite a shock, as along with our son, Kristie has never showed any signs of illness, aside from the usual colds and flu that every 5-year-old comes down with. She does exceptionally well in school and does not have any learning problems.

So, here we were with two beautiful, seemingly healthy children, who were now diagnosed with a rare metabolic disorder that we knew absolutely nothing about. We searched for hours on the internet trying to find more information on the disorder, when we finally connected with OAA. What a wonderful support group. OAA has helped us understand and cope with this disorder more than anyone could know. Dr. Kaplan and our children's nutritionist are wonderful, but the greatest help has been being able to talk to parents whose children have the same problems as ours. Since these disorders are so rare, it is great to be able to talk to someone who is trying to understand and learn more just as we are. We have already connected with a 3-MCC parent who has been so very helpful to us.

Our son will be having a skin biopsy done in February, and this parent had a child who already had this done, she assured us that it was not as bad as we thought it would be. She has been there for us, helping us with our questions and concerns. She has told us "We are Family" and we are special families with special children helping one another. We are so thankful we have OAA for support.

Our son Johnny is doing fine, he weighs 15 pounds. He has his weight checked every 2 weeks and his regular Similac Formula is adjusted according to his weight. He is now allowed 30 ounces of Similac per day anything he drinks after that is a special prescription formula called Profree.

We had some major problems with our insurance company not wanting to cover the Profree. We were lucky to have a good friend, who works in our children's Pediatrics office, who

fought for several weeks with the Insurance Company explaining that this formula was necessary and that Johnny would probably be on it the rest of his life. With the help of this woman, the Insurance Company has finally decided to cover the cost of this special prescription formula.

Our daughter, Kristie, just had a dietary evaluation. Her nutritionist decided that she can continue eating her regular foods, her only restriction for now is milk. She must drink three eight-ounce glasses of Rice Dream per day.

We will meet with Dr. Kaplan and the nutritionist in February and they will make any necessary dietary changes if needed. We are very fortunate. Both our children were diagnosed with a mild form of 3-MCC and that because of the advanced newborn screening tests the disorder was diagnosed early and that so far they show no signs of complications.

We don't know what the future holds for our children, but one thing we know for sure is that the wonderful people of the OAA help us with and support us and for that we are eternally grateful.

Wishing you all a Happy and Healthy 2001.

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Five Years of Living and Coping with MMA

by Menta Pitre, mom to Ashtyn, MMA, Age 5



I have so much to be thankful for. Ashtyn has really not been a sickly child. She has been eating better than ever! It appears her vision seems to be clearer for her. Her mobility has been remarkable. Even though her language is limited, she is able to communicate and let someone know what her wants and needs are. Overall, I 'm extremely pleased in knowing that with as many obstacles as Ashtyn has encountered, she is the happiest child you'll ever meet.

Ashtyn has showed me what unconditional love really is. She has opened my eyes to see the simple things in life. I don't take things for granted like I've done in the past. I have learned the smallest milestone a person accomplishes is such a blessing. I'm so lucky to be able to manage and care for such

a unique and precious child. She has taught and nurtured me as much as I've done for her. I'm not trying to say it has always been easy; but as time goes by, you learn to adapt and do what works for you. I try my best to do whatever I have to do, for my family and I try to be happy and live each day to the fullest.

Ashtyn's vision has surprised many of her teachers, therapists and family. I'm not sure if she sees better, or just understands what she sees better. In February 2000, she had eye surgery to correct her strabismus (eye's crossing). I can tell it has definitely helped her depth perception. She also seems to run away from me much faster now, especially if she's in trouble or has something she is not supposed to.

One thing I've been working on as a parent, is trying to be less overprotective. I am trying my best to let Ashtyn be an independent person. She needs one-on-one assistance for many of her learning and self-help skills. She mostly has problems with fine motor. This makes it difficult to give her all the space she needs. I have noticed that since she has been enrolled in the preschool program, she has grown tremendously and I am extremely proud of her.

One area that has been challenging for us lately has been expanding Ashtyn's attention span. She is so hyperactive; it's hard for her to focus on one object for a lengthy time. I don't know if this is because she receives massive amounts of B12, or maybe because she was born with microcephaly (abnormally small head due to failure of brain growth) that causes her to be developmental delayed. Or, it may be that Ashtyn has Attention Deficit Disorder (ADD). Who knows, it may be one of these conditions or a combination of the two or three of them. I'm hoping it will get better as time goes by. Someone told me that she's just going through her 'terrible two's.' She'll get better as she gets older. I hope it will be that simple. I guess time will tell.

There is one thing that really concerns me. From day one, Ashtyn never had a normal EEG. She has always had irregular brain activity. Back in 1995, and 1996, she only presented some transient sharp activity every now and then. But the EEG she had in April 2000, showed 'bilateral paroxysmal activity accentuated over the right hemisphere, which was more frequent in sleep.' The paroxysmal activity in sleep consisted of polyspike-spike wave

activity. The maximum duration of the discharges in sleep was approximately six seconds. It's more noticeable when she first goes to sleep, but it also happens when she's awake and in deep sleep, just not as often and as long of a duration. My neurologist told me this activity is unassociated with clinical seizure activity. This was an abnormal tracing characterized by bilateral paroxysmal discharges consistent with, but not diagnostic of a paroxysmal disorder (balance disorder). Also, these discharges might be seen with an underlying encephalopathy (a disease of the brain) in a patient who does not have clinical seizures. I've always noticed when Ashtyn is stressed from not getting enough rest, or if she is sick, she gets very lethargic. When she does fall asleep she constantly moves and twitches. Lately, I've noticed it more often than in the past. After we did an EEG to see if this activity was seizures, they ruled it wasn't. Really, they can't explain why this is happening. It's so confusing that this activity is happening - even though she is metabolically stable and we have had no changes in treatment. A few weeks after we had the EEG test done, Ashtyn did have a partial seizure for a couple minutes. Ever since that one episode, we haven't seen any more seizure activity. We're closely monitoring her to see if it happens again. I am afraid to start her on anticonvulsive medication due to the many side effects with those kinds of drugs. So, it's a waiting game at this moment. We're hoping it's just a bizarre thing that happened. If anyone reading this can relate to this neurological activity please notify me so I can learn and understand what exactly is going on.

I've tried to gather both negative and positive things that I've encountered with having and raising a child affected with MMA cblC.

Some disadvantages I've had with having a child with MMA

- Giving daily injections of B12.
- From baby to toddler age having to constantly work for each feeding.
- Restricting your child from foods they like.
- Weighing everything that enters their mouth.
- Having food the right texture, temperature and color so it is enjoyable to eat.
- Constantly mixing formula that you know they won't drink.
- Collecting urine and blood samples regularly.
- Because of the acids and ammonia levels being elevated and being born with microcephaly, your child suffers from being developmentally delayed.
- Going to so many therapy appointments.
- Constantly doing insurance referrals. Also, having to always call your insurance company about bills they don't pay on time.
- Driving 3 hour round trips to therapist and doctor appointments.
- Not knowing what the future holds due to limited research.
- Losing close friends that suffer from the same disorder.

Some positive things I've learned with having a child with MMA

- I'm grateful there are treatments that we can follow to maintain Ashtyn's acid levels:
 - B12 injections
 - L-Carnitine
 - Diet
- I'm thankful God gave me the patience to do the 24-hr. feedings when she was a baby. I'm glad I've learned different methods of ways to manipulate her feedings. Such as feeding her when she is falling asleep, doing games like airplane to trick her to open her mouth.
- I'm so happy Ashtyn didn't have to resort to tube feedings. I wanted her to be able to eat and enjoy food like the majority of this so-called normal world. I'm lucky

because I didn't have to work on her social skills at mealtime. Since Ashtyn was my first child, closely monitoring and weighing all her intake seems to be a normal routine for me.

- I'm glad there is a special formula that we can back up on if she decides to stop eating.
- I'm lucky our insurance has paid for most of her labs and doctor visits- including all her hospital stays. (That's with a fight sometimes). Since Ashtyn is developmentally delayed (mild-moderate) we can enjoy her younger days longer. She'll want to play and be around her parents longer than other children her age.
- I'm fortunate to have many professionals and therapists who work and care so much for her.
- I don't have to go out of state for Ashtyn to see a Biochemical Geneticist. Having a chance to become close friends with other MMA families and the ability to share information with someone who understands what we're going through.

Having to summarize 5 years into a short article was quite a challenge for me. I hope the information I've shared with you is uplifting and helpful. I know it makes me feel good when someone is willing to share and teach me what might help me out one day. I encourage other parents to also write an article for this newsletter so we can learn from one another.

Take care, stay healthy and hang in there.

Remember:

"We're all in this together."

My family sends our love,

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Why Neurological Assessment is Important

What is a Neuropsychologist?

A neuropsychologist is a doctoral-level psychologist who has additional specialized training in the evaluation of cognitive functioning. This includes (but is not limited to) general intelligence, attention and concentration skills, academic performance, abstract reasoning, language skills, visual-spatial processing, fine motor control, memory functioning, general mood, effort, and (when appropriate) personality. Pediatric neuropsychologists specialize in the assessment of children. They often work within a medical setting conducting assessments of children and adolescents to determine how a child's disease might affect his or her brain functioning, daily life, educational needs, and ultimately, the course of his or her developing skills.

A neuropsychologist should have completed a Ph.D. or Psy.D. program in clinical psychology, often with additional coursework in neuroanatomy, neuropathology, and advanced methods of assessment. Neuropsychologists complete two years of additional, highly-specialized postdoctoral training that focuses on specialized test administration and interpretation, case conceptualization in the context of known brain-behavior relationships, and integration of a patient's medical and social history, behavioral observation, and objective test results. The purposes and goals of the neuropsychological assessment include facilitating patient care and rehabilitation, documenting the child's current status, delineating the child's strengths and weaknesses, and documenting improvement or deterioration of functioning."

What is a neuropsychological evaluation?

A neuropsychological evaluation studies the "work" of the brain. This is a comprehensive assessment of attention, learning, memory, "think ahead" ability, language and visual-spatial skills, and sensory-motor functions. Several hours are required to complete this evaluation because most of these skills are made up of component parts. The evaluation does not have to be administered in one session or in one day.

When is a neuropsychological evaluation indicated?

A neuropsychological evaluation is indicated whenever complaints of problems with attention/concentration, learning and memory, language, and visual-spatial skills need an objective assessment. Complaints in these areas often occur in neurological and other physical conditions, in psychiatric disorders, in learning disabilities, and in developmental disorders such as Attention Deficit Disorder.

At what age should a neuropsychological evaluation be performed?

Age-appropriate tests are used for child, adolescent, and adult evaluation. Therefore, an individual of any age can be evaluate.

How does a neuropsychological evaluation differ from a learning disability assessment done at school?

Learning disability assessments usually focus upon measuring IQ-academic achievement discrepancies. If attention is assessed, it is usually done by having an observer fill out a

behavior rating scale. All of this provides information about comparing a student to his/her peers for identifying problems. A neuropsychological evaluation is an interactive assessment that uses standardized procedures to understand the process of how and why an individual behaves, struggles, or fails. The results should be linked to interventions, which may or may not be school based.

(I would like to thank Dr. Steven J. Hughes, Ph.D., L.P. and Dr. Robert Gray from the University of Minnesota Hospitals and Clinic for their input into this informative article.)

John Tate, Jr.

MMA, mut⁰, 1 year



Our son John was born on January 20th, 2000. What an incredible day. It was snowing in and around Philadelphia and everything was pure and white. It was the first snowfall of the millennium for us. John was beautiful from the moment he was born. We had a great 1st day with our son from beginning to end. The second day was just as perfect as the first. However, since John was jaundice, we needed to stay another day to monitor him and put him under the bili lights. By the 3rd day, we knew that there was something wrong but at this point, we really had no idea. His bilirubin levels for jaundice were climbing so, we knew we had to stay for day 4. Also, my wife was breast-feeding and, as most mothers know, the beginning is slow. So, the combination of the two things, bili lights and breast feeding, contributed to what we thought was dehydration. So, by the end of day three, they put IV's into our little six-pound baby boy to keep him full of fluids, not to mention all of the monitors for heart and lungs, just to be safe. My wife and I still weren't really scared. We thought that it was due to lack of fluids and the bili lights. The turning point was when

we witnessed the labored breathing. My wife was immediately concerned. We waited patiently to speak with the NICU doctor. After some time, we sat down to discuss what is going on and how we were going to treat and monitor John. They drew some blood and kept him on IV's overnight. They also decided to move him from the maternity ward to the NICU since his labored breathing was a concern. I think that the blood work detected abnormal levels of gas in the blood, which they treated by giving him bicarbonate or bicitra in the IV. This was probably the beginning of saving his life and keeping him metabolically stable. After a few days in the NICU, we thought that we were getting ready to go home. We still attributed everything to dehydration and jaundice. The only prevailing problem was that John was still breathing rapidly. His respiratory rate was still in the 60's. A week after John was born, we thought we were preparing to take John home. Instead, we received the results from the pre-screening. John had a metabolic disorder. The pre-screening was the second most important event that contributed to treating John and keeping him stable. On day 6, we were transferred to Children's Hospital in Philadelphia, (CHOP), where the metabolic specialists were located.

The next 2 weeks were probably the toughest 2 weeks of our lives. I had to watch as they poked and prodded, drew blood, did exams and kept our little baby hooked up to all sorts of monitors. They determined that John had MMA and my wife and I were in shock. A biopsy later confirmed his gene defect as MUT0. The good thing was that John was interested in eating and he kept up with the minimum required amount of formula that appeared to be a complicated mixture that the pharmacy prepared. The doctors told us that his MMA levels were high and, since he presented at birth, he was in a pretty severe category. However, they were also surprised with his appearance and stable appetite. It was hard to look at him and not want to treat him as a healthy little baby boy. We learned a lot about the disease within about 10 days. We gradually tested John's tolerance for protein and measured his levels of MMA in the urine. We were able to progress toward taking John home and, at the time, our only concern was measuring and monitoring his protein intake. About 3 weeks from the day he was born, we were able to take our son home.

Well, the last 9 months have been the toughest, most stressful, yet most rewarding months of our lives. It wasn't long after John was home that he did not eat as much as he needed to. We had some tests done and determined that John also had clinical signs of reflux. We got by a few months until we resorted to an NG-Tube. That lasted less than a month. We admitted that the feeding problem was not short term, and we had the G-tube put in on June 1, 2000. Immediately after the operation was probably the scariest time for Lourdes and I. It was our rock bottom, I hope, as we struggled with putting John through the pain of the operation. I guess that anyone who has resorted to a g-tube for their child knows how much it helps. With MMA, being able to push fluids through to dilute the acid levels in the blood and brain is critical.

Thanks to the g-tube, John's 1st summer was a little easier for us than the spring. John progressed as he got bigger and stronger. Since we had the tube in his stomach, we didn't let him crawl on his belly too much, so he arched his back and kicked his feet and moved from one end of the room to the other on his back. It was a sight to behold for a couple of months. When John was 7 or 8 months old, sometime in late summer, he started to crawl on his belly.

September to December - if it wasn't for the feeding problem, people would not be able to tell that John has a serious metabolic disorder. The feeding problem does include intermittent vomiting and, with MMA and reflux, it has been more than intermittent. We have constantly looked for ways to prevent the vomiting. There were a few months, maybe September and October, that seemed especially difficult with more frequent vomiting. We have been lucky so far. John has only been mildly sick twice in the past 11 months. We have had two trips to the ER since birth. Both times, we were scared and did not know if John was going into a metabolic imbalance. We had IV fluids pumped in, ran some blood work, and went home within a couple of hours.

The past 2 months have been a little better. The vomiting is under control and John has not had a cold or flu since September, when he had his last set of shots. There have not been any setbacks as far as his development and John has been trying to walk lately. He has actually taken a few steps, but he does not have his balance yet. He is around the 25th percentile for both weight and height. January is a big month for us. We have a developmental test on the 2nd, the initial meeting with a feeding team on the 10th, his birthday on the 20th, and a visit with GI on the 29th. So if we make it to February, I think we'll be OK.

All in all, we have been very blessed. We have been able to care for John from the day he was born. The doctors at Abington helped save John's life. The NICU doctors and especially the nurses, at CHOP, provided the best care during the second and third weeks of John's life. Our list of heroes would not be complete without mentioning the best team of metabolism doctors and nutritionists that a child could ask for.

John has a big sister, Morgan, that he loves very much. She is wonderful with him and makes him laugh whenever she is within sight. He always crawls up the steps and goes directly to her room. Morgan is 11 and does not have MMA, but she knows how difficult it is to take care of her little brother. John also has many, many friends and family members praying for him.

Please feel free to contact us anytime if you have any questions about John's diet, medications, acid levels, or any details that may help someone.

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MMA, mut-0 Research Underway

Dr. Chuck Vendetti from the Children's Hospital of Philadelphia (CHoP) has begun research on MMA mut-0 with a goal to cure this metabolic disorder. A layman's definition of the project has Dr. Vendetti creating a mouse model of MMA mut-o which includes knocking out the good gene to replicate the human defect in the animal. Ultimately he will begin gene therapy experiments on the mouse models with the hope that some day this can be applied to humans.

The research began with the cooperation of CHoP and a \$50,000 grant that was the result of an MMA parents Marty and Kate Moran (Kayleigh, MMA, mut-0, age 16 months) working with their State Representative and Speaker of the House of Representatives in Pennsylvania, Matt Ryan. Mr. Ryan is an unbelievable person, with a passion for healthcare issues, who didn't blink an eye at the opportunity to help this research. Our heartfelt thanks go out to Mr. Ryan.

To further this research Marty and Kate Moran and Dennis and Bonnie Meisel (Blake, MMA, mut-0, deceased and Alyssa, MMA, mut-0, age 2) have teamed up to turn on the fundraising/grant efforts across the country and around the world. They will be in contact with all known MMA mut-0 parents as well as anyone interested in joining the effort. Some near term plans include a formal foundation, publication of an MMA mut-0 brochure, and the creation of a web site.

Feel free to contact the Meisel's at meisel@pa.net, 717-582-2195 or the Moran's at golfer@dvol.com, 610-399-8268.

Treatment of Propionic Acidemia Patients in Saudi Arabia

by Pinar T. Ozand MD, Ph. D.

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(Dr. Ozand graciously responded to one of our parent's request for information on the treatment of propionic acidemia. Please remember to consult your own physician when considering treatment changes).

Yes. I have many propionic acidemias under follow up. The frequency of this disease in this country is probably 100 times higher than that in the West. The Saudi disease is of two types: (1) very severe; (2) moderately severe and as such not much different in its clinical course from other organic acidemias. We have the gene defect in both of our types identified at Willink Biochemical Institute at Manchester, UK. Both types are different in their mutations which explains the difference in the clinical behavior of our infants.

Propionic acidemia is almost always, in all types, is a vicious disease. It affects brain and immune system. The central hypotonia is due its toxic affect in the brain. The central toxicity also causes chronic vomiting and anorexia.

Physical therapy might help the hypotonia. Over the many years I have never been able to find an effective management for their anorexia and vomiting. Nowadays I generally use domperidone as suppository, 10 mg 2-3 times a day for an infant less than two years and 30 mg for a child older than two years.

Even the most indolent form will cause acute metabolic decompensation from time to time particularly during a minor illness, minor vomiting diarrhea.

During any such episode the patient should be immediately hospitalized. We have found that during such repeat attacks, our patients almost always (more then 67% of the time) have a sepsis with unusual bacteria. Therefore I advise your primary physician to take these episodes very seriously and obtain blood culture regardless covering the patient with broad spectrum antibiotics. Most of the brain damage occurs during these repeat episodes. Therefore they should be very vigorously treated by giving 10 % glucose + alkalinizing agents as required. This should be continued for 5-7 days in a hospital setting. Another must is the use of intravenous carnitine. This is an essential drug used in many organic acidemias including propionic acidemia. Its dose is 50 mg/kg/dose IV given over 10 minutes. Its administration is continued until the crisis is over.

We advise the parents and the nurses to check daily urine ketones, simply by the dipstick used for urine testing. The crisis is heralded by ketonuria and is over when the ketones disappear from the urine. At this time usually the platelets also start to become very low. Therefore such an infant in crisis under therapy is monitored by daily urine ketones and daily platelet counts. The infant is discharged only after platelet count starts to rise.

We also find that during crisis the blood ammonia level increases which is a significant contributor to brain damage. We monitor daily blood ammonia and if increases above 100 micromolar, we start the infant on IV sodium phenylbutyrate 500 mg/kg/day given in 3-4

equal doses. Most pediatricians don't realize that propionic acidemia is also a hyperammonemia disease and a bad one at that. This is caused by the inhibition of urea synthesis by propionyl-CoA in the liver.

We use Metronidazole (Flagyl) during crisis. This has to be given orally. Another significant source of propionic acid is from the intestinal bacteria. We try to reduce this source by giving 10 mg/kg/ dose Flagyl repeated four times a day.

Our protocol for the management of such an infant in between episodes is:

1. The propionic acidemia formula; preferably a British formula that contains NO FATS.

A significant source of propionic acid is odd-chained fatty acids that keeps accumulating in the fat tissue of the infant, enriching it with these fatty acids. Therefore most of the times the repeat episodes occur after 1-2 years, after enough odd-chain fatty acids accumulate in fat tissue.

2. We add to such a fat free formula about 2-3 ml. of synthetic fat, Medium chain triglycerides to cover the nutritional need for fat. We also add about 0.5-1.0 ml. of canola oil to formula to prevent the deficiency of essential fatty acids. We start this very soon after birth. These infants frequently develop "nappy rash". It is either due to deficiency of essential fats or in poorly controlled cases due to candidiasis. This is treated as needed by mycolog or if severe and bacterial and not fungal in nature by bactroban ointment Nowadays we rarely encounter oral moniliasis as well as perineal moniliasis or other types of rashes because of our effective protocol.
3. We add about 2 g/kilo/day L-alanine to their diet again soon after birth. These infants very quickly develop protein malnutrition. The formulas don't provide enough protein. The disease thus gets complicated by protein malnutrition which only aggravates the clinical condition.
4. Oral L-carnitine is an essential therapeutic drug. It has no side effects. We use 200 mg/kg/day given in two-three equally divided doses. The liquid form contains sorbitol which will cause diarrhea. Tablets are better. Also, from time to time its intestinal fermentation causes a "dead-fish" smell in the patient. During those times the use of Flagyl (as described above and below) will get rid of the smell in 3-4 days.
5. We always use Polycitra (equal mixture of sodium and potassium citrate) at a dose of 3 ml/kg/day as added to the formula. Methylcitrate is an unusual compound that accumulates in tissues in propionic acidemia. It is very toxic to normal metabolism. Citrate achieves two things: (A) competitively gets rid of methylcitrate which is a serious toxic compound to the energy generating oxidative phosphorylation and (B) it provides alkalization and thus alleviates acidosis.
6. For severe form of the disease we routinely keep our patients on oral sodium phenylbutyrate since in between crisis the patients show chronic hyperammonemia. When oral sodium phenylbutyrate is given, one also has to give 5 mg. folic acid and 25 mg pyridoxine daily.
7. Again for severe cases we use Flagyl off-on at three months alternating periods. The dose recommended is 10 mg/kg/dose given four times daily.
8. We routinely ask for blood count, blood ammonia and blood amino acids once every 2-3 months. This is to monitor for nutritional anemia, iron deficiency and adequate protein nutrition. Your physician will find that these infants will have chronic insidious elevated levels of ammonia in between crisis unless sodium phenylbutyrate is used. Oral iron should be supplemented if needed. The efficacy of the odd-chain fat restriction is monitored by measuring C13, C15 and C17 unesterified fatty acids in the plasma by GC/MS. Most places don't have this facility.
9. The EEG consistently shows the presence of a metabolic disease even in very well controlled patients. Unless clinical seizures are observed we don't use anticonvulsants. The preferred one for seizure treatment is Phenobarbital and if needed also Rivotril. Your physician in such instances should never use depakane. The drug is contraindicated in the treatment of seizures in organic acidemias.

10. Once a year CT or MRI brain is also advisable if you can afford it. This is to document the state of the brain atrophy and basal ganglia disease. An inadequately treated patient with basal ganglia disease shows choreoathetosis and dystonia. These are minor jerky movements, grimacing at the lips and abnormal posturing of the extremities particularly in the hands.
11. I usually never use biotin, since the molecular genetic studies in our population showed the mutation not at the binding site of biotin but somewhere else. There is only one biotin-dependent propionic acidemia infant reported.

Biotin also is a harmless drug/vitamin. If your pediatrician will more comfortable by using it, the dose is 5-10 mg/kg/day given in two equal doses.

As you see our management is very detailed and comprehensive. Despite all these efforts a severe variant will slowly deteriorate over the years, mostly manifesting after two years of age. I advise you to identify a good and compassionate dietitian. She will be your best ally in fighting against the disease. Such a person is much more important than a physician. Don't forget this is a lifelong disease and you must secure as much help as possible and keep your spirit up. I have several infants, albeit only a few, who are leading the normal life style of a child. I also understand from my colleagues in the West that propionic acidemia there is rare but apparently not as vicious as it is in this part of the world.

As to the gene therapy. This is a long way to go. Its protein has two parts and the interaction is very complex. Propionic acidemia is a liver disease and so far none of the liver type diseases could be treated by gene therapy. Liver transplantation may be effective but its benefits in the long run is not yet described in detail. If it is opted for, maybe a small segment or lobe transplantation will be better than an entire liver transplant. In my patients the disease doesn't seem to affect kidney which is an advantage for transplantation.