



Organic Acidemia Association



OAA Newsletter • Family Stories • Family Matching • Family Conferences • Research Funds Awarded • National Advocate for Newborn Screening

Parent Support, Education & Awareness www.oaanews.org

A support group for families living with methylmalonic, propionic, isovaleric, and other organic acidemias

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Conference News!



Happy Holidays! Hard to believe we will be welcoming 2020 in a few short weeks. OAA has been very busy on many fronts. In our last newsletter, we announced that we would host our family conference in April 2020 in Austin, Texas. Due to a number of circumstances - one of them being the price of hotels in Austin - we have made the decision to change course and not host a formal conference in Austin. We may instead have an informal gathering of families in the Austin area in April. So Texas families - stay tuned! The summer months historically is a much better time to host a conference and we have the opportunity of host next year's conference with Dr. Jerry Vockley's INFORM Network (<https://informnetwork.org>) and Mitoaction (<https://www.mitoaction.org>).

We have changed the date for the conference to July 25-26, 2020 (Saturday/Sunday) in Pittsburgh, PA. The venue hotel will be the Wyndam Hotel (<http://www.wyndampittsburghuniversitycenter.com>) right on the campus of the University of Pittsburgh. More information will be in the next



newsletter - and we will also post in our private OAA Facebook Group. Reach out to our conference coordinator Erin MacLean or myself if you would like to volunteer or have questions.

This past fall, OAA had several opportunities to bring awareness to our community. Karen Dalton and myself hosted a table at the SIMD/NAMA (North American Metabolic Academy) training here in the Twin Cities. Erin MacLean also represented OAA at the New England Rare Disease Conference in Portland, Maine. We have plans to host at other conferences in 2020 - if you are interested in helping to represent OAA - please let me know. This is an important outreach to bring awareness of our rare organic acidemias.

Health and Happiness for 2020.

Kathy

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Lucy

PROPIONIC ACIDEMIA

AGE 21

My daughter Lucy is 21 and has Propionic Acidemia. Lucy had a metabolic crisis at birth and the neonatologist immediately suspected an organic acidemia. It took about a week to confirm a diagnosis but the excellent team of doctors at the University of Kentucky's Children's Hospital began treating her for an organic acidemia right away. She was in a coma for several days and required dialysis. She had seizures with her initial crisis. We ultimately traveled to Atlanta to see a specialist in the field where we met Dr. Rani Singh who has guided us through the years with Lucy's care. Our life with Lucy has never been easy and I live daily with the fear of when the next crisis will be, but she is doing well right now. We went to the NIH to participate in a study to develop newer treatments for PA this past spring. She was poked and scanned and interviewed. We collected every lab sample you can think of. While we saw many of the same results as others with PA, we were happy to see that some things continue to remain normal for Lucy. Her heart pumping function and kidney function are currently normal. Her amino acid levels were as normal as they can be for PA after a 10 hour fast. And yet she has very little enzyme function. She does have autism and her IQ has dropped significantly

since middle school. What does all this mean? Who knows, but we have hope that one day maybe there will be a treatment that will allow less dietary restrictions. We struggle more with her medical needs and fearing loss of medical stability than with her autism. We are constantly on our toes, waiting for the other shoe to drop. It is hard to enjoy the stability and achievement we have in the present. I remember being given an OAA calendar during the first days of Lucy's life and seeing stories of other children with PA. I was grasping for some hope of a future for her. Would she talk, walk, have friends, go to school, have tea parties, play dress up, graduate, have a job. It was and is still scary. That calendar and the stories that went with it gave me a little hope. I want to do that for others.

Lucy does talk (a lot). She walks, rides a bike and an electric scooter to the local Rite Aid and her favorite - Yard Sales. She belongs to a special needs dance class. She has a strong passion for helping others with disabilities and has found a way to fulfill that by going into schools and the Down syndrome meetings where she assists the instructor with the Allegro Dance Program (a special needs dance program). She has lots of friends. She eats a large variety of foods. She had tea parties, played dress up, cheered, she graduated from high school, has a job at a childcare center. She took a college class and with help studying was able to pass the test required to get a national certification for childcare (Child Development Associate). She is a beautiful young lady and enjoys her life. Although we struggle daily with the constraints of her needs due to Propionic Acidemia, there is hope.

JULIE
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In November, The Stagni family had the privilege of sharing the OAA story to LogicBio in Boston, MA. LogicBio is working on a gene therapy for MMA.

Interventional Clinical Research: What to know, what to ask, is it right for my family?

KIMBERLY A CHAPMAN, MD, PHD, CHILDREN'S NATIONAL RARE DISEASE INSTITUTE, WASHINGTON DC

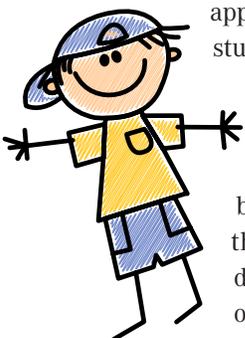


So you are thinking in enrolling yourself or your care into a research study, thank you for considering to help us understand your family's disorder and search for treatments.

As we discussed last time, research is a process to understand the world in which we live. The most simplistic divisions include very basic research (i.e. the search to understand fundamental processes) and clinical research (most simplistically divided to observational and clinical trials). Last time we discussed observational clinical trials like registries and natural histories. Here we are focusing on clinical trials.

Clinical trials are interventional studies which are often designed to determine whether an intervention works. This is often a medication (or things like gene therapy). It can also be for a surgical device or technique. It may also be a new measurement technique. In research, the patient is often referred to as the subject so we will use that language from now on in our discussion

The "gold standard" type a trial is called a placebo controlled clinical trial. In this type of trial, the design is that the subject will either 1) receive the intervention (i.e. medication, intervention, etc.) or 2) a sham (i.e. a sugar pill or pretend intervention) and an outcome is measured. This way whether the intervention impacted the subject or whether it is just them thinking they got intervention (instead getting the sham treatment also known as placebo) helped the subject can be determined. It is well known that in some people, the sham or placebo can result in the measured outcome. It is amazing how powerful our brains can be. The whole idea of this type of study is to decrease bias and make sure something really works. As you can see in the placebo controlled study, the advantage is you may receive the intervention, the disadvantage is you may not. However, it does prove that an intervention works or not (and the FDA who approved interventions really likes these kind of studies).



There is a variation in this type of study in which a known beneficial intervention is used instead of the sham and compared to that being tested intervention. In organic acidemias, there are only rare occasions in which this design method would be able to be used instead of a placebo controlled mostly because there are few known beneficial interventions.

Usually placebo-controlled or comparison of two interventions/therapies needs lots and lots of subjects to reach a statistical difference—the fancy math needed to show something works or not. As you can imagine this is hard in rare diseases, because, well they are rare—like organic acidemias. So sometimes, a subject can be their own control and so they receive or do not receive the intervention for some time and then for the next part of the study receive the opposite of the first part. Few subjects are needed and so more common in rare disease and this is an advantage.

The disadvantage is it takes more time to do these studies as the subject since there are two parts.

Less useful, but sometimes the only option are intervention only studies. Sometimes having a sham section is unethical since the process of doing the sham procedure is too dangerous or the disorder is so lethal that if the intervention works it is lifesaving. Sometimes interventional only studies will use natural history data as their control group (sort of like a placebo group but without a group getting placebo). For this type of interventional clinical trial, good natural history studies (and registries) are essential—part of the goal of the OAA natural history registry with NORD is to help provide this data. This is why sometimes a company with an intervention may try to start a natural history—they are looking for their control group.

Now with every research study, risks and benefits are weighed. The goal is for the potential benefit to outweigh the risk of the trial. In trials which are thought to have little benefit to the individual participating then the trial must be very or no minimal risk. Clinical trials by definition introduce some risk—the intervention as well as sometimes the way to figure out it works because laboratory blood and urine collections introduce risk, as does biopsies, as do radiology interventions. It is important to examine the risks for any study you consider. It is also important to think about not just the procedure related risks, but risks like time commitment (okay maybe not a risk, but could be if it is more than your employer allows). Since time is an issue, some studies reimburse for time. Some reimburse for travel and food during the study.

To help with designing the consents and to determine if the risk and benefits are as balanced as possible, researchers have to present their research plans for interventional clinical trials (and any clinical trial for that matter) to their institutional review



board (IRB for short) or ethics board (usually name in Europe). The

IRB or ethics board makes a decision about whether the research can be done with the goal to keep the subject safe. Consents are the legal

document you sign in which you agree to participate and understand the risks and benefits. These are approved by the

IRB/ethics board. Different IRBs and ethic boards may weigh the risks and benefits differently and so often different institutions who are participating in an interventional study will have slightly different consents if their boards are different. We will talk more about consents in a subsequent Research Corner.

So how do you decide whether a study is right for your family? Ask yourself whether you think the benefits outweigh the risks? You are the only one who can ultimately make this decision. To help you, you can talk to your metabolist or primary doctor. Talk to the researchers and ask questions about anything you do not understand. Evaluate the consent and what the design of the study.

Some questions you can use to evaluate a study include the following: Is there a placebo arm? Are you your own control with some placebo/standard of care compared to the intervention? Is it a comparison study looking at intervention compared to standard of care? How much is the time commitment? Will I need to travel and how often? Are the answers to these questions okay with my family? Also ask yourself, if the intervention works, what does this mean to me/my care, my family, to OAA community at large? In addition ask yourself, if the intervention does not work, what does this mean to me/my care, my family, to OAA community at large? What is the risk of dying or worsening and is this known? Am I okay with the risk of worsening, if there is a chance to get better? What chance of getting better am I or my family willing to take?

For some, the information about whether a particular intervention works or not, is enough for them to say, "this is a good thing", and decide to participate. For others, this is not a motivation and their calculations are different. My hope is that you and your family participates in research at the level of your comfort. Only you and your family can balance the risks and benefits. As you know, we NEED you to help us take better care of you or your cares.



OAA

Financial Status

In the fall of each year, after filing the annual 990 report with the IRS, the board of the OAA publishes the organization's financial status. The statement shown here recaps years 2018 and 2017.

Contributions/donations for 2018 were the highest in the history of the OAA, enabling us to sponsor the largest parent/professional conference in our history held in Minneapolis during June 2018. This funding allowed us to cover conference expenses and end the year with a strong cash balance that will be used to support future programs and grants.

On behalf of everyone associated with the OAA, we thank our financial contributors - because without their support we would not be able to deliver the services for parents and professionals that have become the hallmark of our organization since its founding over three decades ago.

	FY2018	FY2017
REVENUE		
Donations/Contributions	\$116,266	\$24,122
EXPENSES		
Grants (NIH/Family)	\$10,000	\$1,000
Family Support	\$2,036	\$2,679
Accounting	\$1,700	\$700
Office Expenses	\$1,390	\$697
Conferences	\$73,337	\$450
Insurance	877	\$877
Newsletter/Publications	\$9,519	\$5,929
Telephone/Internet	\$2,389	\$2,381
Programs	\$5,101	\$2,072
Total Expenses	\$106,349	\$16,785
Fund Change (Revenue-Expenses)	\$9,917	\$7,327
Opening Fund Balance	\$36,401	\$29,074
Fund Change	\$9,917	\$7,327
Ending Fund Balance	\$46,318	\$36,401

Q & A with HemoShear

BRIAN WAMHOFF, PHD, IS CO-FOUNDER AND HEAD OF INNOVATION AT HEMOSHEAR THERAPEUTICS, A BIOTECHNOLOGY COMPANY DEVELOPING DRUGS TO TREAT METABOLIC DISORDERS WITH SIGNIFICANT UNMET PATIENT NEED.



Tell us about HemoShear – What progress have you made in inherited metabolic disorders?

HemoShear was created around a powerful technology that accelerates discovery of novel treatments for complex diseases. To address the urgent need to improve the lives of children born with metabolic disorders, we partnered several years ago with the Children's National Rare Disease Institute (CN-RDI), located in Washington, D.C., in an ambitious effort to create relevant biological models of methylmalonic acidemia (MMA), propionic acidemia (PA) and maple syrup urine disease (MSUD) in our laboratory.

Working with CN-RDI, several patients donated their diseased liver tissue to us after receiving transplantation, in order to help our team study MMA and PA. The patient cells helped us gain a deeper understanding of these diseases than what is possible with traditional animal research. Our technology enabled our team to uncover the biological processes of MMA and PA and assess different ways of potentially treating the root causes of these diseases.

Based upon our discoveries, we are planning to advance a new drug treatment that has the potential to improve the lives of MMA and PA patients. In fact, our hallways are lined with photos of patients – they are the inspiration that motivates our scientists during long days and challenging obstacles to finding a treatment. You and your children are our source of energy and the reason we do what we do.

Have you been able to discover a drug that might treat MMA and PA?

Yes - we are excited to share that we have developed a promising potential oral drug treatment for MMA and PA called HST5040. Our laboratory and animal research has shown that HST5040 may reduce the toxins that cause harm in PA and MMA patients.

As an oral drug, HST5040 would be convenient for patients and families to administer at home as a tablet, in a liquid form or through a gastric feeding tube. We believe that the dosage could also be adjusted over time if required. MMA and PA are complex diseases that manifest in every organ of the body. Because HST5040 is a 'small molecule,' it has the potential to enter tissues and thus be active throughout the entire body. We also believe that patients who have had a liver and/or kidney transplant may also be able to take this drug to further complete their journey toward a healthier life.

What have you learned from families and patients?

While HemoShear scientists have dedicated significant time in the lab to understanding PA and MMA, it has been important to us to combine this knowledge with the day-to-day experience of patients.

We have spent time with the community of families affected by metabolic disorders to better understand what would be truly meaningful improvements in your children's quality of life.

We held a day-long session with parents last year where we learned about the challenges and tribulations associated with diagnosis, evolving regimens for disease management, triggers that lead to metabolic crises, impact on child development, managing family dynamics, and much more.

A talented graphic recorder captured insights at the meeting in several illustrations that we display in our offices as another powerful daily inspiration to us.

We will continue to listen and collaborate with families to ensure that we are doing our best to understand and help meet your medical needs. We look forward to spending additional time with you to learn more about the disease experience.

What do you want families and patients to know?

It is an exciting time for the MMA and PA communities as potential new therapies advance into clinical trials.

In Memoriam



Mateo

MMA

FEBRUARY 23, 2017 –
AUGUST 22, 2019

Mateo André was born on February 23, 2017, in Escuintla - Guatemala, he was born into a family with limited resources. Four days after he was born Mateo was diagnosed with a rare disease called Methylmalonic Acidemia (MMA). Mateo had the most severe mutation - he was MUT 0. This disease currently has no cure, there are only treatments to keep the disease under control in developed countries. In Guatemala nothing is known about these diseases, there are no specialists, there are no treatments. There are no medications, trying to control this disease in a country like Guatemala is a real nightmare.

When he was diagnosed with Methylmalonic Acidemia, Mateo was given a life expectancy of 2 months, but with the help of God and good-hearted people in the USA, Mateo managed to reach the age of 2 and a half years. In his short life, he spent a lot of time hospitalized because of his illness. He suffered a left hemiparesis and lost the mobility of half of his body, with home therapy he was able to recover part of the mobility he had lost, it was truly a little warrior. The disease was damaging his internal tissues and caused him a general delay in development. After much suffering and struggle Mateo unfortunately lost the battle against the disease and died on August 22, 2019. He was a child that gave us much joy. He smiled a lot, he was very affectionate, a beautiful little angel. We strive to give him a quality of life to the best of our ability and we try not to miss anything he needed. Today Mateo is in heaven and has left a void and a pain in our heart, however, we are certain that Mateo is in heaven and is now free to play, run, jump, and that somehow comforts our heart. We love him and miss him very much. Now he is an angel in heaven.



Janelle

MMA MUT 0

FEBRUARY 18, 1977 –
SEPTEMBER 6, 2019



In Memoriam



“Beautiful flowers only bloom for a while, and our beautiful Lily was no different. Strong, delicate, vibrant, and energetic; she blossomed into our lives and left seeds of strength and love in our hearts!”

~ Michael and Erin



At St. Elizabeth’s Hospital, she appeared to be improving every day. She would keep down some food from her bottle and the rest through a feeding tube. She greeted her mom and dad with beautiful blue eyes and smiles on many visits even though she was going through multiple tests in order to reach a diagnosis.

After ten days, test results came back showing high amounts of hydroxyglutaric acid in her body, and she was transported to Children’s Hospital of Milwaukee. Even after receiving her terminal diagnosis, Lily fought through many medical procedures to give us beautiful memories and time spent together in the hospital.

Lily is survived by her mother Erin; her father Michael; her grandparents Misty and Craig and Ed and Mary; her godmother Kim; her godfather Matthew and aunt Adrianna; and her Aunt Meghan.

The family would like to thank Fiss & Bills-Poklasny Funeral Home, St. Raphael Church, and the caregivers of Oak Hill Cemetery for their very kind support and care during this very difficult time. A memorial fund will be established in lieu of flowers to the Organic Acidemia Association to provide support in research and management for all inheritable genetic metabolic disorders including 2 Hydroxyglutaric Aciduria types D and L combined.



Lily

2-HYDROXYGLUTARIC ACIDURIA TYPES D AND L COMBINED

JULY 13, 2019 -
NOVEMBER 3, 2019

Liliana Marie was born in Neenah, WI on July 13, 2019 and died on November 3, 2019 in Wauwatosa, WI at Children’s Hospital of Wisconsin due to complications from the rare metabolic disorder 2 Hydroxyglutaric Aciduria types D and L combined.

Liliana came home and filled her parent’s house with joy. Unfortunately, she had some feeding issues that led to her be re-hospitalized. After seeing many doctors, a neonatologist also found out that she had other symptoms that are difficult to diagnose in an infant (such as seizures, hypotonia, and different responses to stimuli). She was sent from Mercy Hospital to St. Elizabeth Hospital where she resided for ten days.

Clark

ISOVALERIC ACIDEMIA

AGE 5



It was Mother's Day 2014 and we'd just found out that I was pregnant. It was a bit of a shock, as we had only recently started trying for a baby after returning from our honeymoon in Australia! But we were very excited, and even though I tried not to get too far ahead of myself - it was still very early days after all - I couldn't resist buying our baby's first set of Babygro's, with little Superman logos emblazoned on them. This turned out to be very fitting, as a few months later we found out we were having a little boy that we would eventually go on to name Clark... our little superman.

Two weeks before my due date, my waters broke unexpectedly so I was admitted to hospital and induced. Unfortunately that didn't work, and so after 50 long hours of labour, Clark was born by emergency caesarean to two very tired and relieved parents! Two days later we were allowed to bring our little boy home, and were ready to start finding our "new normal"... we had no idea the journey we were about to embark upon.

For three days at home, we struggled to get Clark to feed - he seemed to only drink a tiny amount and then go to sleep. It got harder and harder to wake him for feeds,

and he seemed a bit cold despite lots of skin to skin contact. We had been seen by breastfeeding support workers who assured us we were doing well, so we put Clark's issues down to the fact he was a little jaundiced and we were completely new to all this.

When Clark was five days old, the midwife came out to do the newborn bloodspot screening and check him over. I remember the next bit like it was yesterday... she weighed Clark, typed some numbers into her calculator, and then picked up the phone without saying a word. Snippets of the phone call floated through my head... "five days old... lost 14% of birth weight... parents done all the right things... yes, to admit him please...". It was at this moment that we realized something a little more serious was going on. We were given an hour to get our bags packed with everything we'd need for a hospital stay, and get ourselves to the children's unit in our local hospital - luckily we only lived a five minute walk away so we made it with time to spare. Clark's observations were taken immediately. The nurse thought there was something wrong with the

thermometer as it wasn't going high enough, but on the third attempt it was realized that Clark really was that cold... his temperature was 33.9°C (93°F).

The next few hours were a blur as the doctors and nurses started addressing Clark's problems, one by one. First up was a "hot-cot", which turned out to be just that - a small bed for Clark to lie on with a 'grill' above him, warming him up. The first impression was that Clark may have meningitis and septicaemia, so they added in urine tests, blood tests, an IV drip, and a lumbar puncture. The results back from these tests painted an unclear picture, meaning the Consultant on duty that night had his work cut out for him. He got on the phone to specialists at Great Ormond Street Hospital and stayed on for hours past the end of his shift to try and figure out what was wrong. This night, Saturday 22nd November 2014, remains to this day the single worst and most terrifying day of our lives. The image of Clark lying on the hot-cot attached to numerous wires and sensors, hearing the alarms all start to go off, and stepping back to let the nurses who had rushed in the room to save him, will forever be etched in our memories.

Clark made it through the night, but the next day gave more questions than it answered. He did not have meningitis or



septicaemia, but nobody knew what else it could be. The Consultant on duty the night before was back in, and following chats with the specialists, now had three drugs for Clark being couriered from two hospitals from across the country. It was at this point that the first hints of a diagnosis were thrown around the room... "Organic Acidemia". Of course, we were straight onto Google to provide us with some information but ended up even more confused.

The next day saw more tests - x-rays and brainwave activity scans - before we were told at lunchtime to go home and pack a bigger bag, as we were being transferred to Great Ormond Street Hospital in London. This was a scary thought, GOSH was renowned for being the best in the world for children's care and knowing that we were on our way there was both reassuring and terrifying. That afternoon, Clark was placed carefully in a transportation pod, put on a trolley and wheeled into the back of an ambulance. I went with him while Shane was chauffeured in our car and followed behind for the two hour journey, blue lights all the way.

The ambulance arrived first, and got Clark up to the ward that we would be calling home for the foreseeable future.

After Shane had joined me, it suddenly hit us - we had no food, no transport, no accommodation, nobody we knew... we were truly on our own and fully reliant on the medical staff to make our son better. After Clark was hooked up to his drips and various medications, we sat at his bedside and waited... what for, we didn't know. That night, the lovely nurses found a fold-out bed and put it up in one of the lesser used staff rooms for me to sleep on; Shane spent the night dozing in a chair at Clark's bedside.



The next morning we helplessly watched as Clark was given more medications and antibiotics, cannulas were removed and replaced, x-rays and tests were scheduled. We felt both terrified at the situation, and reassured that Clark was receiving the best care possible. We were at a loss as to what to do with ourselves - we were new parents who, at this point in time, could provide nothing towards the care of our new baby. I did at least manage to get a bed sorted in the mother's unit on this day, which was a weight off our minds - sleeping on a camp bed the night before was less than ideal only one week after major surgery!

The next day saw more blood tests and imaging scans, but the scariest thing was walking with Clark to an operating theatre where he was placed under general anaesthetic to insert a central line for bloods and medication. A fairly simple procedure... but he was so tiny, still well below his birth weight... and we were terrified. We were told to go to the canteen for a drink but ended up just pacing the corridors, waiting for the moment we could see our little boy again. Finally we got the call that Clark was back on the ward so we made our way back and were seen by the consultants shortly afterwards. We now had a diagnosis... Clark had Isovaleric Acidemia (IVA). The doctors explained this diagnosis to us and gave us a booklet, but we were swimming in all this new information. Over the next few days our research gave us a glimpse into the life we were now about to embark upon, filled with medication, food control, hospital appointments and admissions, and constant vigilance. Even then we had no idea about what this really meant. These few days also saw Clark become neutropenic and so he was moved from the four bed ward that he had been on since his arrival, into a private room. Although this was obviously worrying due to the risk to Clark's health, it did at least mean that after 5 days of sleeping in a chair next to Clark's cot, Shane now had his own pull-down bed to sleep on every night.

The next two weeks were a blur of weaning Clark off his IV feeds back on to milk, getting him to gain all the weight he had lost, making sure he had the correct balance of the right medications, and getting him healthy enough that he could be discharged home. Two weeks doesn't sound a lot in retrospect, but at



the time almost every day felt like two steps forward, one step back... progress was being made but it was slow, and new problems arose almost daily. Towards the end we were expecting to be discharged, only to be told last minute that Clark's potassium levels were too high and so he would need to stay in for another few days. To have "freedom" ripped away from us at the eleventh hour was devastating at the time, although we understood that it was in Clark's best interests.

Finally after 3 weeks at GOSH, the day finally came for Clark to be discharged! We were so glad to be able to bring our little boy home in time for Christmas, but those first few weeks were tough. We had various hospital appointments at both our local hospital and back at GOSH to attend, and a strict schedule of medication and milk to give to Clark. At one point we had 11 alarms set throughout the day to ensure we didn't miss anything!

Over the next year, we had to take Clark in to be admitted due to sickness several times but the frequency of these admissions slowly decreased. With each check-up with his consultant, we were permitted to leave a little longer between his feeds... the relief we felt when we were

able to drop Clark's milk feeds to every 4 hours, and then every 6 hours a few months later, is indescribable! Finally at one year old, Clark was well enough to be left for 12 hours at night... and we could finally start trying to get a full nights' sleep.

Clark has started to have a little understanding of his 'special tummy' and what this means for him. We have not had to take him to hospital to be admitted for over a year now, as he understands why he has to eat what we give him, and the implications if he doesn't eat his specified amount of protein every day. Life dealing with Clark's IVA has got a little easier, but is still hard. Occasionally we will be turning in for the night and suddenly remember we need to sort his meds before we can go to bed! We keep a record of what he eats throughout each day, so that we can plan his evening meal to ensure he meets (but doesn't exceed) his protein allowance.

IVA has changed so much of our lives. The 25% risk of having another child with the same condition was a huge factor in our decision to even have another baby, but our youngest son James is just a carrier, like Shane and I. We consider ourselves very lucky as our boys absolutely adore each other, and we know that they will always look after each other.



Clark deals with his situation amazingly and we are so proud of him... he takes his own medication twice a day (4 syringes in total), and never complains that he always has something different to eat than his friends. Clark is now five years old and has recently started school... a day that, when he was a baby, we didn't know if we would ever see. It is truly amazing to see the lovely young man that he is becoming, and watching him play with his friends without a care in the world - just the way it should be for a five year old... until his next mealtime, that is.

DAWN

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Parent Support Group for MMA/PA in China

China Methylmalonic Acidemia & Propionic Acidemia Care Society (CMAPACS) is a nongovernmental non-profit public organization founded by parents with MMA and/or PA kids. CMAPACS originated from an internet-based chatting group in 2012 and is set up formally in 2019. The number of members by now is around 500. CMAPACS aims to offer help to families with MMA and/or PA kids on the following aspects: guidance on finding proper hospital and doctor, guidance on daily care, platform of exchanging experiences, populating knowledge of MMA and/or PA, transferring advances of new medicines or curing methods, and applying medical insurance policies from the government.

There are some problems for MMA/PA families at present.

1. About medicines: The oral liquid of levocarnitine produced in China uses trace alcohol as stabilizer, which is not suitable for children, and some children are not able to use because of alcohol allergy. The price of levocarnitine imported from regular channels is too high for ordinary families to afford. There is no production of bicitrate in China. The potassium citrate and sodium citrate are not suitable for our children's long-term use. We are now finding our way of purchasing them.
2. About specialty food: Formula powder produced here is made of amino acid powder. The cost of material is low but the price of product is high due to low production capacity and inventory, while the foreign manufacturers do not have selling permission here. We ask our friends abroad to buy some and ship to us.
3. About curing techniques: There are only a few doctors who know MMA and PA in China. Children come to see a doctor after a long journey, but the level of doctor's diagnosis and treatment is slightly behind the international level. In particular, China's medical system has not achieved multi-disciplinary diagnosis and treatment. Children need to see different doctors in different hospitals and departments to solve complications, such as hydrocephalus, epilepsy, rehabilitation treatment, nutrition, etc.

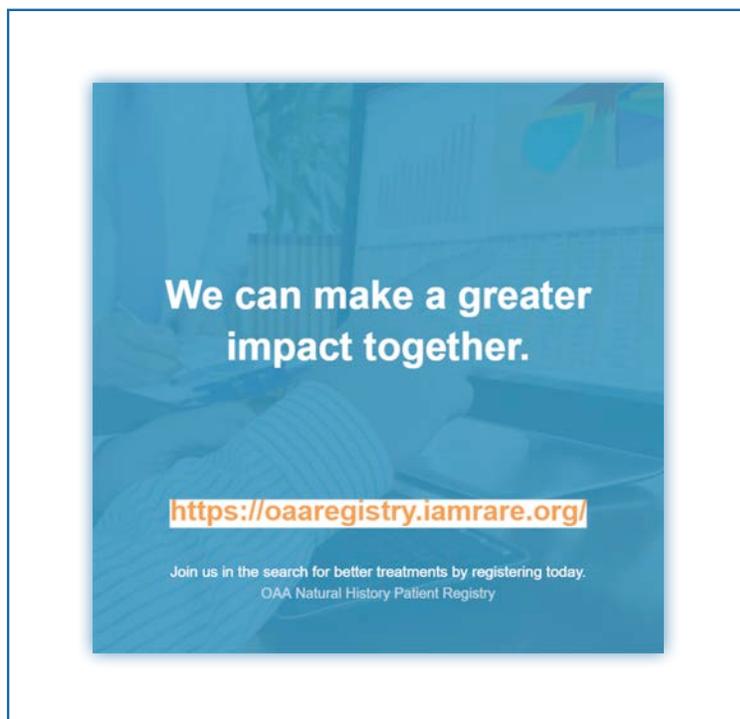
4. About the treatment cost: Rare diseases have not been included in the scope of medical insurance in most areas here. Most families buy drugs and special food at their own expense, resulting in poverty due to illness.

We are now actively engaged in public fund-raising, and are trying to contact different kinds of foundations. Now some foundations have expressed their intention to make directional donation for CMAPACS on special formula powder. We are now working on import approval of specific brand of formula such as Abbott and Nutricia.

The above are the current problems facing us, which is the existing intention of our organization. Things are becoming better compared with situation in the year of 2012 and we are still on the way.

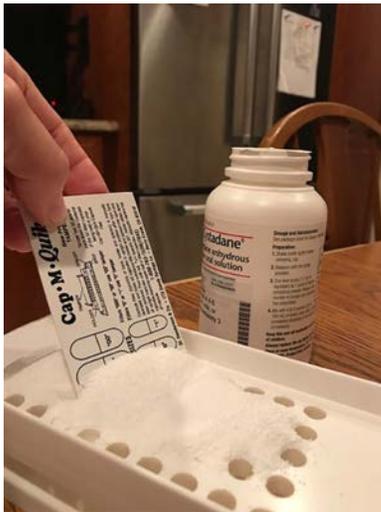
Yours

Zhaohui





Medication Management Made Simple



Hello OAA families. My name is Josephine and my 25 year old son Michael who has CbIC. Since birth Michael has been taking Cystadane (betaine anhydrous) oral powder. I would mix it in juice but he would have a difficult time drinking the entire amount due to bitter taste. I found capsule filler on Amazon that allows us to fill empty gel capsules. It's a great do-it-yourself gadget that has helped us with daily medication management and reduced the stress of taking Cystadane. Some of you may have already seen or may already have capsule filler. If you don't and your child does well with swallowing pills, then I highly recommend you try this. Michael takes 5 scoops of Cystadane 3x per day. This is the equivalent of 26 pills daily. I KNOW, this sounds like a lot, and it is, but we break it up throughout the day. We use double "00" gelatin capsules. He takes 8 in the morning, 6 at lunch, 6 at 4:00pm and 6 in the evening. The Cap-M-Quik allows me to make 50 pills at a time and I usually make enough in one sitting to last the week. We recently went to NIH to visit Mike's medical team. They thought this was worthy of sharing with other OAA families. Mike's homocysteine levels have never looked better and the team felt that maybe part of the reason was the way he is taking the Cystadane. Taking it throughout the day may be keeping it in his bloodstream longer or more consistently. Just a thought, but it made sense to all of us.

Thanks for listening to our little success story!!



Kathy Stagni represents OAA in October at the NORD IAMRARE™ Registry Leaders Community Meeting in Washington DC. This is an annual meeting of NORD Patient Registry Leaders.

Renal Findings in Propionic Acidemia

NOT AS RARE AS PREVIOUSLY SUSPECTED

OLEG A. SHCHELOCHKOV, MD, AND CHARLES VENDITTI, MD, PHD

Propionic acidemia (PA) is a serious metabolic disease which can impact many organs. For example, it has been known for some time, that propionic acidemia can cause poor heart function (cardiomyopathy) and inflammation of pancreas (pancreatitis). But what about other organs? Because PA is relatively rare, its low frequency makes it difficult to spot an uncommon complication or measure how often a complication happens. We are conducting a natural history study of PA at NIH (<https://clinicaltrials.gov/ct2/show/NCT02890342>). With the help of PA community, we were able to gain new insights into how PA can affect kidneys, and recently published a paper summarizing our findings (<https://www.ncbi.nlm.nih.gov/pubmed/31249402>). Below we share some important questions raised during the study:

Question: What prompted the study of kidney function in propionic acidemia?

Answer: It has been known for many decades that methylmalonic acidemia, a disease in many ways similar to propionic acidemia, can lead to poor kidney function. A loss of kidney function in methylmalonic acidemia (MMA) can significantly impact the quality of life and may require special treatments. In recent years, there have been isolated reports of patients with propionic acidemia who also developed kidney disease later in life. Our European colleagues had noticed that some older PA patients in their studies also had lower kidney function. Although kidney problems in PA were not as severe as in an isolated MMA, the frequency of this complication and the age of onset was not known. It prompted us to examine renal findings in patients, who were seen at NIH as part of the PA natural history study.

Question: What type of kidney problems did we find in PA patients?

Answer: We discovered that when we used the most common way to estimate renal function using blood creatinine, 50% of adult PA patients had some degree of the chronic kidney disease. We also found that a blood chemical called “cystatin C”, can be helpful to spot a renal function decline sooner. Importantly,



patients who had chronic kidney disease had a higher chance of having cardiomyopathy. We don't know yet, how exactly cardiomyopathy and chronic kidney disease are connected to each other. We are conducting additional studies to look into this association.

Question: What would doctors do if they discover chronic kidney disease in a PA patient?

Answer: Patients with chronic kidney disease will benefit from establishing care with a renal doctor (a nephrologist). Nephrologists will order and review blood and urine labs, which help them come up with a better care plan. Interval renal ultrasounds can be helpful to follow the size and appearance of kidneys. Some patients may need to have their diet adjusted to control for how much water, calcium, phosphorus, vitamin D and other food ingredients they take each day. Doses of some medications will need to be adjusted in more advanced kidney disease. For example, doses of some anti-epileptic drugs may need to be adjusted if the kidney disease becomes severe.

Question: Can chronic kidney disease of PA be prevented?

Answer: At this point, we don't know how to stop the chronic kidney disease of PA. But we believe that early diagnosis of chronic kidney disease, good control of blood pressure, avoidance of drugs toxic to kidneys, and prevention of chronic metabolic acidosis, may help slow down the progression of kidney disease.

We wanted to thank all families who participated in the study and we are looking forward to meeting new families at NIH. We are grateful for patients' generous gift of time and efforts to make our protocol a reality. Every patient contributes in an important way. As we carefully study each patient, we gain new knowledge that we can share with patients, families, healthcare providers, and researchers. Please feel free to contact the team with questions or comments. You can email Dr Oleg at oleg.shchelochkov@nih.gov or contact our research nurse Susan Ferry, RN at susan.ferry@nih.gov.



Organic Acidemia Association

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Golden Valley, MN 55427

oanews.org

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Suggested membership donation is \$25 (US) and \$35 (international). Extra funds are welcome and can be designated for research, OAA operating expenses, or to help others attend conferences.

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Organic Acidemia Association

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

Association" in the blank line on your pledge card.

Donations can also be made at OAA's website through the "PayPal" and the "Network for Good" option.

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- This newsletter does not provide medical advice. You should notify your health care provider before making treatment changes.



IS ON FACEBOOK - donations can be sent through our "Cause" Page, connection with other parents can be found through our private "OAA Group" and private "Fan" Page.



OAA Google Group

OAA's main mission is to empower families with knowledge about organic acidemias. If you would like to connect with other families who share the same or similar diagnoses, please join our private OAA Group. Visit the OANews.org web site to sign up.

