The Inherited Metabolic Disorders News

Winter 2015 Volume 12 Issue 1

In this Issue

From the Editor

Hello Everyone!

I hope everyone is keeping warm and enjoying our Canadian winter weather!

Plans are well underway for the 11th annual Metabolic Family Day (Friday, May 8, 2015) and Low Protein Cooking Demonstration (Saturday, May 9, 2015). The brochure for the events will be mailed out shortly. We are really encouraging electronic communication, so please send your email address to **janice.little@lhsc.on.ca** to receive communications by email.

Thank you!

Janice Little

From Dr Chitra Prasad

Dear Friends,

Greetings!

Hope you are staying warm through this winter. My trip to India this December reminded me how lucky we are to have central heating in Canada. It was very cold in New Delhi and nearby regions. However I did get to see the Andaman and Nicobar Islands (union territories of India). These are close to the Bay of Bengal. Weather was nice and sunny and the water was beautiful. I also ventured into Scuba diving (my first time!). Please see some pictures of these beautiful islands.

The metabolic team would like to invite you all for the 11th metabolic family workshop on the 8th May and low protein food demonstration on the 9th May. More details are available in the newsletter. Please inform Janice or Kara about your attendance at the metabolic family workshop. Story by Luke's parents (Lindsay and Mark) is extremely inspiring. The diagnosis of a urea cycle disorder (argininosuccinic acid lyase deficiency), management and then Luke receiving a liver transplant from his uncle is incredible. The metabolic & transplant care teams at London Health Sciences Centre, Windsor Hospital, Hospital for Sick

From Dr Chitra Prasad - continued

Children and Lindsay & Mark all have been involved in Luke's care. I wish Luke and his family the very best as they go forward on their journey.

With best wishes to every one.

Your friend
Chitra Prasad

"There are only two ways to live your life. One is as though nothing is a miracle. The other is as though everything is a miracle."
-Albert Einstein

Personal Stories

Lucas Lee Gerard arrived 10 days late into the world on December 24, 2012 weighing 8 lbs 4 oz. I am convinced he knew what was to come and had decided to stay comfy and warm a little while longer. He was born by all appearances, healthy and happy and was able to head home just 24 hours later, on Christmas night, to see big brother Joshua.

On the morning of December 27, 2012, Luke began to show signs of not wanting to eat and began vomiting. We took Luke to his scheduled maternal newborn check up that afternoon at Windsor Regional Hospital (WHR), where we expressed our concerns for his symptoms. We were sent home and told to return after 4-6 hours if he did not begin to eat. At 6:30 that evening we returned to WRH and Luke was eventually admitted, first to the pediatric floor of the hospital, and then transferred to the NICU where Luke's vital signs raced through the roof. He began having seizures and became unresponsive as he fell into a coma. We were terrified as news of his X-ray, ultrasound, MRI and spinal tap all came back negative. We were told we had the sickest baby in the NICU and yet we had no answers as to why or what could be done to help him.

In the meantime, Luke's uncle contacted us to remind us that his daughter, Luke's first cousin, has a rare metabolic condition and to ask to have his ammonia level checked. I just remember not even being able to pronounce the word in the text, and just showing the doctor and nurses the phone and telling them that this condition existed within our family. Could this be affecting Luke? The answer given back to us was a resounding "NO".

Personal Stories - continued

Twenty-four hours later, after the doctor consulted with doctors at London Health Sciences Centre(LHSC), Luke had a blood draw taken to check his ammonia. It came back at over 950. Luke was rushed Code 4 via ambulance to Victoria Hospital in London as we drove shortly behind him. On our way to London we researched ammonia in the body, normal levels and what high levels meant. We read a normal ammonia level ranged from 15-55 and that hyperammonemia, or high blood ammonia levels, are toxic to the brain, can cause neurological damage and can even be fatal. We had no idea what to think at this point. We were so scared for our new baby. Once Luke arrived in London, he underwent two rounds of hemodialysis to clean the toxic ammonia from his blood as quickly as possible and he was also given a cocktail of medications. He responded well, not only to treatment but to the caring foot massages given by the dialysis technicians taking care of Luke. (All of the monitors would start beeping as soon as his foot massage stopped!) His ammonia level came down over the next 16 hours. It was during this time that my husband and I met Dr. Chitra Prasad. She gave us the news that Luke has a genetically inherited, recessive metabolic condition of the Urea Cycle called Argininosuccinate Lyase Deficiency (ASA), that among other attributes, involves being deficient in an enzyme that is located throughout the body, but specifically the liver, where its job is to break down protein into urea and excreted through urine. Because of the deficiency in this enzyme, Luke's body creates a byproduct called ammonia. Dr. Prasad explained that Luke has a great chance of having neurological damage due to the extreme hyperammonemia and that we would be keeping a close eye on his future development. Luke was transferred out of the Pediatric Critical Care Unit and to the sixth floor pediatric care 4 days later. Luke had a nasogastric tube (N/G tube) to give him a special recipe of medicated formulas that at times involved mixing 4 different formulas plus breast milk which gave Luke the precise amount of protein he could handle. It was imperative for Luke to have exact amounts of his recipe (that changed very regularly) and at exact times to avoid fasting. He also had a Broviac catheter placed when he was 1 week old that gave easy access for the very frequent blood draws required to monitor ammonia levels, liver enzymes and other blood tests. Luke was discharged from hospital after 25 nights and arrived safely at home on January 21, 2013.

Since Luke's initial admission, he has had multiple hospital admissions to WRH due to high ammonia levels despite a strictly monitored diet, medications and weekly or usually more frequent blood ammonia levels. Our life was consumed with watching for symptoms such as lethargy, vomiting and over all being unwell. Not really an easy thing to do with a newborn.

Personal Stories - continued

Luke had a gastric tube surgically placed into his stomach at 4 months of age. He suffered from a septic and terrifying blood infection in his Broviac line, was rushed Code 4 via ambulance yet again and spent 15 days in LHSC to have the line removed, given IV antibiotics and a Port-a-Catheter surgically inserted in its place when he was only 9 months old.

It cannot be predicted when or why Luke will suffer from hyperammonemia or at what point neurological damage may occur. It was for this reason that Luke was referred to Sick Kids Hospital in Toronto where he was assessed for liver transplant. Liver transplant is not a typical treatment for ASA, but is becoming more widely considered for severely affected patients in order to avoid a hyperammonemic crisis, in turn avoiding the possibility of fatality or neurologic damage. By replacing Luke's liver, the new organ would have a fully functioning enzyme to hopefully enable him to have a regular diet, avoid liver damaging medications and optimally a better quality of life. At the advice of the Toronto Liver Transplant and Metabolic teams and the London Metabolic team, we made the difficult decision to place Luke on the liver transplant list.

We learned that a liver can be donated by a live donor seeing as the liver is an organ that regenerates. We as Luke's parents were the first to see if we would qualify for donation, but were devastatingly told that we were not matches. We then reached out to family and friends to ask if anyone would be willing to donate. Luke's Uncle Pat stepped forward and after a 3 month long assessment process, he was approved as a match for Luke.

Tuesday, April 8th, 2014, Luke and Pat Gerard underwent surgery for transplant. Both did well through their 11 and 8 hour surgeries respectively. Not only did Luke make Sick Kids history by being the first infant to come out of liver transplant surgery extubated, but he came out of surgery not requiring any of the medications needed to keep his ammonia level normal. The road to recovery has had its challenges for both Luke and Pat, although all in all they have each healed exceedingly well. Of the 3 months we were expecting to be in Toronto for Luke's surgery and recovery, we spent less than one months' time there. We are now home and adjusting to an unfamiliar life, one that is not ruled by ASA. At this time there are not any restrictions on Luke's protein intake. He does not require any of the multiple formulas that we had countless recipes for and Luke is no longer taking any of the metabolic medications that were life sustaining prior to transplant. Although these changes are beyond welcomed, life post-transplant is not without its challenges. We have new specialists and new symptoms to watch for. We have become family to a different set of people who have children and family members who are transplant

Personal Stories - continued

recipients, usually for very different reasons. New medications are part of daily life and there are a different set of rules and worries to be thoughtful of. Liver transplant is not a cure for ASA as we are aware that the enzyme is present in other areas of the body as well as the liver. That is really all we understand about it. There are other characteristics of the disorder to watch for such as brittle hair, hypertension, ADHD and learning disabilities and perhaps more that are not yet identified as the effect of the deficiency of this enzyme are not yet fully understood. At this time Luke is not showing major signs of cognitive or neurological damage and is meeting milestones as he should be. He attends the John McGivney Children's Rehabilitation Centre for physiotherapy, occupational therapy and speech pathology to ensure he is developing accordingly. A challenge for Luke at this time is his unwillingness to eat orally. He is fed primarily through his G-Tube, but is working diligently to change this behavior. Luke is also struggling with speech and is not using many words to communicate, but he is working hard at overcoming this obstacle as well. We have recently been made aware of other patients with ASA describing difficulty in forming thoughts and words and we wonder if this is a characteristic of the disorder, or if past episodes of hyperammonia are effecting speech development or it is just the fact that he is a child that has been through a lot and is wanting to control his development in the only way he knows how. Luke's journey during his 2 years of life has been difficult and challenging. He has shown such courage, bravery and resilience throughout it all. He has an infectious smile, and as his parents we have to wonder how he can be so happy considering e verything he has had to go through. Perhaps a day will come that he will tell us. Until then we will live life through his eyes, seeing everything for the first time and taking constant notes on what he has to teach us.

Featured This Issue

Argininosuccinic Acid Lyase deficiency (Urea Cycle Disorder)

Argininosuccinate Lyase (ASL) is a cytosolic enzyme which catalyzes the fourth reaction in the urea cycle and the first degradative step, i.e. the breakdown of argininosuccinic acid to arginine and fumarate. Deficiency of ASL results in an accumulation of argininosuccinic acid in tissues, and excretion of argininosuccinic acid in urine leading to the condition argininosuccinic aciduria, ASA. ASA is an autosomal recessive disorder and is the second most common urea cycle disorder. In addition to the accumulation of argininosuccinic acid, ASL deficiency results in decreased synthesis of arginine. There are two main presentations (severe neonatal form and a late onset form). The clinical presentation of the severe neonatal onset form is indistinguishable from that of other urea cycle disorders and is characterized by hyperammonemia (increased ammonia) within the first few days after birth. Tachypnea (rapid breathing) leading to a central respiratory alkalosis, hypothermia, vomiting, seizures and lethargy are commonly observed clinical features. In contrast, the manifestations of the late onset form presentation range from episodic hyperammonemia triggered by acute infection, to cognitive impairment, behavioral abnormalities, learning disabilities in patients without any documented episodes of hyperammonemia. Unique features of ASA are hepatomegaly (enlarged liver), elevations of liver enzymes to severe liver fibrosis. The treatment is for rapid control of hyperammonemia during metabolic decompensations and interval therapy to prevent the primary manifestations and long-term complications. Arginine is frequently supplemented. Liver transplantation can help with the biochemical abnormalities however it does not correct the arginine deficiency or the elevation of argininosuccinic acid in other tissues that are thought to account for the long-term complications of ASA. Long term follow up is essential for these children.

Newborn screening is available for ASA however index of suspicion should be high and an ammonia level should be promptly ordered when any newborn infant presents with lethargy or coma.

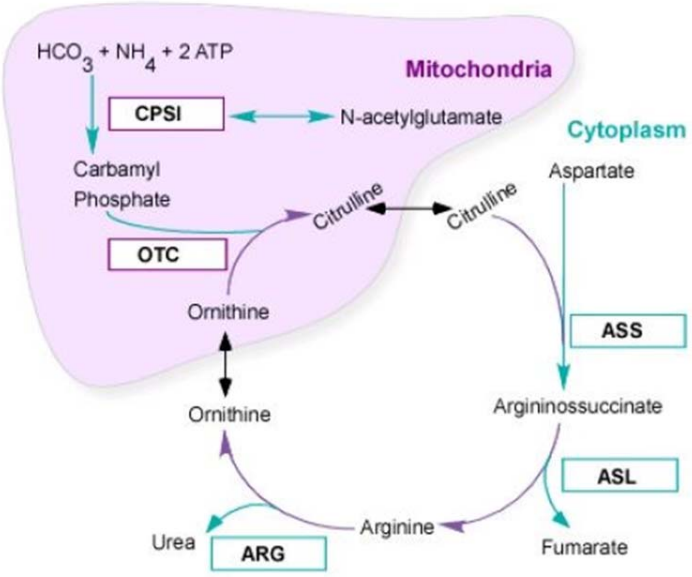


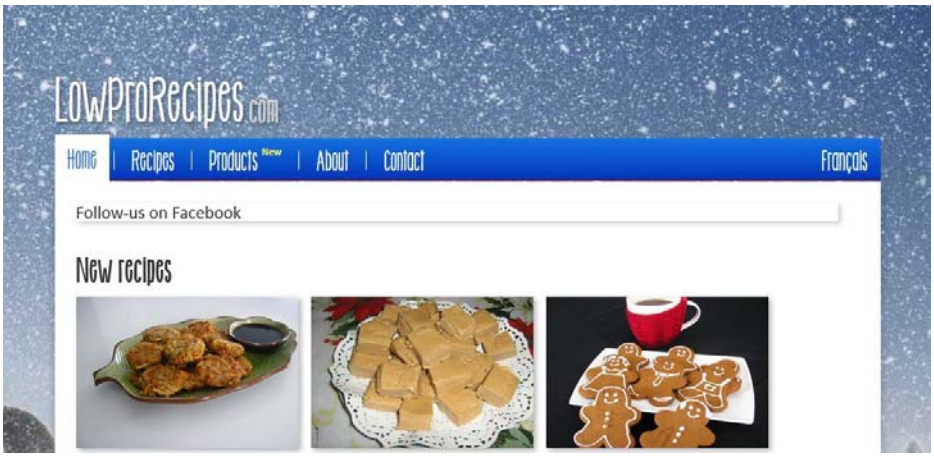
Figure: The Urea Cycle." Used with permission from: Lanpher BC, Gropman A, Chapman KA, Lichter-Konecki U, Urea Cycle Disorders Consortium, Summar ML (2011) Urea Cycle Disorders Overview. GeneReviews

Reference:
www.ncbi.nlm.nih.gov/pmc/articles/PMC3073162

Suzanne's Corner

Please check out the following website by Genevieve Lafrance, Dietitian-nutritionist from Quebec: **www.lowprorecipes.com**

Genevieve has created this amazing website for families who follow low protein diets. It provides easy to make and delicious recipes.



Other news:

Periflex Jr, unflavoured is being discontinued and replaced with Periflex Jr PLUS Plain. This newer version for PKU patients has DHA and fibre. All families who currently use Periflex Jr, unflavoured, are aware of this change. If by chance, I have forgotten a family, please call me to discuss the transition to Periflex Jr PLUS Plain.

Polycose powder has been discontinued. Limited supplies are availaible in Toronto and Montreal. The replacement at this time is SolCarb which is covered; however, your dietitian must update your ordering form. If you are using Polycose powder, please contact your dietitian: Sarah Denomme (MCADD only) or Suzanne Ratko.
A new Inherited Metabolic Diseases (IMD) Program listing was released on December 9th. The following additions were added to the list:

Cambrooke All Purpose Baking Mix (2 lbs)
Cambrooke MixQuick Multi Purpose Batter (2 lbs)
MMA/PA Cooler 15 Red
Periflex LQ Berry (PKU)
Periflex LQ Orange (PKU)
PKU Air 15 Gold
PKU Air 15 Green
PKU Air 20 Green

Sarah Denomme
519 685 8500, ext 52486

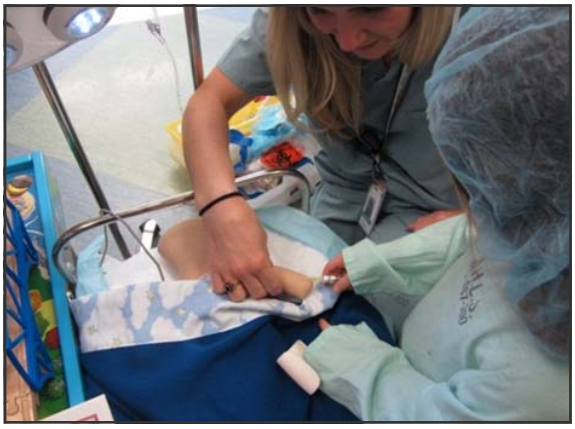
Suzanne Ratko
519 685 8500, ext 52469

Resources

Child Life - Empowering Children and Families

Children today confront a wide variety of stressful and potentially traumatic events that can overwhelm their natural ability to cope and heal. Experiences related to health care and hospitalization can lead to feelings of fear, confusion, loss of control, and isolation that can inhibit their natural development and have negative effects on their physical and emotional health.

Child life specialists are trained professionals who help children cope with the stress and uncertainty of illness, injury, disability, and hospitalization.



WHAT IS A CHILD LIFE SPECIALIST?

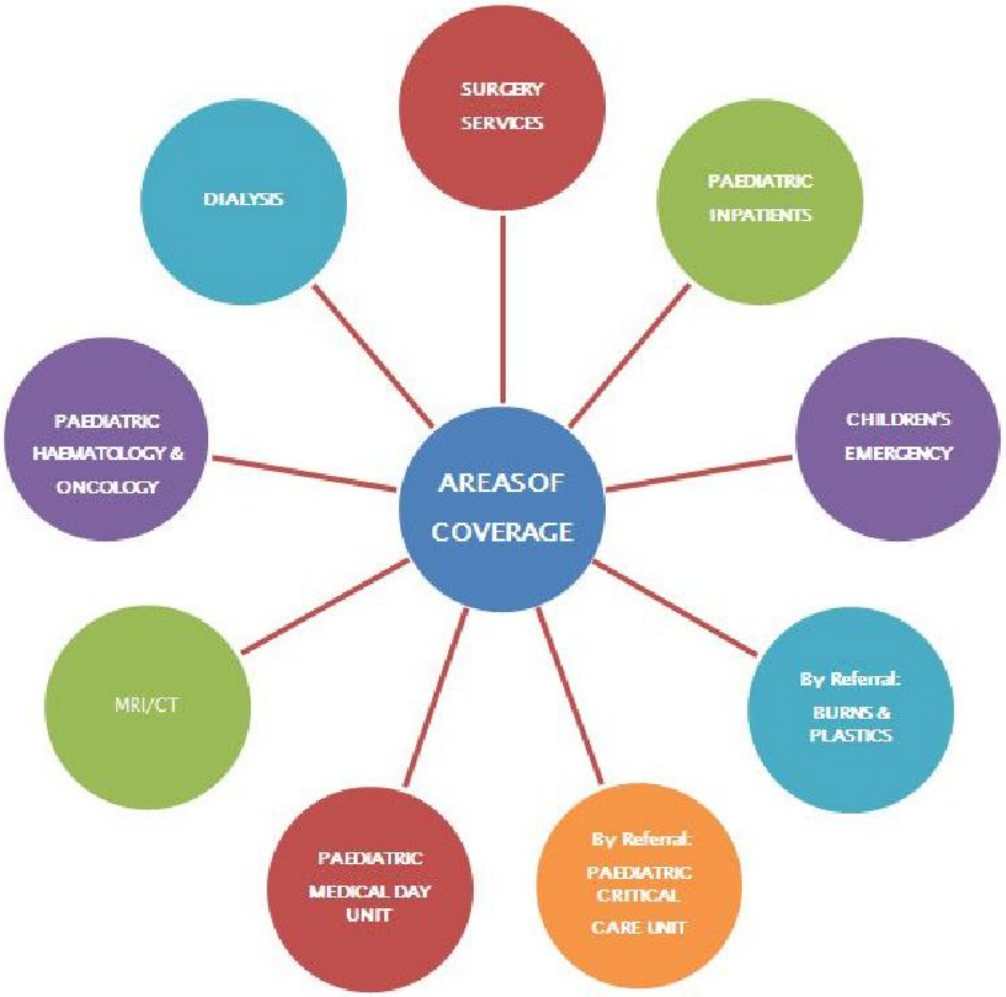
Child life specialists are child development experts who work to ensure that life remains as normal as possible for children in health care settings and other challenging environments. They promote effective coping through play, self-expression activities, and age-appropriate medical preparation and education. As advocates of family-centered care, child life specialists work in partnership with doctors, nurses, social workers and others to meet the unique emotional, developmental and cultural needs of each child and family.

Resources- continued

SERVICES PROVIDED BY CHILD LIFE SPECIALISTS

Child life specialists focus on the psychosocial and developmental needs of children, collaborating with families and other health care providers to:

- Prepare children for medical procedures or treatment using language that children understand
- Introduce coping strategies to help reduce anxiety and enhance cooperation with the health care team
- Provide support and distraction during medical procedures
- Offer opportunities for play and expressive activities, to encourage normal development and a sense of FUN in spite of challenging circumstances
- Promote family-centered care by providing information, advocacy and support to families of pediatric patients
- Specialty services include Bravery Beads, Upopolis (an on-line social networking site for pediatric patients) and SMILE (a new multi-sensory environment on B6)



For more information please contact Child Life Services:

Erika Clements
BA, CLSt Dipl, CCLS
519-685-8500, Ext. 50298, Pager 17362
erika.clements@lhsc.on.ca

Brandy Straub
BA, CLSt Dipl, CCLS
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brandy.straub@lhsc.on.ca

What's New

Genetics Education Day

The Medical Genetics Program at LHSC hosted our first "Genetics Education Day" for health care providers on October 22, 2014, marking 35 years of service. As a comprehensive team, we provide clinical genetic services to patients and families for various indications including prenatal, cancer, cardiac, metabolic and general pediatric and adult genetics.

Farewell & Welcome Back!

Farewell to Nicholas Watkins (Nick), who has done a fantastic job covering the metabolic genetic counsellor position while Melanie Napier was off on maternity leave. You will be missed!

Welcome back to Melanie in March! We are all looking forward to having you back with us.

What's New - continued

Presentations/Publications

Strauss KA, Jinks RN, Puffenberger EG, Venkatesh S, Singh K, Cheng I, Mikita N, Thilagavathi J, Lee J, Sarafianos S, Benkert A, Koehler A, Zhu A, Trovillion V, McGlincy M, Morlet T, Deardorff M, Innes AM, Prasad C, Chudley AE, Lee IN, Suzuki CK.CODAS Syndrome Is Associated with Mutations of LONP1, Encoding Mitochondrial AAA(+) Lon Protease. Am J Hum Genet. 2015 Jan 8;96(1):121-35.

Ferrand A, Siu VM, Rupar CA, Napier MP, Al-Dirbashi OY, Chakraborty P, Prasad C. Biochemical and Hematologic Manifestations of Gastric Intrinsic Factor (GIF) Deficiency: A Treatable Cause of B12 Deficiency in the Old Order Mennonite Population of Southwestern Ontario. JIMD Rep. 2014 Oct 12.

Prasad C, Rupar CA, Campbell C, Napier M, Ramsay D, Tay KY, Sharan S, Prasad AN. Can J Neurol Sci. Case of multiple sulfatase deficiency and ocular albinism: a diagnostic odyssey. 2014 Sep;41 (5):626-31.

Prasad C, Rupar CA and Prasad AN. Presentation on Twinkle gene mutations causing cerebro-hepato -renal syndrome at the All India Institute of Medical Sciences New Delhi India December 2014

Prasad C. Presentation on Newborn screening at Maulana Azad Medical College New Delhi India December 2014.

"In the Clinic"

Shane (Fabry patient), Dr. Prasad, Megan (Medical Student), Nick (Genetic Counsellor)

Children's Hospital
London Health Sciences Centre

Metabolic Family Workshop

Friday, May 8, 2015

Best Western Lamplighter

591 Wellington Road London, ON

Low Protein Cooking Demonstration

Saturday, May 9, 2015

Real Canadian Superstore

825 Oxford Street E London, ON

For further information, contact Janice Little at 519-685-8453

janice.little@lhsc.on.ca

Metabolic Family Workshop
Friday, May 8, 2015

Number Attending: _____

Names: _____

Contact Name: _____

Phone Number: _____

Email: _____

Morning Workshop Attending: (indicate names)

Diet _____

Other Metabolic Disorders _____

Lysosomal _____

Afternoon Workshop Attending: (indicate names)

Youth (8-13) _____

Adolescents (14-20) _____

Adults (with metabolic disorder) _____

Parents _____

Low Protein Cooking Demonstration
Saturday, May 9, 2015

Number Attending: _____ Names: _____

Please return above information to:

Janice Little **janice.little@lhsc.on.ca** **Tel : 519-685-8453**
LHSC Victoria Hospital **Fax: 519.685.8214**
800 Commissioners Rd E London, ON N6A 5W9

Children's Hospital
London Health Sciences Centre

"Our Kids"

Carver
Age 5 years
Methylmalonic Aciduria

Justin
Age 8 years
MPS I

Karson
Age 4 years
PKU

Save the Date 2016!

Metabolic Family Workshop
Friday, May 13th

Low Protein Cooking Demonstration
Saturday, May 14th

Things to Remember

- Life is what's coming… not what was
- Life's precious moments don't have value unless they are shared
- Life is a journey… not a destination. Enjoy the trip!
- Success is getting up one more time
- He or she who laughs… lasts

Going Paperless !!!

In an effort to streamline newsletter production and help the environment, we are going to email future newsletters to as many people as possible. Please help us by sending an email to **janice.little@lhsc.on.ca** using the title "Newsletter" indicating that you would like to receive the newsletter by email.

Thank you!

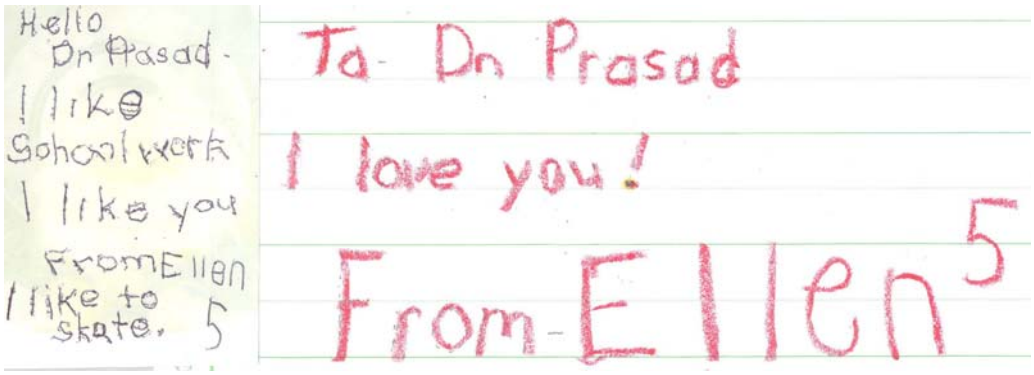
How to Make a Donation

Donated funds are used for future Metabolic Family Workshop Days as well as further teaching and education. If you wish to make a donation, do so on the **The Children's Health Foundation website** www.childhealth.ca

Ways to Give/ Under Giving Options: donate now/ Select: Make a Donation or Join Caring Heart Monthly Giving /Follow the prompts and it will give an online form with a comment box that you can type in and instruct the funds go to the *Inherited Metabolic Disorders program.*

If you would like to donate by phone with your credit card, please call 519.432.8564 or toll-free at 1.888.834-2496, Monday to Friday, 9 am to 5 pm.

Your donation is tax deductible, and an income tax receipt will be mailed to you. ***Thank you!***



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Parent Support Contact: Jennifer Culp

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Email: jennc2011@hotmail.ca