

October 2000 OAA Newsletter

Use of Metronidazole for the Treatment of the Body Odor Associated with Oral L-Carnitine Administration

by Susan C. Winter, MD

**Director, Medical Genetics/Metabolism
Valley Children's Hospital
Madera, CA**

Oral L-carnitine is poorly absorbed when taken orally, with about 75% excreted by the bowel. In about 7% of individuals, the normal bowel flora metabolizes the unabsorbed L-carnitine into trimethylamine which smells like rotting fish. The absorption of this bacterial metabolite results in the patient smelling similarly. This can be extremely obnoxious and often results in patients stopping needed therapy or leads to serious social acceptance problems.

We have had success in treating our patients with Metronidazole in low doses to alter the bowel flora; this results in rapid disappearance of the odor. Metronidazole is available as a tablet of 250 mg. or a capsule of 375 mg. In patients under 20 kg., we use ½ of a 250 mg. tablet or ½ of a 375 mg. capsule once daily orally for 10 days. Over 20 Kg., we use a 250 mg. tablet or a 375 mg. capsule daily. Since Metronidazole has a terrible taste, the capsule has been the preferred form of dosing. Parents open the capsule and mix the contents into apple sauce or a concentrated juice. Occasionally, the body odor returns requiring a repeat course of therapy. In a few patients, usually those on large doses of L-carnitine, once daily administration has been necessary for years. There is a hereditary disorder of Choline Malabsorption that results in individuals having the same trimethylaminuria and body odor. This disorder also responds to daily Metronidazole therapy.

Transplantation in Organic Acidaemias

by James V. Leonard, MD

**Biochemistry, Endocrinology and Metabolism Unit,
Institute of Child Health,
London, UK.**

Transplanting organs can be used to provide a source of the enzyme missing in patients with inborn errors of metabolism. It is natural to think that this could be used to improve both the metabolic control and the quality of life of some patients with organic acidemias. At the International Congress of Inborn Errors of Metabolism in Cambridge UK, (September, 2000) a workshop was held to examine the role of transplantation in organic acidaemias comparing it with conventional treatment.

Despite advances in our understanding of organic acidaemias, the management of propionic acidemia (PA) and methylmalonic acidemia (MMA) remains difficult. The mainstay of the management of PA and vitamin B₁₂ non-responsive MMA is a low protein high energy diet that may incorporate the use of supplementary aminoacids omitting those that are metabolised to propionate (valine, isoleucine, threonine and methionine). The importance of maintaining good nutritional state is now well recognised and naso-gastric or gastrostomy feeds are essential in the patients with a poor appetite. Overnight feeds may be helpful; not only to maintain good nutrition but also to reduce problems associated with fasting. The diet must always be closely supervised to ensure the protein intake is neither too high nor too low and that it is nutritionally complete.

Metronidazole, an anti-bacterial compound, is used to reduce propionate production in the bowel. Carnitine is given to prevent deficiency, usually in a dose of 100mg/kg/d, although higher doses are used by some. Sodium bicarbonate is often given, particularly in MMA. Sodium benzoate is now more widely used to

prevent hyperammonaemia in organic acidaemias despite initial concerns about its potential toxicity. However no harmful consequences have been reported and it reduces both plasma ammonia and glycine concentrations. Growth hormone and alanine have both been used but their value is unclear.

Each patient needs a 'crisis' or 'emergency' regimen that is used during any metabolic stress such as infections. These regimens are not nutritionally complete so they must not be continued for longer than is absolutely necessary to avoid prolonging the illness and causing additional complications such as skin rashes.

Although the conventional management has improved, complications in the severe forms of both PA and MMA are common. Poor appetite and gastro-esophageal reflux are very frequent. Developmental delay is also common, particularly in those who present in the neonatal period. All patients are at risk of developing a movement disorder that may be severely disabling as well as cardiomyopathy (weakness of the heart muscle) and pancreatitis (inflammation of the pancreatic gland) although the cause and the frequency of these are not known. Patients with MMA are also at risk of progressive kidney disease that commonly reaches a critical stage in adolescence.

In view of all the complications it is not surprising that the overall outcome of the severe variants of both PA and MMA presenting in the newborn period has been disappointing. In one older study only 1 patient out of 11 with neonatal PA was still alive at the age of 6 years. Furthermore all these patients were handicapped with IQ/DQ of less than 75. In the same series only one late onset patient died, but many of the survivors did not do well having a wide scatter of ability and almost half had a movement disorder. However on conventional treatment alone the survival is improving. In the current series from Manchester, UK of 17 patients with PA presenting in the newborn period 6 had died, but 3 of these were following liver transplantation. However learning disabilities were still common. Of those over the age of 4 years, only 2 out of 5 survivors were of normal ability (IQ/DQ greater than 80).

In earlier studies of non-B₁₂ responsive patients with MMA the outcome of early presenting patients was not good. Only 20% were alive at 8 years although there was no mortality in late onset patients. However complications were common. In the more recent series from Manchester two patients out of 12 had died but of the seven patients over the age of 4 years only 1 was of normal ability (IQ/DQ greater than 80).

Understandably those who cared for the patients with severe variants looked for ways to improve the outcome. By transplanting patients a source of the missing enzyme is provided. This is most likely to be effective if the liver is transplanted but even a kidney transplant might make a difference. The current 5-year survival for liver transplantation is approximately 80% so it seemed that liver transplantation in infancy could offer better survival. The quality of life and neurological outcome might be better and further organ damage prevented. For patients with MMA in end stage renal failure a kidney transplant would be necessary but combined liver and renal transplantation could offer a better outcome since, without reducing the urinary excretion of methylmalonic acid, survival of an isolated kidney graft was likely to be reduced.

The results of liver transplants have, however, been disappointing with many problems. In both PA and MMA there was initially high perioperative mortality. This has improved with better preparation but the overall mortality remains high. The 2-year survival is approximately 60%. However the quality of life for the survivors does appear to be better.

From these findings it is clear that liver transplantation is not a straightforward option. Whilst some patients have done well it is essential to recognise that liver transplant does not correct the enzyme deficiency in other organs, most importantly in the brain. In one patient the cerebrospinal fluid concentrations of methylmalonic acid remain high. (more information is needed about this problem). If it is decided to proceed then preparation prior to operation must be meticulous to prevent complications. Technical advances may improve the problems at the time of operation but there is a high risk of neurological complications. There is an urgent need to understand the cause of the neurological complications and how to prevent them. This is important for all patients, those having transplants and those receiving conventional therapy. The kidneys are also easily damaged in patients being transplanted.

The patients in end stage kidney failure may become more stable on regular haemodialysis but this is not regarded as a long-term solution. The outcome of both isolated kidney and combined liver and kidney transplants has not been good. Of three patients with MMA who had a kidney transplant alone, one has died. Of those who had combined transplants at one centre one had done well one moderately well and one

had died. Again there had been a particularly high incidence of serious neurological complications. There is a suspicion that the patients are more sensitive to the drugs used to prevent rejection.

Late complications may also occur. One child with MMA had a severe neurological insult whilst recovering from a chest infection without any severe disturbance five years after transplant. She has been left severely disabled. Another patient was reported who, despite a transplant several years earlier, is now developed chronic renal failure and has progressive hypotonia.

In conclusion transplantation does not cure the patients who remain at risk of developing new problems. Furthermore there appear to be more complications than would expected from other transplants for metabolic disease. At present the indications for liver transplantation are not clearly defined. More detailed information is essential and it was agreed that a register of all patients who are being considered for or who have had a transplant for PA and MMA should be established. Parent organisations all over the world can play their part to make sure the details are as complete as possible. This will help to answer some of the outstanding questions more quickly.

Jenna Lynn Delima

Propionic Acidemia (PA), Age 22 months



You were born on Nov. 18, 1998, a healthy 7 lbs. 13 oz. little girl in the presence of a large number of family and friends. It was a joyous occasion as you were eagerly awaited, the first-born grandchild. You relied on Mommy's breast milk as your only source of food, which kept your health and development well. When you were four months old, we started feeding you pureed foods, but you immediately showed signs of unhealthiness. Your physical development receded, as if you were stepping back to a newborn phase. You slept most of the day, did not have the appetite to eat, and had such rare bowel movements. Naturally, we shared our concerns with the family physician on several visits, but were told you probably just had the developmental "slumps" that babies commonly experience. On that advice, Mommy and Daddy were reassured that your health would be back on track. Then on May 10, 1999, Mommy's first day back to work, you were rushed to BC's Children's Hospital by grandma because she felt uneasy with your lethargy and poor breathing. There, they did numerous tests on you, and you were so brave that you did not even cry as you were being pricked for blood samples. The Biochemical Diseases physicians were already suggesting that you may have a metabolic disorder called Propionic Acidemia, but Dr. Lillquist didn't confirm it until your third day at the ICU, you were then 6 months old. She said your ammonia at the time of admission was 189, which was at a toxic level. She also reassured us that with a strictly monitored low-protein diet, you would be just fine. So we grieved your newfound condition very briefly. We were going to show you how strong we could be in the face of this trial. Our initial hospital stay lasted one long month, where they taught us how to calculate and measure your foods. Your dad and I were experts at NG-tube placements by the time we were released from the hospital. You, on the other hand, could not bear to have the NG-tube up your nose.

The first six months out of the hospital was hard for all of us. You had to re-learn how to eat orally and gain some muscle control. Since you had an "episode", your development was drawn back. Your development has been slow, but that is due to your low-protein intake. You kept vomiting your feeds while Mommy would catch, estimate how much you vomited, and then contact your dietician, Carol Hartneft, to inform her of the incident. You got so chubby during your first year from a diet consisting of Similac Advance with Iron, Propimex 1, Product 80056 and approximately 1-1.5g natural protein.

Today, your protein tolerance is at approx. 2g/kg, and still increasing at a good pace. Your daily medications consist of 20 ml Carnitor®, 5 ml Lactulose, 2.8 ml Iron, 10 ml Biotin, 12 ml Cisapride and for one week each month, 4.5 ml Flagyl. For a child with low albumin count, you have gone through your illnesses without major complications or seizures to date. Most of your feeding is done through your g-tube, but you are showing eagerness in oral feedings. At present, you have bimonthly physiotherapy at home done by the Infant Development Program. They are there to monitor and give suggestions in your physical development. You have regular visits at the Blood Lab for Ammonia checks to ensure you are tolerating your diet well.

On April 8, 2000, your dad and I were thrilled to find out that you would have a sibling by the time you were two years old. However, three months into the pregnancy, we lost the baby. We believe that was God's way of telling us to place our undivided attention toward you.

You have now mastered crawling, climbing and attracting attention. However, you still need to practice your sense of balance, so you will be able to walk soon. We really enjoy your sweet words like "mama" and "dada", but we cannot wait to hear you say, "I love you". Although you are not that vocal or physically active, you still find a way to make us proud and happy with your silliness. Always keep your strength, little "stinky" girl, because you have us beside you and God carrying you through.

Love Always, MOMMY and DADDY

Our special thanks to: Carol Hartnett (Dietician), Biochemical Diseases Team, Anne Ryner (Physiotherapist), Beth Hutchinson (Consultant), Deb Gwynn (Speech Pathologist), our very supportive family and friends, and of course, to God, the Almighty, "Thank you Lord for all the blessings you have bestowed upon us".



We would love to hear from other parents who want to share their unique experience with PPA or other metabolic disorders.

Aubrey and Greg Delima
aubrey.delima@shaw.ca

Ashtyn Pitre

MMA, cbl C, Age 5-1/2 years



Hi everyone, my name is Ashtyn Nicole Pitre and I'm a 5 1/2 year old little girl who is very active. I'm going to start my 3rd year of preschool in the fall of 2000. I've always loved to go to school. I'm so happy my mom decided to hold me back one more year in preschool. Even though I'm 5 1/2 years old I really act like a 2 1/2 or 3 year old. All my peers are so much bigger than I am and they seem to pick up on things much quicker than I do. Giving me an extra year of preschool will give me time to catch up with them. I really like to ride the school bus. The monitor on the bus keeps me entertained when I ride in my car seat. I feel like a big girl when my mom doesn't have to pick me up from school.

I am a very friendly little girl. I used to prefer just to play with adults. But now, I will play with anyone. Of course it is easier to play with big people because they play and do what I want them to do. If I play with other children I have to share toys, and sometimes they don't do what I want them to do. Now that I've been in school for two years I've learned how to socialize with my peers much more. I sometimes side play and sometimes play directly with them. I don't always need to have an adult.

My favorite game is to point out colors to someone. I know all my colors. I can say and sign the majority of them. My favorite color used to be purple, but I think it's blue now. I can also point out some shapes and animals; I don't say or sign them. As far as the animals, I usually make the sounds they make. It's fun to do those sounds. If you're wondering if I know my ABC's and 123's, well I'm not quite ready to learn all of them. I can recognize a couple letters like A, B, P and sometimes T but not all the rest. If you start to count for me and you say 1 then I'll say 2. And if you ask me how old I am I will tell you "ive" (I don't know how to make the F sound yet), and I will show you 5 fingers. But as far as saying or recognizing numbers I can't do that just yet.

I'd like to tell you a little about the way I communicate with others. It's very hard for a stranger to understand what I try to tell them. The words I say are not always clear. I sometimes say my words so fast I sound like I'm speaking a foreign language. It kind of sounds like cluttered speech. The words sound like they are all on top of each other. I also make up my own words for certain objects; for example I like to call silly putty, 'mini mini.' I know it doesn't sound like the word I'm suppose to say but that's the way I want to call it. I prefer to say some two and three syllable words. My mom tries to figure out how and why I'll say some hard words, but can't say some short and simple words. The hard words I like to say are aluminum, elevator, alligator, umbrella, brassiere, basketball, watermelon, rubberband, and Dr. Pepper. As far as saying easy words like one, yes, open and more I just choose not to. I'll just wait until I'm ready to say them. I don't use two word responses and I don't understand pronouns. I often say a word two times when I talk, for example: pretty pretty, little little, go go. I do have to mention that my receptive language is much better than my expressive. If you ask me to go get something in one room and bring it to you in another, I can do it. Also, if you want me to point out what certain objects are, I can do it. But if you expect me to say everything I see or do, I can not do it.

I use some hand-signs to help me tell someone what I want. The signs I know and use a lot are: out, on, more, please, jump, music and all my colors. As you can tell, I have a severe delay in speech and language. If someone would want to know what age level I am on speech and language, my mom would tell them I range in the age of a 1 1/2 to 2 year old with some scattered skills at higher levels ranging as far as a 3 to 3 1/2 age level. My speech therapist was surprised I knew all my colors so well. That's if you compare to what other things I can say and understand. Surely, I don't want to be any ordinary patient. I have to do some things to keep everyone wondering at what level of development I am. I like to use certain gestures for different moments such as I like to say 'Lordy Lordy Lordy' or 'Ooh La La.' And If I smell something that stinks I'll wave my hand and say 'poo-woo.' If I see it raining or if I hear water flowing I say it's 'pee

peeing.' If someone asks me what's in my nose or if I hear someone say I need to get a kleenex, I'll tell them 'booger booger.' I like to make a sound like a squeaky swing or door. And you should hear the silly laugh sound I make, It's hilarious. I like to imitate animal sounds like what a bird, duck, dog, cat, pig, cow, or frog does. I can do a cute whistle. I like to suck the air in my mouth to make my whistle. My mom likes when I make a sound like an Indian girl.

Since I've learned how to say my mom's real name, I just call her Menta now. I don't call her momma any more. I also learned how to say my first and last name and my daddy's name too. How you like that? As you can tell I have a very unique talking voice and personality. I've really been working hard at repeating some words my mom wants me to say. Everyday it'll become easier for me to talk because I'm growing up to be a big girl now.

I have been exposed to so many sensory things in my short life. I used to really be defensive to lots of different textures, both in my mouth and when touching things. But, I can say I overcame lots of those obstacles. I am still sensitive to certain sounds that I can't see or understand. These include blowing air in balls or balloons, stretching an accordion and letting the air in it, strumming a guitar, hitting a wire doorstop and letting it vibrate, hearing a dog bark or putting a stethoscope or headphones to my ears. My mom and me work on sensory integration every day. Maybe one day I will overcome all my sensory problems.

I am also a very picky eater. Although, when I was a baby and a toddler, I was much worse. My mom had to feed me when I was going to sleep. I sucked my bottles and infant feeders when I would go down for a nap. I just didn't like to eat or suck anything when I was fully awake. But, since I was about 3 years old till now, I am trying different foods and my appetite has seemed to grow. I really prefer salty foods to sweet ones. My favorite snack is popcorn. I also like Puff Corn made by Golden Flake - It's just like buttered popcorn but it doesn't have any kernels. It just melts in your mouth (Yum Yum)! I really enjoy eating beets and any kind of pasta. I eat bread, rice, cereals, grits, chips, crackers and all kinds of vegetables. I guess you can say that I basically eat vegetables and starches. I also love to add butter on most of my foods. I sometimes eat baby food, but I prefer to eat the real stuff. I always have had sensitivity to certain textures. I don't like to chew a lot. I guess that's why my mom still gives me some baby food. This works out well because I won't eat some foods by themselves but will eat them in baby food. These foods include certain vegetables, yogurt, and creamed spinach and corn. Once a day, my mom gives me either a vegetable & meat baby food, pudding, or yogurt or cheese so I can get the raw dairy product since I can't have real meat or milk. But I can't just live on vegetables alone, so my mom tries to balance my diet as best as she can. I'm just beginning to eat a small portion of a banana and an apple. When I was younger I would make some funny faces when my mom would make me taste fruits. Most of the time, I'd give it right back to her. But lately, I've been a big girl about tasting different foods, and you know, my mom is very proud of me. As far as eating free foods, my favorite two are blue Jell-O and ice cream cones. I especially like the colored ice cream cones - it makes it fun when it's a colored one. Here's a secret my mom does to my oatmeal so I'll eat it- she adds blue food coloring in my oatmeal for me to enjoy it better. Of course I do prefer the Gerber oatmeal cereal to regular oatmeal with all the lumps in it (Yulk).

My nutritionist has allowed my mom to increase my diet two extra grams of protein a day. It's only a trial basis, until we receive my levels back from the lab. I am so excited to be able to eat a little more each day. I hope it can stay that way. I am now allowed to have 18.5 grams of whole protein a day.

Believe it or not, I don't care to drink my formula. To fix this, my mom adds most of my milk (that's my formula) in oatmeal or cereal. I'm just starting to drink a little of Dr. Pepper or Root Beer, but my favorite drink is plain water. I also like coffee too. My mom is experimenting with my calorie supplement in my coffee. Sometimes I can tell if she puts too much in it. It's amazing how sensitive I am to smell and taste. I like to drink fluoridated water it helps my teeth stay strong and healthy.

When feeding me, my mom has to let me taste it on the end of my tongue before I eat a spoonful. If not, I might spit out everything. Even if I really like the food, I need to get my taste buds ready. Here's one other secret that works good on me, are you ready? You know those multi-vitamin pills you have to take in the morning time? Well, I find it just simply tastes better when my mom calls it a morning candy. Even though I don't like candy, it sounds better with that name. I don't like it if you call it a vitamin. And the only kind I like is One a Day for Kids no other kind. It probably sounds like I'm a difficult person to feed, but I really have come a long way. My mom has worked very hard to make eating a fun thing instead of a task. Looks like all the work she did paid off.

As far as potty training, I'll pee pee when I'm brought on a regular schedule (most of the time). I sometimes have accidents in my pull-ups if I wait too long. I don't really ask to go to the potty, they just have to keep bringing me. But as far as the big job, I just don't have the patience to sit through the time it takes to finish. I usually make a big mess because I don't sit still enough. So my mom says we will wait until I'm ready before I have to reach that goal. If for some reason I do have a 'number-two' accident I definitely do not like to be dirty. Sometimes I get in real big trouble when I strip my clothes and dirty pull up off without telling my mom. One day I'll learn that I'm just not supposed to do that.

My mom wants me to tell you about me not wanting to take a nap during the day. I don't like to miss anything that's going on.

But, you know if I wake up early in the morning, by the time the afternoon comes around I really need to rest my body. I am so lively when I'm awake I use up every ounce of energy I have in me. I could go all day without resting, but I usually get either really aggravated or giggly when I'm tired. Also, when I don't rest enough my eyes move a lot and it looks like I can't focus on things well. Another thing that makes me really tired is when I get sick. I sleep a whole bunch, especially if I have a fever. Then, I usually stop eating and drinking and I have to get IV fluids for me to feel better again. One last thing that affects my body is the heat. If I get overheated it tends to slow me down. I don't sweat a lot when I'm hot. But, I do get really red in the face. I also have a high tolerance to pain, it takes something really bad to make me cry.

Everyone knows the two favorite people in my life are Menta (my mommy) and J.J. (my daddy). They spend so much quality time with me. I also have some wonderful grandparents. They all play with me and make me so happy. And they help my mom a bunch when she needs time to do things. I love when my grandparents baby-sit me; we have so much fun. I have a cousin, Leslie, who plays and spends time with me. I also have two close friends that I call by name, Lee and Natalie. They are around my age, and we all get along very well. One other special person I have in my life is Ms. Diane. She's a paraprofessional who helps my teacher at school and also baby-sits me at my house when my mom and dad go out on a date. I really like Ms. Diane, she sits down with me at my table and let's me play with messy things like play dough, chalk, stamp pads, and markers. All the things I can't be left alone with. She also brings me to the park so I can play on the slide and swings. It's so fun to be outside. Of course, I have many more other special people in my life. These are the people that know me best and help me learn what I need to know. And of course, they play with me too.

There's one last person I'd like to thank so much; he is my godfather Marc. He has helped my mom proofread all the stories she has written about me. I will never forget the help you've given to her. One day when I get older, I will be able to read the stories and know exactly how I lived when I was a younger girl. Thanks again, and I love you.

Here are some things Ashtyn doesn't like or doesn't like done to her

- Getting an I.V.
- Wearing a urine bag to collect urine for the doctor.
- Taking medicines. Especially the sweet ones.
- Eating sweet foods like candy, cake and ice cream.
- Drinking her formula.
- Sitting down to watch T.V.
- Sitting in a car seat for long trips.
- Having to be quiet and still when we go in public places.
- Real animals. They tend to scare her.
- Getting her hair fixed. She doesn't like barrettes and pony tails.
- Giving good bye kisses.
- Crying babies make her sad.
- When she sees a baby with a pacifier in their mouth.
- Real guitars. The look and sound of them.

- Noises that she doesn't understand what they are and where they are coming from.
- Taking a nap when there's noises in the room.
- If you pull her hand to do something, she pulls the opposite way. She prefers you to guide her from the elbow.

Here are some things Ashtyn really enjoys

- Loves playing outside.
- Swimming or taking a bath.
- She likes to suck her right thumb and play with her mom's hair with her left hand when going to sleep.
- When other people clap for her.
- Playing with silly putty. It doesn't stick to everything like play dough.
- Playing at McDonald's or Burger King in the balls and on the slide.
- Swinging.
- Feeding her babies and stuffed animals with a spoon and a bottle.
- Cooking in her pots on her play kitchen.
- Listening to Barney shows.
- Listening to Shania Twain and Cajun music.
- Throwing velcro balls on a felt board and basketballs in the goal.
- Throwing beanbags. We are working on underhand throws.
- Blowing raspberries on other people if their arm or leg goes too close to her face.
- Whistle like a bird.
- Fluttering her hands when she gets excited.
- Someone imitating what she does.
- Flipping furniture.
- Throwing her toys in back of her bed or the sofa.
- Playing with a VW car that she calls a bee beep.

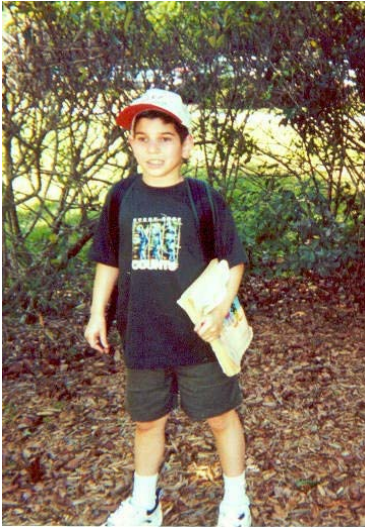
I hope you enjoyed me telling you about my personal life, and thanks for listening!

Enjoy life to the fullest and be happy.

Ashtyn Pitre
The Pitre's
207 East 14th Place
Cut Off, LA 70345
(504) 798-5631
menta@cajunnet.com

Robert Bazy

Isovaleric Acidemia, Age 9



Our Family's Life Line!

Robert is full of different challenges everyday. No day goes by, without Robert making our life interesting. As his sister always states "A family is a team", no baseball, football or basketball organization can survive without a "team effort". This is true when raising a "special child".

We know that Robert protects the ones that love and care for him. Robert is truly our "Family's Life Line".

As Robert grows, so does our family and we are so fortunate to have Robert as our "Family Teacher".

Robert teaches us that it's better to give than receive.

Robert teaches us that it's OK to be different and be part of a family.

Robert teaches us that life is full of patience, care and love.

Robert teaches us that it's better to love than hate.

Robert teaches us that children are a gift and that we should be thankful.

Robert teaches us that it's better to deal with life, than to walk away.

Robert teaches us that a "Family is a Team".

Even though Robert is only 9 years old, he has taught us important lessons of life.

Robert is truly our "Family's Life Line". We are honored to have Robert as a family member and family teacher.

Richard Bazy

johnnyba@worldnet.att.net

Amber Wist

MMA, mut⁰, Age 16

Amber, MMA with her grandparents.



Amber is 16 years old; a junior in high school, on the National Honor Society; favorite subjects – science and math; just completed driver's-ed, and hopes to get her license in November, is saving to hopefully buy a pickup truck in 2001 (currently has \$4,000); has a dirt bike/-motorbike; works part time at a florist; has a boyfriend; has been a choir member and altar server at our church; is becoming somewhat of a pool shark - to name some of her interests and accomplishments. She also has a 24 year-old brother who is healthy. Amber is truly a sweet, loving girl.

Amber is 5' tall and weighs approx. 100lbs. She makes a special drink mix consisting of 120g of 80056, water and Tang which she drinks each day. She is also on sodium bicarbonate, Rocaltrol and Carnitor[®]. Her daily protein intake is 32g. She has always done very well with her diet.

Amber was almost two years old when she started walking, precariously at that. She walked before she crawled. Her fine and gross motor skills are not her greatest strengths, although, she is not limited in her activities. I would say her cognitive skills are her greatest strength.

Amber started on the bicarb when she was about two years old, which helped with her illnesses. Before the bicarb, she would always end up in the hospital whenever she had an illness. She has had many hospitalizations, some in PICU, most from when she was very young. After starting the bicarb, Amber was able to get through a lot of illnesses without becoming acidotic. I believe the bicarb helped with her acid level. I believe her last visit to the emergency room was in 1995 where she was treated with IV and briefly admitted, due to vomiting. Her hospitalization prior to 1995 was in 1990 and was much more frightening. She had a metabolic stroke, affecting the basal ganglion portion of her brain. I was in the hospital room with her (fortunately, I've always been able to stay with her during her hospitalizations) and noticed her right hand was in a slight, claw-like position. As the day progressed, she became more affected. Her right arm began to jerk back uncontrollably, then she lost control of her neck and then her tongue. She had a tube inserted down her throat for feeding. As I said, it was very frightening because we did not know what the outcome would be. Thankfully, she recovered. It is extremely important to get our children to the hospital early when they become ill.

Amber's kidneys have been affected by her MMA, which is why she takes Rocaltrol. It is thought that she may one day need a kidney transplant. Actually, when this first became apparent some years ago (perhaps in '95) I believe it was thought she may have needed a transplant by now. However, Amber's lab results have been stable, and she has been doing very well. I have stopped keeping track, mentally, of her numbers, and so cannot give you any exact levels off the top of my head. As far as I know, there is no immediate concern about her liver.

Take care and God bless.

Denise & George Wist
12105 Lanham Severn Rd.
Bowie, MD 20720
301-262-1360
dw120@umail.umd.edu

Joshua Johnson

Propionic Acidemia (PA), Age 21



Our names are Mark and Kim Johnson. We are the parents of Joshua, who has PA. Since 1980, when Josh was originally diagnosed, we felt very isolated because we had no way to find out any information about this disorder. Just recently we discovered the OAA - through the miracle of the web.

Mark and I were young parents (he was 19, I was 18). Josh was diagnosed with Propionic Acidemia shortly after he turned one year old. During the first year of his life, Joshua seemed to be a normal, healthy baby.

The first time Joshua got sick, Mark's parents were watching him. Joshua's symptoms were running a fever, rapid breathing and he was so lethargic he seemed almost lifeless. Concerned, they called us immediately. When we arrived and saw his condition, we brought him directly to the emergency room.

The first hospital that we brought him to couldn't help us. They said they didn't know what was wrong with him and immediately dispatched him, by ambulance, to Children's Hospital in St. Paul, Minnesota. They also had no idea what was wrong with Josh.

That's when the doctor's started throwing out all these wild scenarios -i.e. Had he recently fallen, where he could have hit his head? Was it possible that Josh somehow had gotten access to and drank antifreeze? Was it also possible that he could have gotten access to and eaten what would have been an entire bottle of aspirin? The only thing that we could think of to tell the doctors that had changed recently, was that we had just switched him from formula to milk.

As the night progressed, the doctors, still unable to come up with any answers, turned their suspicions toward us. Were we hiding something and afraid to admit it? After all, in their eyes, we were so young.

So, once again, they returned to the wild scenarios. Only now adding "Are you sure?" or "Isn't it possible?" Putting such doubts in our own minds as, "Was it possible that he got into antifreeze?" What about the aspirin and where could he have gotten it? "DID he fall?" With all those doubts running through our minds it made it almost impossible to think clearly. We just kept going back to the recent switch to milk even though there was no apparent connection.

On top of all this, they were running all these tests on Joshua. Just poking around in the dark hoping to come up with something. They even wanted to pump his stomach because they still believed he had aspirin in his system. However, we refused to allow them to do this. Josh had been through too much already. Within the next few hours Josh had slipped into a coma.

Just when things were looking truly grim, finally, some good news had arrived. After that long evening of questions, suspicions and doubts, Josh had been diagnosed with a rare metabolic disease called Propionic Acidemia. It was the milk after all that had made him sick. That was what my gut had been telling me all along.

We will never forget how the doctor broke the news to us. "I've got some good news and I've got some bad news." (Yes, those were his actual words to us.) "The good news was that they knew what Josh had, a "mild" form of Propionic Acidemia. The bad news was that, in all likelihood, he would probably be retarded and may not live into his teens. They told us, because all the others (only twelve or so other cases IN THE WORLD at that time) had been severely retarded and no one, to his knowledge, had lived into their teens. He went on to explain to us that even if Josh did really well with his PA, he'll still never have a completely normal life. He said, for example, that Josh may never be able to go out and do normal things

that other people take for granted, such as, go out and eat pizza or grab a hamburger. He also said Josh would never outgrow this and probably be on some sort of medication for the rest of his life.

Considering Joshua's problems with his immune system, due to the PA, he has been relatively healthy with only a few hospital stays. Of course with every cold, flu or other illness it was always much worse than your average person. Josh only relapsed once shortly after he was first diagnosed. We have been to the hospital over the years for other things. As you all know, fighting infections was difficult for him and he had to be hospitalized while antibiotics were fed intravenously. And everytime flu season came around, it would be another trip to the hospital. We get flu shots now and that really helps.

Josh has a mild case of PA and is not on any medication for it now due to his choosing. However, he was taking Biotin and Carnitine for many years before that - 35 pills a day. He is not considered mentally-retarded and has some learning disabilities. He doesn't drive due to some spatial problems and by not being able to process things quite fast enough. But he is determined to get his license somehow. Occasionally he has a piece or two of pizza and can even eat a hamburger. Josh also seems to get very tired especially after doing something physical and will sometimes eat nothing at all except for some chips for the whole day. On those days, I try to get him to drink some Ensure - it's a high calorie drink (it also contains vitamins) and has 9 grams of protein per can. He gets dehydrated more quickly I'd say than others and is constantly drinking Mountain Dew. I think the Mountain Dew must also supply him with some needed energy.

Now here it is, 20 years later. Joshua has exceeded almost all of our expectations. He is no longer on any medications, he is not retarded, he can eat pizza and can even grab a hamburger just like normal people. Some good news... he has recently become a father to a boy, Josh Jr. Who thankfully does not have PA.

If there are any questions or comments, we can be reached at the following web address:

Mark, Kim and Josh Johnson
650 Third Street
St. Paul Park, MN 55071
KimJ@FMFRATTALONE.COM

Christopher Anderson

MMA, mut⁰, Age 2-1/2



Christopher Patrick was born on February 18, 1998. His delivery went well and he was considered healthy on his first day, he ate well. On the second day he didn't seem to have an appetite and "spit up" a lot, but was sent home. Since he had a circumcision before he left the hospital, we were told to expect him to have a deep sleep for several hours. He did sleep well that day, we told. However, through the night he would not wake up to eat. At 4AM after several attempts to feed, I called a nurse on the "well baby" unit. I told her that he would not eat, had lost his sucking reflex, was groggy and his eyes were rolling back somewhat. While on the phone, my husband, Brett yelled to me that Christopher had stopped breathing! I ran to the bedroom, shook him and pressed on his chest. He started breathing again, but it was labored. We rushed to Wilford Hall Medical Center.

The nurse examined Christopher carefully. At that point, he was flaccid and unresponsive. The doctors were called in and ran labs. After running labs twice, to verify that indeed his ammonia level was in the 1200's. (normal range is 50 to 100) and rushed him to the NICU.

Christopher was put on a ventilator, and had several catheters placed. There were so many healthcare workers around our little baby, that we could not even see him. And being a registered nurse myself, I didn't want to see what Christopher would endure. Though it seems strange, now, Brett and I returned home, feeling very helpless.

While at home, Dr. Heiman (the neonatologist) called and said they had an idea of Christopher's diagnosis of Methylmalonic Acidemia (MMA). He wanted to try an experimental procedure — hemodialysis. Brett, my mother and I went back to the hospital after praying that the dialysis would work.

Dr. Heiman and Dr. McLean (the geneticist) explained the speculated diagnosis of MMA. Since Christopher's ammonia level was in the 1600's at that time, it was thought that his chances were slim—but hoping for recover and minimal brain damage, they started the procedure quickly.

At the start of the hemodialysis Christopher's ammonia level maxed to about 2400. By the end of that day, the ammonia dropped and hovered at about 800.

The next morning, his level still had not changed. Throughout the day the level gradually dropped into the 200's. Thankfully! His hemodialysis was then stopped. Though he had experienced seven seizures when his ammonia levels were high, they did not reoccur.

In the days following, Christopher managed to wean himself off the ventilator and become stable. It took several days for him to open his eyes and a week for him to cry, but what a joyous sound that was!

After 6-1/2 weeks in the NICU, he reached his birthweight of 7 lbs. and 11 oz. He had an outpatient blood transfusion and weekly follow-ups, but was doing well. He had Phenobarbital, B12 shots and Carnitine for meds. His formula was a mix of Similac, Propimix-1 and Prophree.

Everything went well. However the metabolic specialist at Santa Rosa Hospital who oversaw his care were not optimistic that his immune system would handle even his first cold. Waiting to see how Christopher would do being sick was very difficult. I wanted to treasure every day with Christopher, yet protect myself from being hurt if he did not make it. Thankfully, he made it through his first cold easily and several since.

Over the last 2-1/2 years, Christopher had a g-tube placed and has been hospitalized about 12 times with various minor illnesses. Having IV fluids with bicarb added, and IV Carnitine, he does very well bounding back to health.

He now takes Carnitine (16cc daily) and Zyrtec and Flonase for allergies. His formula is a mix of Propimix-1, Prophree and ProVimin. Since he had testing to show he has type mut0 of MMA, he B12 shots were discontinued, as was the Phenobarbital.

We are so thankful to the staff at Wilford Hall and Santa Rose Hospital. Dr. Heiman and Dr. McLean have earned a reward for the first hemodialysis of an MMA patient recorded in the medical journals.

Since this is the first time I have written Christopher's story for OAA, I will just briefly mention his progress since his initial diagnosis.

Christopher raised his head at 4 months, crawled at 1 year,

and has just begun walking. We are so excited! He has speech, occupational and physical therapy.

Though he does not talk, Christopher is very social and expressive. He is an affectionate and loving child. He loves to hug, clap, give high-fives and climb everything. Christopher's relaxed personality goes well with his younger sister's spunky personality.

Katie, who is now 1-1/2 years old, has been diagnosed as "healthy". It is amazing to see how accepting they are of one another, just as they are.

We would like to thank OAA for such valuable information and support from other families. We welcome hearing from other families with metabolic disorders, who face similar challenges.

Our phone and email sites are as follows:

Brett and Mary Anderson
113 Ferson Loop
San Antonio, Texas 78236
210-670-1528
brettmary@hotmail.com

Our prayers are with all families of children with metabolic disorders. May God bless you and take care.

Stacey Erickson-Coyle

Propionic Acidemia (PA), Age 27



My name is Mrs. Stacey Coyle (maiden name Erickson). I am 27 years old and I live in Red Deer, Alberta, Canada with my husband, Kevin and our son, Nicholas James. Some of you may have read my story in the OAA newsletter in the past. Well, a lot has happened since my last story and I thought it was time for an update. I am pleased to report that I am doing great! I haven't been sick and haven't been in the hospital since my son was born. My husband and I married on June 14, 1997 at the Gaetz United Church in Red Deer. After a few months we moved to our first home, a old-fashion house on a corner lot with a big yard and lots of trees. Two years later we decided to try to have a child, despite the risks, but we did everything we could to educate ourselves, asked my doctor in Edmonton many questions regarding the pregnancy, my health and the baby's health so we were prepared for what was to come. On March 28, 1999 I found out I was pregnant! I called my husband at work that day and asked him to pick me up after work at the medical laboratory. I gave him the exciting news that I was pregnant and it was the most exciting moment of our lives! From then on I began to prepare for the arrival of the new "weeone" and I had to keep myself healthy. I had to take six glasses of formula, followed a strict diet and get lots of rest and exercise. I managed to keep my glycine level close to normal, down to 350. On

January 12, 2000 our son Nicholas James Coyle was born at 6:12 pm at the Red Deer Regional Hospital. He weighed 7 lbs., 6 oz. and 20-1/4 inches in length. He has red hair, blue eyes and the cutest little boy you ever say – quite the ladies man too! He was born perfectly healthy – normal baby boy and I am pleased to report he doesn't have Propionic Acidemia! He was tested for PA once when we was born and a few weeks after I brought him home from the hospital by the doctor up in Edmonton.

We haven't been doing much this past summer, just being a wife and mother keeps me pretty busy and I just love taking care of Nicholas. My husband has been busy at work, working a lot of hours so we could afford to go on summer vacation. My husband works as a journeyman cabinet maker and works at Thomson Cabinets in Red Deer. When I am not busy and find some free time, I like to spend write to my penpals, family and friends. I also read, work on crafts, which includes designing teddy bears and work on family history research. I currently have 12 pen-friends who have PA who I write to, but I am always interested in knowing more who have the same disorder and hearing about their lives and what life is like for them living with PA. I would like to hear form more people who have PA and get to know each other better, because everyone needs a friend.

I hope all the reads like my updated story and I look forward to hearing from you soon. Take care and have a nice day!

**Mrs. Stacey Coyle
4030-50 A St.
Red Deer, Alberta
Canada T4N-1Y7**

Metabolic Research Funds

The **Scott C. Foster Metabolic Research Fund** benefits individuals with inherited metabolic diseases including phenylketonuria (PKU), maple syrup urine disease (MSUD), homocystinuria (HCU), tyrosinemia, organic acidemias (OA's), and urea cycle disorders (UCD's).

Each of these rare diseases occurs because of an enzyme deficiency affecting metabolism of dietary protein or other nutrients. Each of them can cause serious medical problems. When untreated or poorly controlled, all of them cause mental retardation, and some even death. There is a great need to improve the quality of treatment for children and others affected by these diseases.

Although each of these inherited metabolic diseases is unique, there are similarities that link them. Each requires a very difficult and very restrictive diet. Usually, an expensive synthetic formula is also required. Dietary treatment is for life.

Given adequate funding, there are many research projects that could greatly improve the quality of life for affected persons. The Scott C. Foster Metabolic Research Fund will help support such projects.

Who Was Scott C. Foster? Scott Foster was the first child with MSUD to be identified through the newborn screening program in Massachusetts. Because of the newborn screening program, Scott began treatment within days of his birth. He survived a metabolic crisis when he was 18 months old. His diet was well controlled throughout his life and he developed well both physically and intellectually. He graduated from college, had a steady girlfriend, and worked for the Massachusetts Bay Transportation Authority. One night, he came down with the flu and went into an irreversible metabolic crisis. Scott died at age 22 with his family by his side.

The Scott C. Foster Metabolic Research Fund is the first of its kind in the United States. The monies raised will be designated for research that will help all of the disorders that are included in the fund. Please help spread the word about this fund so that together we can make a difference. To date, they have generated \$200,000.00.

Please think about the Scott C. Foster Metabolic Research Fund when you want to make a tax-deductible contribution, when you want to organize a fundraiser or in lieu of flowers in memory of a loved one.

Donations can be made to:
Scott C. Foster Metabolic Research Fund
65 Bromfield Street
Somerville, MA 02144
Anyone with questions can contact:
Herb Foster at (617) 625-6635

NORD's Research Grant Program

The National Organization for Rare Disorders (NORD) has a fund open for research on Methylmalonic Acidemia. Currently there is \$2,316 in the fund.

NORD's mission is to promote the diagnosis, treatment, and cure of rare disorders through programs of education, research, advocacy, and service to families and health professionals. **NORD's Research Grant Program** provides small "seed money" grants to academic scientists studying new treatments or diagnostic tests for rare diseases. The small clinical trials supported by NORD's research grants provide preliminary data indicating that a treatment (drug, device, or medical food) will be safe and effective when used for a larger number of patients. Researchers can then use the preliminary data to apply for larger multi-year government grants, or to attract a commercial sponsor who will manufacture the orphan product and get it approved for marketing by the Food & Drug Administration (FDA).

Donating for Rare Disease Research

Donors may specify that their gift to NORD be used for general research and related activities, or they may restrict their gift to research on a specific disease.

Disease Specific Research

Gifts restricted to a single disease will be used to support clinical research on that disease, including new treatments, diagnostic tests, or genetic studies. However, a Request for Proposals (RFP) will not be issued to the scientific community until the disease-specific fund reaches \$35,000 to \$50,000. This is because scientific research is very expensive, and scientists cannot accomplish meaningful results unless they have enough money to support their work.

Out of funds restricted to specific rare diseases, NORD uses only \$5,000 to cover the direct costs of the RFP, which include advertisements in leading medical journals and a mailing to every academic research facility in the United States. Additionally, research institutions in Canada and Europe may also be notified of the RFP. After the grant is awarded, NORD monitors the progress of the research, processing biannual reports to NORD's Medical Advisory Committee.

In the past, when donors gave small sums restricted to research on specified diseases, the gifts languished unspent for several years because the sums were too low to support medical research. Therefore, NORD's Board of Directors decided if the funds donated to a specific disease do not exceed \$1,000 within two years, the gifts will be transferred to NORD's general research account. Exceptions can be made if NORD sees continued donor activity for a specific disease, indicating that there is a determined effort to reach the minimum \$35,000 goal. In many instances, families will launch fundraising campaigns in their communities that raise several hundred dollars at a time. NORD encourages these activities and recognizes that it can take several years to reach the necessary sum that triggers a request for research proposals.

Selection of Grantees

The initial Request for Proposals asks scientists to submit a brief description of their proposed research project along with their qualifications and a draft budget. Once that information is received, NORD's Medical Advisory Committee (composed of leading academic scientific experts) reviews all of the applications and selects finalists. The finalists are invited to submit a full grant application describing their proposed project in detail. NORD's Medical Advisory Committee then reviews the full grant applications (peer review) and ranks them through a scoring system. The highest scoring grant applications are recommended for funding to NORD's Board of Directors who vote on the final grant awards.

NORD's grant review process is based on the same peer review system utilized by the National Institutes of Health (NIH). Scoring of grants is done individually by each medical expert, and

scores are added together to determine the final ranking of each proposal. Any reviewer with a conflict of interest is excused from voting on a specific proposal.

Donors who wish to support research on rare diseases are encouraged to contact NORD's Department of Development to find out more about this unique program at (203) 746-6518 Fax: (203) 746-6481 Toll-Free: (800) 999-6673.