# The Inherited Metabolic Disorders News

Winter **2018** **Volume 15 Issue 1**

Children's Hospital
London Health Sciences Centre

## In this Issue




## From Dr Chitra Prasad

Dear Friends,

Greetings!

I am very pleased to let you know that Sheila Tingley (current metabolic administrative assistant) and Reem Mewafi (who also covered for Rana, metabolic administrative assistant) have together helped with this current newsletter. Janice Little (our resource associate) has been guiding them.

Newsletters give us a chance to communicate, to share stories and successes with everyone. Our current newsletter brings you the story of Justin and his remarkable family. I have known Justin for many years. Justin has Hurler syndrome Mucopolysaccharidosis I or MPS I). This diagnosis is extremely challenging. I still remember the day when I shared the diagnosis and the courage that Chantal and Pierre (parents) showed. They were first time parents. Since then Chantal has ensured that I receive regular updates about Justin's health care. He received cord transplant, a relatively new therapy for Hurler syndrome. Justin is an amazing boy. Some of you might remember his dancing video a couple of years ago at one of our metabolic family workshops. Justin does not allow any of his various medical challenges to slow him down. The family is also very fortunate to have Chantal's dad, Justin's grandpa who is always there for Justin. I saw how much Justin loved his grandpa, how he would readily settle into his arms. Extended family also plays a big role when we are faced with such enormous challenges. The Massicottes (especially Chantal) have become a driving force for Justin's care. With this being a multisystemic condition, there are numerous tests and appointments. Chantal is a wonderful advocate for Justin's care. She is also a great team player.

Our next metabolic family workshop will be in May of 2019. We will keep you posted about the details.

Suzanne Ratko (dietitian) was nominated for the President's Award at London Health Sciences Centre. Congratulations Suzanne! The field of inborn errors of metabolism remains exciting and challenging with all the recent improvements in diagnosis and newer therapies. I would urge all of you to remain involved with new updates about your respective condition.

With best wishes
Your Friend,
Chitra Prasad

***From caring comes courage (Lao Tzu)***

## From the Editors…

Reem and I are honoured to be a part of such an important and inspiring venture. Thank you to Dr. Prasad and Janice Little for your patience and helpful guidance as we continue to learn and refine our skills to keep this wonderful communication available to everyone!

SHEILA TINGLEY - I have been an employee at LHSC for approximately 10 years and have worked in a variety of departments. Genetics is a new area for me and I am really enjoying the learning experience. Outside of work my life is dedicated to my family and volunteering to help those in need in our area with many different community groups. I am active in my local Optimist Club, helping to "Bring out the best in kids". I love to laugh and enjoy cooking and needlework.

REEM MEWAFI - I first came to be involved with genetics in 2014 when I spent several weeks as a co-op student in the Medical Office Administration program at Westervelt. Shortly after graduating I was fortunate to be hired as a registration clerk in Womens Ambulatory Care. Recently I had the pleasure of returning to Genetics and joining the metabolic team when Rana, Dr. Prasad's Secretary, began her maternity leave. It has been such a great learning experience, dabbling in different areas of general genetics, prenatal, and metabolic. It really helps that I am surrounded by passionate, determined caregivers who really do give their all to their patients.

Thank you to many of you who have shared your emails so that we don't have to send printed copies of newsletters. Please send us your email address if you haven't already done so.

Please continue to send your contributions, ideas and stories for the newsletter, as well as topic ideas for the Metabolic Family Workshop to **sheila.tingley@lhsc.on.ca or reem.mewafi@lhsc.on.ca**

## Our Story

Our lives changed forever when Justin was born November 1, 2006. We had no idea what the future would hold for our little family.

My husband and I had questions about the best nutrition for our growing boy and we decided to consult with a Pediatrician. Upon initial examination, the Pediatrician recognized certain traits related to a type of "*Mucopolysaccharidosis*" and decided we should have some testing done to confirm his intuition. We were shocked by the possibility and determined to have a proper diagnosis. We were referred to London Health Sciences Centre for genetic testing.

After what felt like the longest day of our lives from multiple tests being administered to our son, Dr. Chitra Prasad confirmed the Hurler's Syndrome MPS1 diagnosis on December 17, 2007, and our lives completely changed forever. Along with all the fun and normal activities a toddler would engage in, Justin also started weekly ERT (Enzyme Replacement Therapy) on March 31, 2008 and the process began for a cord blood / bone marrow transplant. We received the news on March 7, 2008 that SickKids Hospital had found a perfect match (unrelated cord blood 6/6) for our son. We arrived at Sick Kids Hospital Ward 8B in Toronto on April 13, 2008. Justin received his unrelated cord blood transplant on April 24, 2008. He did extremely well during transplant from both a physical and emotional point of view, (our main goal with no exception was to make sure he continued to eat well through chemotherapy, and laughed every single day). When the chemotherapy protocol pre-transplant was complete, the new cord cells engraphed and his counts were on the rise, we knew we were on the right path.

On May 31, 2008, Justin achieved a Chimerism (number of cord cells in his body) of 92%. He continued to receive weekly ERT during and after transplant. His last ERT was October 31, 2008 (total of 31 weeks). Following the transplant, Justin and mom were essentially isolated to the house and hospitals (Sick Kids initially following transplant and then to the Children's Hospital in London) for at least a year until his immune system was built up again, his blood "counts" normal and immunizations up-to-date.

He started school in September 2010 with an Individual Educational Plan (IEP) and a full time Educational Assistant with him. He is fully bilingual in French and English. He is followed at school by a Physiotherapist, an Occupational Therapist and a Social Worker.

On June 5, 2012, Dr. Ali (Ophthalmologist SickKids Hospital in Toronto) performed a partial Corneal Transplant of his left eye. It was so amazing to "see" our son's excitement with his "new" sight. A few months later, on October 20th, Dr. Ali transplanted his right eye cornea. The transplant was a huge success! He wears prescription glasses, reads, writes and is a wiz at creating and editing his own videos.

On November 29th, 2016, Justin had 8- plates inserted in the growth bone of both knees to straighten his legs. Dr. Carey performed the surgery. The 8-plates will be removed once his legs are straight (approximately 12 to 18 months). The 8-plates did not stop Justin from doing what he loves which is swimming, riding his scooter and now his skateboard.

Since birth, Justin had tubes in his ears (now removed) and had his adenoids removed. He completed many sleep studies to determine the cause of sleep disturbances which concluded that anxiety affected his sleep. He has mild carpel tunnel but that does not stop him from building and creating amazing domino tricks. He has minor leakage from his mitral valve and mild dilation of the left ventricle. He has kyphosis of the spine and his hips are not formed properly because of the deposits of muccopolysaccharides. He has mild hearing loss but does not wear hearing aids. He was recently diagnoses with ADHD and mild anxiety disorder.

It's been 10 years of ups and downs. So many appointments, so many doctors, so many trips to London and Toronto… It's all worth it when we see him smile, laugh and play with his friends. Friends and family ask us "How do you do it?" "You just do!" I tell them. You find strength you didn't know you had! You are an advocate for your child! One day at a time, one clinic appointment at a time, one surgery at a time. We try to stay positive and embrace every second with our son.

Just to "put things in perspective" from an outsider point of view… Our family is somewhat normal. Other than appointments that we manage in our busy schedule, I work part time, my husband works full time and Justin goes to school full time. When Justin is not at school he enjoys creating videos of his dominos and posting them on YouTube. He loves watching his favorite "YouTubers" on his tablet, playing videos games, and ridding around our neighborhood on his scooter, attempting "tricks". This past October, Justin was granted his "Wish to fish in Hawaii" from the Make-A-Wish Foundation in London. What an amazing trip we had! Make-A-Wish Southwestern Ontario Chapter organized the most unbelievable trip which included snorkelling, a submarine tour and 4 hours of fishing aboard a Private Charter. We spent 7 days in Paradise. Everyday Justin would ask us "Am I dreaming? Are we really here?"

We know with a diagnosis of MPS1 comes new dreams and new challenges in our lives. We are ready for the future…


This is a picture of Justin and his family on a submarine (that's why its blue) - a part of his Wish trip. Doesn't look like he is having fun, does it? :-)

Justin before transplant - Christmas 2007

Justin's 3rd grade school picture -2014


Justin's 6th grade school picture - 2017


Justin with a goat fish - Wish Granted October 2017

## Featured This Issue

**Mucopolysaccharidosis I (MPSI/Hurler Syndrome)**
*Compiled by Dr. Chitra Prasad*

Mucopolysaccharidosis type I (MPS I) is a condition that affects many parts of the body. Children with MPS I often have no signs or symptoms of the condition at birth, although some may have an umbilical hernia or lower abdomen (inguinal hernia).

Children with severe MPS I generally begin to show other signs and symptoms of the disorder within the first year of life, may have a large head, a buildup of fluid in the brain (hydrocephalus), heart valve abnormalities, distinctive-looking facial features that are described as "coarse," an enlarged liver and spleen (hepatosplenomegaly), and a large tongue (macroglossia). Vocal cords can also enlarge, resulting in a deep, hoarse voice. The airway may become narrow in some people with MPS I, causing frequent upper Respiratory infections and short pauses in breathing during sleep (sleep apnea). People with MPS I often develop clouding of the clear covering of the eye (cornea), which can cause significant vision loss. Affected individuals may also have hearing loss and recurrent ear infections.

Some individuals with MPS I have short stature and joint deformities (contractures) that affect mobility. Most people with the severe form of the disorder also have dysostosis multiplex, which refers to multiple skeletal abnormalities seen on x-ray. Carpal tunnel syndrome develops in many children with this disorder and is characterized by numbness, tingling, and weakness in the hand and fingers. Narrowing of the spinal canal (spinal stenosis) in the neck can compress and damage the spinal cord. Without treatment (such as cord cell/bone marrow transplant along with enzyme replacement therapy) individuals with severe MPS I can experience a decline in intellectual function and a more rapid disease progression.

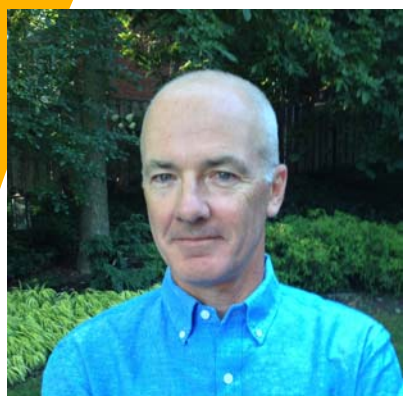
Mutations in the *IDUA* gene cause MPS I. The *IDUA* gene provides instructions for producing an enzyme that is involved in the breakdown of large sugar molecules called glycosaminoglycans (GAGs). GAGs were originally called mucopolysaccharides, which is where this condition gets its name. Mutations in the *IDUA* gene reduce or completely eliminate the function of the IDUA enzyme. The lack of IDUA enzyme activity leads to the accumulation of GAGs within cells, specifically inside the lysosomes. Lysosomes are compartments in the cell that digest and recycle different types of molecules. Conditions that cause molecules to build up inside the lysosomes, including MPS I are called lysosomal storage disorders. The accumulation of GAGs increases the size of the lysosomes, which is why many tissues and organs are enlarged in this disorder. This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Successful HSCT (hematopoietic stem cell transplant) has been performed for children with Hurler syndrome since 1980. The immediate benefits include correction of the enzyme deficiency and clearance of glycosaminoglycans (GAGs). Long-term benefits include the possibility of long-term survival by protecting the heart, lungs, and brain from the effects of progression of the MPS disorder. Other organs and tissues can also show benefits from the HSCT; these include the eyes and ears, liver, spleen, joints, airway, etc. However, it should be noted that many children are still requiring a variety of orthopedic surgeries despite a successful transplant.

**References**

Genetics Home Reference:
*https://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-i#diagnosis*

MPS Society: *https://mpssociety.org/learn/treatments/*



**Orthopedics and Mucopolysaccharidosis I -**
**Dr Tim Carey MD, FRCS (C)**
**Pediatric Orthopedic Surgeon, Associate Professor**

The mucopolysaccharidoses are a group of metabolic disorders that occur as a result of enzyme deficiencies leading to accumulation of sugar molecules called glycosaminoglycan's in many cells of the body. Frequently involved are the cells responsible for bone and cartilage formation and as a result multiple skeletal abnormalities can be associated with these conditions.

Involvement of the musculoskeletal system can be widespread and often typical abnormalities are seen on x-rays, such as widened and shortened bones of the hands and feet, abnormal growth and development of the hip joint leading to hip dysplasia, and abnormal growth of long bones leading to angular deformities such as genu valgum [knock knees].

Involvement of the spine can result in shortened trunk height and spinal deformities such as scoliosis [curvature to the side] or kyphosis [curvature towards the front]. When the cervical spine is involved there can be abnormal growth and development of vertebral bodies leading to potential instability and possible neurologic symptoms.

Orthopedic surgeons are involved as part of the treatment team to evaluate the effects of the condition on the growth and development of the skeleton. Surgery is sometimes necessary for the above-mentioned conditions. If there is excess motion of the cervical spine occasionally a spinal decompression and fusion is required to eliminate potential for pressure on the spinal cord. Such surgery is necessary for thoracolumbar spinal deformities also. Lower extremity alignment is monitored with growth and will sometimes require bracing or surgical procedures to realign the lower extremities.

**Genetic Counsellor Update:**

As many of you are aware, Samantha Colaiacovo (right) was covering the maternity leave Melanie Napier (left) from October 2016 -September 2017. Melanie has recently been seconded from her position of Genetic Counsellor to work within the hospital to ensure that it is ready for its upcoming accreditation with Accreditation Canada. She will be in this position for up to one year. During her absence Samantha will rejoin our team and continue to provide genetic counselling services to patients and families seen in our Metabolic Genetics Clinic.

# Research Publications/Projects

**Dr. Chitra Prasad and Dr. Tony Rupar**

## Research to develop new therapies

There is exciting research focused on developing new therapies for inherited metabolic diseases. The dream of gene therapy is becoming a reality. We are contributing to a Canadian clinical trial of gene therapy for Fabry disease. The participating researchers are from Halifax, Sherbrooke, Toronto, Hamilton, Calgary and London. This first in the world clinical trial of gene therapy for Fabry disease has now treated two patients.

In December, Dr. Rupar and Dr. Prasad led a team that met in Ottawa with Health Canada officials to discuss planning for a gene therapy clinical trial to treat another disease, Metachromatic Leukodystrophy.

## Recent research publications

Jamie Kramer, Farhan S, Nixon K, Everest M, Long S, Segal D, Knip M, Arts, H, Chakrabarty R, Wang J, Robinson J, Mirsattari S, Siu VM, Poulter M, Lee D, Rupar CA and Heglele R. 2017. Identification of a novel synaptic protein, TMTC3, involved in intellectual disability and seizure susceptibility. Human Molecular Genetics 26: 4278-4289.

Kerkhof J, Schenkel LC, Reilly J, McRobbie S, Aref-Eshghi E, Stuart A, Rupar CA, Adams P, Hegele RA, Lin H, Rodenhiser D, Knoll J, Ainsworth PJ, Sadikovic B. 2017. Clinical Validation of Copy Number Variation Detection from Targeted Next Generation Sequencing Panels. The Journal of Molecular Diagnostics 19: 905-920.

Jamie A. Abbott, Ethan Guth, Cindy Kim, Cathy Regan, Victoria M. Siu, C. Anthony Rupar, Borries Demeler, Christopher S. Francklyn, and Susan M. Robey-Bond (2017). The Usher Syndrome Type IIIB Histidyl-tRNA Synthetase Mutation Confers Temperature Sensitivity. Biochemistry 56: 3619-3631.

Ju Huang, Aneal Khan, Bryan C. Au, Dwayne L. Barber, Lucía López-Vásquez, Michel Boutin, Michael Rothe, Jack W. Rip, Mona Abaoui, Murtaza S. Nagree, Shaalee Dworski, Axel Schambach, Armand Keating, Michael West, Patricia Turner, Sandra Sirrs, C. Anthony Rupar, Christiane Auray-Blais, Ronan Foley, Jeffrey A. Medin. (2017). Lentivector Iterations and Pre-Clinical Scale-up/Toxicity Testing: Targeting Patient Mobilized CD34+ Hematopoietic Cells for Correction of Fabry Disease. Molecular Therapy - Methods & Clinical Development 5: 241-258.

Yildirim ZK, Nexo E, Rupar T, Büyükavci M.(2017) Seven Patients With Transcobalamin Deficiency Diagnosed Between 2010 and 2014: A Single-Center Experience. J Pediatric Hematol Oncol. 39: 38-41 Camilla Raya Halgren, Jenna Lakhani, Samantha Colaiacovo and Chitra Prasad. Bulging anterior fontanelle and dense bones in an infant. Submitted to Paediatrics and Child

Health.Christine Le, Asuri N Prasad, Charles A, Rupar, Derek Debicki, Andrea Andrade and Chitra Prasad. Infantile-onset Multisystem Neurologic, Endocrine and Pancreatic Disease (IMNEPD): Case Series and Review of the Literature. Submitted to Canadian Journal of Neurological Sciences.

Eugenio Zapata-Aldana, David Dongkyung Kim, Salma Remtulla, Chitra Prasad, Cam-Tu Nguyen , Craig Campbell. Novel mutation in TBCK gene presenting in two siblings and delineation of the phenotype. Submitted to European Journal of Human Genetics .

Canadian Inherited Metabolic Disease Research Network (CIMDRN). Local site investigators: Dr. Chitra Prasad and Dr. Natalya Karp, Melanie Napier Genetic counsellor, Rana Chakrabarti. Principal Investigators: Beth Potter and Pranesh Chakraborty (CHEO)

S Venkateswaran, S Blaser, M Geraghty, S Hayflick, C Prasad, N Prasad, M Srour, G Yoon. Neurodegeneration with Brain Iron Accumulation Survey. (Will be done through Canadian Paediatric Surveillance Program).

Kathleen O'Connor, Tara Jukes, Sharan Goobie, Jennifer DiRaimo, Greg Moran, Beth Katherine Potter, Pranesh Chakraborty, Charles Anthony Rupar, Srinitya Gannavarapu and Chitra Prasad. Psychosocial Impact on Mothers Receiving Expanded Newborn Screening Results. Accepted for publication in European Journal of Human genetics.

Ravi Datar, Asuri Narayan Prasad, Keng Yeow Tay, Charles Anthony Rupar, Pavlo Ohorodnyk, Michael Miller and Chitra Prasad. Magnetic Resonance Imaging in the Diagnosis of White Matter Signal Abnormalities. (Accepted by Neuroradiology Journal).

Balci TB, Hartley T, Xi Y, Dyment DA, Beaulieu CL, Bernier FP, Dupuis L, Horvath GA, Mendoza-Londono R, Prasad C, Richer J, Yang XR, Armour CM, Bareke E, Fernandez BA, McMillan HJ, Lamont RE, Majewski J, Parboosingh JS, Prasad AN, Rupar CA, Schwartzentruber J, Smith AC, Tétreault M; FORGE Canada Consortium; Care4Rare Canada Consortium, Innes AM, Boycott KM. Debunking Occam's razor: Diagnosing multiple genetic diseases in families by whole-exome sequencing. Clin Genet. 2017 Sep;92(3):281-289.

## Ravi Datar

Ravi has been working on a project entitled "Magnetic Resonance Imaging in the Diagnosis of White Matter Signal Abnormalities" with Dr. Chitra Prasad and Team.

This project has been presented at the Garrod Symposium, May 2017, and has been accepted for publication in the journal "Neuroradiology"

## Suzanne's Corner

### Pumpkin French Toast

Nutritional facts

| Serving | |
|---|---|
| Energy | 162 kcal |
| Protein | 0.6 g |
| PHE | 24 mg |
| TYR | 22 mg |
| LEU | 36 mg |
| VAL | 27 mg |
| ILE | 22 mg |
| MET | 6 mg |
| LYS | 29 mg |

Number of servings: 2
Serving size: 1 french toast

**Ingredients**

- 2 slices Homestyle bread (2110)
- ¼ cup (60 ml) pumpkin puree
- ¼ cup (60 ml) vanilla almond milk
- 1 pinch of pumpkin pie spices (see below)
- 1 tsp (5 ml) butter

**Preparation**

- Preheat a pan.
- Mix the pumpkin, almond milk and the spices together.
- Dip the bread in the mix on both sides.
- Cook until it's brown. Flip and cook on the other side.
- Serve with maple syrup!

*Tip : We could replace the pumpkin puree with applesauce, or banana puree and change the spices.*

**Pumpkin pie spice - (2 tsp)**

- 1 tsp (5 ml) cinnamon
- ¼ tsp(1 ml) nutmeg
- ¼ tsp(1 ml) ginger
- 1/8 tsp (1 pinch) clove
- 1/8 tsp (1 pinch) Allspice

Mix together all the spices. Keep in the pantry.

***Loprorecipies.com - http://www.lowprorecipes.com/recipes/category/breakfasts/pumpkin-french-toast***

Children's Hospital
London Health Sciences Centre

# Metabolic Family Workshop

...a day of fun, family and fellowship!!

Coming in 2019…..details to follow in the next exciting issue of the newsletter

## Low Protein Cooking Demonstration

**SAVE THE DATE - Saturday June 2nd**

Vitaflo will be sponsoring our 14th annual low protein cooking demonstration. Chef Patrick will provide an interactive and fun event on Saturday, June 2nd. Great Canadian Superstore, Oxford at Gammage.

More details to follow

***For more information, contact Suzanne Ratko at (519) 685-8500 ext 52469.***

## Students, Residents & Staff

Dr. Camila Halgren

Dr. Jenna Lakhani

“It was a great learning experience to see the diagnostic challenges in the presentation of Osteopetrosis and management with Bone Marrow Transplant. With a rare disease presenting in our centre, we took the opportunity to write up the case report, along with Samantha Colaiacovo and Dr. Chitra Prasad to create awareness regarding Malignant Infantile Osteopetrosis”.

Dr. Rana Chakrabarti

Originally from London, I graduated from St. George's University with an MD and a Master's in Public Health before joining the department in 2016. Since then I have been involved with many of the various research projects being undertaken here including the **Canadian Inherited Metabolic Diseases Research Network (CIMDRN)**. I hope to continue my education with a residency in Medical Genetics. In my spare time I enjoy watching soccer, gaming, cooking and reading. I am fond of exploring different cuisines in the city and trying new dishes.

I am excited to share with you all the new arrival of my fourth child, baby boy Aboudy. He was born October 2nd, weighed 7lbs 10 oz, healthy baby and the delivery was easy, for once! I am off on maternity leave and can’t wait to return to Genetics!

-Rana Elshourafa
Secretary for Dr. Prasad & Dr. Karp

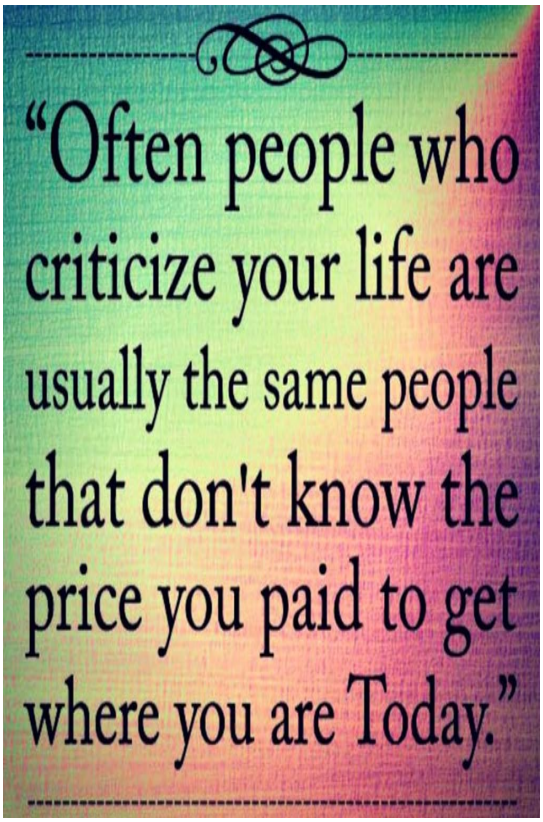
## Our Stars

Karson Gervais is running with his family and enjoying some winter fun!

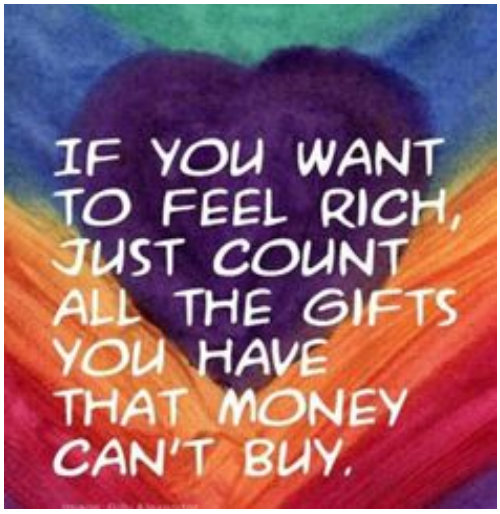
Shaylin MacLeod, working on her gymnastics moves.

*Out of the mud of your fears, struggles, pain and confusion,*
*the lotus flower of your inner heart will spontaneously grow.*

## Inspirations...








## 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, please do so on **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 in the payment area 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!***


Caley Bruhlman, artist and athlete!

## Contact Information

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