SEARCHING FOR A CURE HOPE FOR OUR CHILDREN

Propionic Acidemia Foundation

VOLUME 1, ISSUE 13 FALL 2012

PA Registry is Launched

On September 1st, the Propionic Acidemia Foundation launched a patient registry. Through patient participation, the registry will increase the understanding of the ways Propionic Acidemia (PA) affects those with the disorder. The privacy protected information will help researchers in identifying patterns and trends within the disorder.

Those participating in the registry will be able to view combined information of those who have entered their information. For example, you can view how many of those affected by PA have a feeding tube, how many were newborn screened, and how old the person was at diagnosis. As of the end of September, seventeen individuals have entered information into the registry.

For those affected by PA or their caregivers, they can register by going to www.paregistry.org. There will be a place to create a user account, once approved for access, an e-mail will be sent indicating that the affected person's information can be entered. It is expected that the first series of questions will take only 20-30 minutes to complete. Periodically, additional questions will be added. Relevant lab and test results, like EKGs, can be uploaded.

We encourage all of those affected by Propionic Acidemia to register, so that the data will show as complete information as possible. Information can be entered on those who have passed away with the disorder.

Researchers and physicians can contact the Propionic Acidemia Foundation regarding accessing deidentified data from the registry. The patient registry has IRB approval. A sample of information participating families can view on the registry: 65% of those participating have a feeding tube, 41% eat all of their nutrition by mouth.

INSIDE

MISSION: The Propionic Acidemia Foundation is dedicated to finding improved treatments and a cure for Propionic Acidemia by funding research and providing information and support to families and medical professionals.

VISION: To create a future where Propionic Acidemia can be prevented and any affected individual can be cured and live a productive life.

ALAN'S "CYCLE AWAY THE BEER GUT & MAN BOOBS"

My daughter, Eilidh (Scots Gaelic name pronounced Ayley), is 11 years old, full of fun, the apple of my eye and adored by everyone who knows her. The way Eilidh's personality has evolved as she copes with this awful disease is extraordinary. She takes all it throws at her without complaint, is so brave at the worst of times, and in many ways pulls those who love her through it all. We're all so proud of her.

So, inspired by Eilidh and other children like her, I decided to embark on a mega-challenge to raise much needed funds to support research efforts into a cure. Starting on 8th September I cycled from one end of the UK to the other over 9 days. The route, from Lands End in England to John O'Groats in Scotland, is 968 miles long and involves climbing and descending over 40,000 ft. That means I had to pedal my overweight carcass, complete with Beer Gut and Man-Boobs, up and down these hills for an average of 108 miles per day for the 9 days!!

Well, as you can see from the photo (right) I made it to John O'Groats as planned. Don't be fooled by the 874 miles on the sign – that's the distance as the crow flies or by main trunk roads. Our route was meant to be 968 miles but became 976 as we had an 8 mile diversion due to a road closure north of Glasgow.

The hardest days for me were day 1 in Cornwall due to the 26 deg C heat and 108 miles over the incredibly steep, short hills, and day 7 which took us from Hamilton to the south of Glasgow all the way to Fort William in the Scottish Highlands. That day was meant to be 127 miles but the diversion made it 135 and the first 120 of it was into a 30+ mph headwind. We had to pedal like fury, even on the descents!

I don't mind admitting that cycling through Glen Coe into driving rain and a howling wind, 100 miles into a 135 mile day, is something that nearly had me in tears and will live on in my nightmares! But it's at those moments you think about the kids and their families coping with Propionic Acidemia, and all the generous donors who have supported you, and you dig really deep to get through it.

All in all an incredible experience and I left it with huge respect for the 500+ riders who took part in the 2012 Deloitte's Ride Across Britain, all raising money for causes dear to their own hearts. There was 1 head injury I know of, a broken bone or two, and huge amounts of muscle, ligament, tendon and general exhaustion problems – by the latter part of the week the medics tent was like a battlefield hospital in the evenings and early mornings. But seeing people dig into their reserves of endurance was quite special and I'm very proud to have ridden alongside every one of them.

Thank you so much everyone who's supported my fundraising efforts so far, you really drove me on. Those that haven't yet and intended to, or who were waiting to be sure that I both finished and survived it, can still do so via either link below.

UK http://uk.virginmoneygiving.com/pedalawaythebeergutandmanboobs2012

US http://www.firstgiving.com/fundraiser/cycleawaythebeergutandmanboobs2012/pedalawaythebeergutmanboobs2012

Thanks again.
Regards
Alan Duncan

PAF AWARDS $5000 GRANT

PAF Awards $5000 Grant to the Clinic for Special Children PA Workshop, Strasburg, PA

On September 14th, Dr. Holmes Morton and the Center for Special Children held a Workshop titled: "Propionic Acidemia: The Biochemical Basis of Keto-Acidemia, Encephalopathy, Metabolic Strokes, Heart Failure & Long QTc, and a Discussion of Current Therapies"

Propionic Acidemia is found in Amish and Mennonite populations throughout North America.
The Amish & Mennonite variant (PCCB1606 A>G) is a common European form of the disorder. Heart failure may develop and the Clinic is working with a formula company on developing a new formula that may prevent or reverse damage by targeting the citric acid cycle. More information is available in the Clinic for Special Children Summer 2012 Newsletter. In addition to nutritional therapy, gene therapy, enzyme replacement and chaperone drugs were discussed. The workshop was attended by over 50 people including researchers, doctors, students and families affected by the Amish & Mennonite variant. The attending doctors treat over 70 individuals affected by Propionic Acidemia. The format included brief presentations followed by discussion. A number of collaborations have been started and we are looking forward to seeing what happens next.

Participants were invited to attend a benefit for the Clinic on Saturday September 15th. The benefit attracts over 5000 people for fabulous freshly made food on-site and multiple auctions for a variety of items including beautiful quilts and furniture. (See pg. 7 for more)

Dr. Areeg El-gharbawy, Dr. Georgianne Arnold, Dr. Holmes Morton, Dr. Jan Kraus, and Dr. Loren Pena

2012 PAF EDUCATION DAY/CONFERENCE

On June 30th, the Propionic Acidemia Foundation hosted an education conference in Middlefield, OH. It was held at the DDC Clinic Center for Special Needs Children in conjunction with Rainbow Babies & Children's Hospital and University Hospitals. We were fortunate in having Dr. Kerr; Dr. McCandless; Emily Lisi, GC; and Dr. Morton speak. Judy McConnell, RD, gave a cooking demonstration. The day was attended by over 50 people including 10 families affected by PA. Blake Andres, the Executive Director of the DDC Clinic, gave a history of the facility and a tour of the facility and lab. They are a model of a true medical home, and one that looks to the needs of the family that is affected by rare disorders like PA.

Dr. Douglas Kerr and Dr. Shaun McCandless

Publication Note: The PAF Newsletter *is published twice a year. Readers may subscribe by writing to PAF, registering online or calling 877-720-2192. Letters and article submissions are welcome for consideration and may be sent to paf@pafoundation.com or mailed to Propionic Acidemia Foundation 1963 McCraren, Highland Park, IL 60035. If you would like to be removed from our mailing list or receive the newsletter via email, please contact us. We are deeply appreciative to Publishers Printing Company for donating the printing costs of the newsletter.*

Mel & Elise's Story

The Russell Family

My husband and I recently celebrated 15 years together which might not seem like a long time for many, but we were around 15 years old at the time we met. Our lives were in perfect order; we completed college, secured great careers, married, and bought a beautiful home to grow our family. These were all things that we planned for before we decided to finally have children. We did not know at the time but God was preparing us for many upcoming challenges.

Our PA story began in October 2011 when our daughter Elise (1 week) was thought to potentially have an organic acid disorder based on her newborn screening. Elise was home from the hospital for one week all the while eating and sleeping great when her pediatrician indicated that her screening returned with elevated levels. My husband and I were not alarmed because her older brother Melbourne (18 months) had the same elevated screening when he was born and then it was deemed normal based on the repeat test.

While we awaited Elise's second set of results little Mel woke one morning not wanting to eat/drink, was moaning and running a fever. His right side arms and legs seemed to be limp. We rushed him to urgent care where they indicated that they thought he was having a stroke/seizure. Mel was transported to Children's Hospital of WI where a number of tests, spinal tap, x-rays, and brain scans were performed on him that day. The following day we were told that they did not know what the cause was and we could go home and he would be put on anti seizure medicines. Shortly before our expected release the genetics team which we had met with just days before about Elise entered our room. They indicated that they thought Mel might have what they thought Elise has MMA or PA and he had suffered a metabolic crisis. After about a week in the hospital the diagnosis for Mel and Elise was confirmed; they both have PA.

My husband and I had suspected something was going on with little Mel's digestive system since he had terrible constipation and vomiting episodes since he was about 9 months old; when I stopped nursing and we put him on formula/milk. For nearly 9 months before his crisis we visited with multiple pediatricians, GI specialists, and ER visits to figure out what could be wrong. No one ever mentioned PA, and dismissed my asking if the vomiting/constipation had anything to do with his newborn screenings. We often think back to the signs and symptoms such as vomiting, gaging/choking, lethargy, not thriving, staring spells, wobbling, and acid breath. This was at the time our only child and we depended on experts to help us figure out what was happening to our baby.

Both Mel and Elise are developing well; Mel is walking/running (getting into boy trouble) and starting to speak, he self-eats and drinks well. Since his crisis we have been following the PA diet very close with a Propimex mix and 15-16grams of protein/day. Elise is getting ready to crawl, she says "mama, dada, baba, and me" she is eating and drinking wonderfully a mix of Propimex/breast milk, and solid fruits and vegetables. Both children are taking Biotin, Carnatine, TriViSol, and Flagyl.

Our goals are to continue to closely monitor the kid's diet to take every precaution to keep them healthy. We are researching and considering PGD/IVF and cord blood banking in hopes that our future children will not be affected and can supply Mel and Elise with a potential cure from the cord blood. I have been in touch with newborn screening advocates to find out how we can share our newborn screening failure story with others and changes are made in the processes so other families do not have to face the challenges that we have.

As I stated earlier God chose us to protect these babies and we will continue to fight for them. Elise was brought into our lives to save her brother; just days after her birth her brother started to lose his fight with PA and because of her help the doctors were able to save his life. We feel that our children will always have a close bond with each other and this will be quite the story to share with them when they are older and learn to protect one another time and time again.

Mel & Nicole Russell

PROPIONIC ACIDEMIA AND PREGNANCY

The Biochemical Genetics Program at the University of Wisconsin in Madison has followed four pregnancies in women with propionic acidemia (two women, each woman has had 2 children. The first pregnancy was reported in the literature in 1992 (1). We have also followed several pregnancies in women with Maple Syrup Urine Disease (MSUD), another disorder in amino acid metabolism.

At this time, we do not have enough information to know if propionic acid, or any of the other metabolites associated with PA, are teratogens. Teratogens are compounds that can have adverse effects on a developing fetus. Commonly known teratogens include alcohol and various drugs that can have devastating effects on an infant's outcome. In metabolics, we know most about the teratogenic effects of phenylalanine (phe), the amino acid that cannot be metabolized in PKU. Pregnancies in PKU have been well studied and it is clear that elevated phe levels during pregnancy can cause microcephaly (small head size), developmental delay and congenital defects.

In our PA pregnancies, infant outcome has been good. The children of the first woman with PA to go through a pregnancy are now adults, ages 18 and 23. One graduated from technical school and works as an aid for children with autism; the other graduates from high school this spring. For the other woman, her two infants were born prematurily when the mother developed preeclampsia and required c-section. Preeclampsia is a common complication during pregnancy causing high blood pressure which can lead to seizures and coma if not treated. We don't feel that development of preeclampsia was related to the diagnosis of PA, but given our limited experience, we cannot rule out this possibility. This woman's children are now 3 and 6 years of age and do not have any developmental problems, although the youngest required speech therapy. There has also been one other PA pregnancy report in the medical literature – this woman from Europe delivered a healthy infant (2).

During pregnancy, both energy and protein needs increase. For a woman with PA, this means that both formula intake and protein tolerance from food will increase as the pregnancy progresses. This is especially true during the 3rd trimester when the infant is growing quickly. During pregnancy, fetal growth needs to be monitored closely with ultrasounds. In three of the pregnancies we have followed, slowed fetal growth was noted during the second or third trimester. In these cases, growth improved with increased protein and calorie intake.

Women with PA who are pregnant continue to be at risk for metabolic episodes associated with illness or poor intake. Pregnancy does not reduce this risk. The first trimester has been especially difficult for some of our women because of morning sickness. The nausea and vomiting associated with morning sickness can make it difficult for a woman to take sufficient calories and protein from formula. This can lead to metabolic decompensation, just as it can with women with PA who are not pregnant.

Another time that we have found that women are especially vulnerable to metabolic decompensation is during delivery and the post delivery period. After delivery, a woman begins to "break-down" protein stores as the body changes from pregnancy metabolism to post-pregnancy metabolism. We have found that it is imperative that a woman follow her diet and continue to be monitored for a minimum of 2 weeks after delivery to prevent a metabolic episode (1). After delivery, it can take 6 to 8 weeks before a woman's protein metabolism returns to what it was before pregnancy. The importance of continuing diet after delivery was especially evident in a 2003 publication from Japan (3). This paper reports about a woman with MSUD who was compliant with diet treatment during pregnancy. But, she stopped treatment after delivery and died 51 days later from complications associated with poor metabolic control. This shows the importance of diet management during and after a pregnancy in women with metabolic disorders.

There are women with mild forms of PA that may not require strict diet treatment as an adult and have few, if any, metabolic episodes. BUT, pregnancy is a big stress on metabolism as is the post-pregnancy period. So, even if a woman does not have problems associated with PA when she is not pregnant, this does not guarantee that she would not have problems during a pregnancy. Any woman with PA, no matter how mild it may be, should be followed by a metabolic clinic before pregnancy to assure good metabolic control and continue to be followed during and after her pregnancy. All of our women have been referred to a high-risk obstetrics clinic for more extensive monitoring of the mother and her developing fetus.

References

1. Van Calcar SC et al. Case reports of successful pregnancy in women with maple syrup urine disease and propionic acidemia. Am J Med Genet 1992; 44: 641-646.

2. Langendonk JG et al. A series of pregnancies in women with inherited metabolic disease. 2012; 35: 419-424.

Yoshida S, Tanaka T. Postpartum death with maple syrup urine disease. Inter J Gynelcol Obstetrics. 2003; 81: 57-58.

Submitted by

Sandy van Calcar PhD, RD

Senior Metabolic Dietitian

Biochemical Genetics Program, Waisman Center

University of Wisconsin-Madison

PAF FUNDRAISING SPOTLIGHT

EVENTS AND CAMPAIGNS

- 5/6/2012 **Morgan Stanley Spaghetti Dinner & Silent Auction**, Endwell, NY, raised $10,000! (right)
- 7/2012 **St. Michael's Ladies Guild Bottle Drive**, Binghamton, NY, raised $113!
- 8/25/2012 **Groucho's Poker Run,** Columbus, OH**,** raised $5000!
- 9/8-16/2012 **Alan Duncan's "Pedal Away the Beer Gut & Man Boobs"**, UK, raised over $2005 (and counting!)- see pg. 2
- 9/29/2012 **7th Annual Tailgate Party & Corn Hole Tournament**, Gahanna, OH, raised over $10,500!

Kady Falkenberg, Organizer of the benefit, Connor McKillop, guest of honor, and Dr. Bill Marusich, one of Connor's dearest friends and supporters

EVENTS AND CAMPAIGNS

- 10/21/12 **Tara Gerlach -Columbus Half Marathon (OH)** http://www.firstgiving.com/fundraiser/taragerlach/columbushalfmarathon-2
- 11/18/12 **Brittany Smith- Big Sur Half Marathon (CA)** http://www.firstgiving.com/fundraiser/brittany-smith-2/poundingthepavementforpa2012

Join the PAF Pounding the Pavement for PA team or start your own! Run in any race, around your block, or become a "virtual runner" Contact Brittany Smith for more information at paf@pafoundation.com or 877-720-2192


Michelle Ellis, Billy Whitten & Sue Whitten at the Poker Run for PA

A SPECIAL AUCTION: CLINIC FOR SPECIAL CHILDREN

This auction was held on September 15 in Leola, PA to benefit The Clinic for Special Children. The clinic is a non-profit medical and diagnostic service for children with inherited metabolic disorders in Lancaster County, Pennsylvania. It was established to provide comprehensive medical care for children with chronic, complex medical problems due to inherited disorders. Under the direction of it's founder, Dr. D. Holmes Morton (speaking left), the clinic specializes in biochemical disorders such as glutaric aciduria (GA1), maple syrup urine disease (MSUD), Crigler-Najjar syndrome, medium-chain acyl-CoA dehydrogenase deficiency (MCADD), and other disorders that occur in the Old Order Amish and Old Order Mennonite communities in Pennsylvania. The clinic cares for children with over 100 different genetic disorders and is recognized as one of the leading centers for the treatment of MSUD, GA1, and Crigler-Najjar syndrome. The mission of the clinic is to advance methods of newborn screening, to improve follow-up services, to develop better diagnostic methods, and to further clinical research in an ongoing effort to improve treatment and outcomes for children who suffer from rare inherited disorders. (See pg. 3 for info on the PAF grant awarded to the clinic.)

Photos by Mary Caperton Morton, theblondecoyote.com

We want to hear from you! Have a PA story to tell, event to promote or news? Spring newsletter submissions due by January 31!

FY 2011-2012 ANNUAL REPORT

FINANCIAL REPORT

Revenue:

Contributions: $120,277
Interest Income: $213
In Kind Donations: $784
Total Revenue: $121,274

Expenses:

Research Grants/Registry: $106,502
Programs & Outreach: $3,126
Printing (in-kind): $784
Fundraising: $2,419
Operational Expenses: $1,318
Total Expenses: $114,149
Cash Assets 8/1/2011: $126,726
Cash Assets 7/31/2012: $133,851

BOARD OF DIRECTORS/OFFICERS

Jill Chertow Franks, President
Brittany Smith, Secretary/Treasurer
Ann Marie Young
Michael Rosenson
Board disclosure: Jill Chertow Franks is the sister-in-law of Michael Rosenson.
Donations made by board members totaled $596.

PROGRAM ACCOMPLISHMENTS

Research: Grants Disbursement:

$27,000 Andrea Gropman, M.D., FAAP, FACMG, FAAN CNMC, Washington, D.C.**:** "Biomarkers for Neurological Injury in PA"

$27,000 Marisa Cotrina, Ph.D. University of Rochester, Rochester, NY : "The impact of pa on brain astrocytes: an in vitro model to test mitochondrial therapy in PA"

$15,000 Kimberly Chapman, M.D. Ph.D and Kristina Cusmano-Ozog, M.D., CNMC, Washington, D.C. : "Is there energy deficiency in PA".

$32,000 Sarah Venezia, M.S. and Jan P. Kraus, Ph.D., CDHSC Denver, CO: "Enzyme Replacement Therapy for Propionic Acidemia"

Outreach:

- Distributed fall and spring newsletters to affected families, clinicians, and donors
- Exhibited and attended SIMD Annual Meeting
- Held PAF Education Conference in conjunction with University Hospitals, DDC Clinic, and Rainbow Babies & Children's Hospital; Middlefield OH

Help Us Find the Cure!

*Name*_____

*Address*_____

City, State, Zip _____

*Phone*_____

*E-mail*_____

Please send an acknowledgement to:

*Name*_____

*Address*_____

*City, State, Zip*_____

*Enclosed is my contribution of $*_____ *in honor of/in memory of* _____

If you work for a company that has a matching program, please include the matching form.

Please mail your check made payable to: Propionic Acidemia Foundation 1963 McCraren, Highland Park, IL 60035

Thank you for making a difference.

SEARCHING FOR A CURE
HOPE FOR OUR CHILDREN

Propionic Acidemia Foundation
1963 McCraren Rd.
Highland Park, IL. 60035

Phone: 1-877-720-2192 toll free
Fax: 1-877-720-2192
E-mail: paf@pafoundation.com
Website: www.pafoundation.com

PROPIONIC ACIDEMIA FOUNDATION

Sponsors:

Abbott Nutrition

Vitaflo USA

Mead Johnson

Propionic Acidemia Foundation is run 100% by volunteers and we couldn't do it without you.

Join and follow Propionic Acidemia Foundation on Facebook

Thank you Publishers Printing Company for contributing the printing of the PAF Newsletter.