The Inherited Metabolic Disorders News

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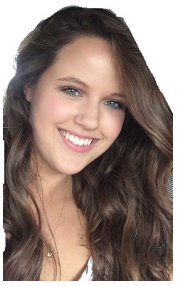
Children's Hospital
London Health Sciences Centre

Winter 2020 Volume 17 Issue 1

In this Issue

From the Editor



Happy New Year everyone! I hope you all had a wonderful holiday. Thank you to everyone who made contributions to this issue of the newsletter. If you would like to be show-cased in the next exciting issue, please send your photos and contributions to meghan.zadorsky@lhsc.on.ca. We love to see what everyone is up to!

Meghan Zadorsky

From Dr Chitra Prasad

Dear Friends,

Greetings.

I am very pleased to bring you another issue of our metabolic newsletter. Jody (Madeline's mom) has written about their journey with lovely Madeline who is now a 21 year old young lady. Many years ago, we had learnt about Madeline and her underlying diagnosis of congenital disorders of glycosylation (CDG syndrome) in our 2005 metabolic newsletter. We had the great honor of hosting Professor Jaak Jaeken who had first described this condition. He met with our families with CDG syndrome from Ontario. As this disorder is still new, we are learning about it all the time. Madeline has taught us a lot about this condition as we have been following her in Neurometabolic and Metabolic clinics for many years. She has a wonderful personality and is very willing to help out in different activities. She has an amazing spirit. Her parents have always been enthusiastic about any advances related to the understanding of this disorder.

Last year I had some of my own personal health challenges. I am extremely grateful to my family, all my patients, my metabolic team (Rana El Shourafa, Suzanne Ratko, Melanie Napier, Dr. Tony Rupar, Dr. Andrea Yu, Dr. Natalya Karp, Sue Mclean), and genetics colleagues, for their support.

In life we need help from our friends and families especially in times of uncertainty and challenges. I hope that metabolic newsletters, Metabolic Family Workshops, and Low Protein Cooking Demonstrations help foster friendships and feelings of a community for everyone.

Meghan Zadorsky, our genetics assistant and editor of the newsletter has summarized life's wisdom on page 11.

We will be having our Metabolic Family Workshop on 14th May 2021. Low Protein Cooking Demonstration will be held this year, 18th July 2020. Please see the details in our newsletter.

I wish you and your family all the best for 2020!

Your Friend,
Chitra Prasad

"Alone, we can do so little; together, we can do so much "—Helen Keller

Personal Stories

Madeline

During the pregnancy of my 2nd child I had a weird feeling that something was wrong. All the tests came out normal and I was told I had a normal pregnancy. Madeline was born on March 28, 1998, 1 day past my due date and a normal healthy girl at 7 lbs. I remember staying up most of the night to look at her, since I was so amazed that my feelings were wrong. After all, she had 10 toes, 10 fingers, high Apgar scores, and looked perfect.

We took Madeline home from the hospital and around the 3rd night she became this colicky, hard to feed baby. I had breast fed my first daughter so I thought I knew what I was doing, but Madeline would never want to feed for more than 3 minutes and would cry and refuse more. Madeline's first checkup showed a very small weight gain so I was referred to the lactation clinic, but Madeline continued to not feed well for months. I tried everything with my diet, always thinking it must be me. I was told she was a colicky baby that was just fussy, which was almost all night long. Surely nothing was wrong, lots of parents have fussy babies. Time passed and at 3 months old, when Madeline still could not hold her head up by herself, I told my family doctor that I thought something was wrong. I remember him telling me that he did not think anything was wrong with Madeline but he decided to send me to a Pediatrician.

We saw a Pediatrician when Madeline was just over 3 months old. The Pediatrician could not find her reflexes, noticed low muscle tone, and ordered some blood tests. When Madeline's PKU counts came back high indicating that something could be wrong, we had more blood work done and a chest x-ray of our little 3 ½ month old baby. We were referred to the Pediatric Neurologist at Children's Hospital in London, and our long road to a diagnosis began.

Our visits to Children's Hospital included many specialists and many tests: EEG, EKG, MRIs, chest x-ray again, and more blood tests. After every test something was ruled out and a new theory developed, then more tests. While we were always happy to hear that it wasn't this or that disorder, we knew that we were still searching for something. When the MRI showed a Dandy Walker Variant in the brain, we were told that Madeline would have walking problems and be off-balance, but did not know more. As the months passed, Madeline was not hitting her milestones: she was still having trouble keeping her head up, she wasn't turning over or crawling, and was still having problems feeding.

Finally, at around 10 months we were sent to Dr. Siu in genetics to try and figure out a diagnosis. After Dr. Siu's examination, she left the room and went to input Madeline's symptoms into a computer database: Dandy Walker variant, failure to thrive, hypotonia, strabismus, developmental delays, large tongue, fatty deposits in abnormal spots, and nipple retraction. It didn't seem like a lot to go on, but out came CDG. Dr. Siu had never heard of CDG, but when she started reading about this disorder it made sense and fit Madeline. We then did another blood test and 6 weeks later had our diagnosis – CDG (Congenital Disorders of Glycosylation). We waited another year to learn the type of 1A, which is now known as PMM2-1A. CDG is a large group of rare inherited diseases affecting glycosylation. Every part of the body requires glycosylation to work normally, which is why people with CDG have many different health problems.

After the diagnosis of CDG, we looked up everything we could about the disorder, and were devastated about this prognosis. Children with CDG had so many complications, with elevated liver enzymes, seizures, feeding tubes, fluid around the heart, endless hospital visits, and an infantile death rate of 25%. This disorder was extremely rare, and Madeline was only the second diagnosed in Canada. In 1999 there were only about 100 cases in the world, and therefore not a lot of information known; we had no idea what Madeline's future would look like. We knew the worst case, and it scared us enough to move our family from Sarnia to London to be closer to the Children's Hospital.

During Madeline's 2nd year we went through very delayed milestones, extreme eating problems, and vomiting constantly every day. We just couldn't get her to eat and keep the food down, but I was determined not to get a feeding tube. Luckily Madeline always seemed to gain just enough weight to ward off the typical feeding tube that most kids with CDG have. These first years were also filled with PT, OT, doctors' appointments, and battles with viruses/infections. Many of the children with CDG spend so much time in the hospitals with viruses, infections, seizures, and stoke like episodes; we felt blessed that Madeline never needed to be hospitalized.

Madeline still had her struggles, and definitely was on her own path with her milestones. She did not eat regular food until after 2, she didn't talk until about 3, and began using a walker around 3 1/2. We continued to monitor the long list of complications that were possible with CDG, and manage her virus/infections without hospital stays. Madeline started daycare around age 3 and the cycle of viruses every 3 weeks began for many years, which was a tradeoff for the social skills she developed. Madeline thrived with her peers and started JK at 4 with everyone else.

Madeline's elementary school years were spent fully integrated in school, and she participated in every activity she could find. Most children with CDG's health stabilizes after the age of 6, so we were happy to be over that hump. She still struggled with viruses and infections that made her very lethargic and her lack of coordination caused many bruises, stitches and even a concussion from all her falls. Her developmental delays seemed to put her further behind her peers as the years went by, but she loved being social and with her peers and sister. Madeline always looks up to her older sister and therefore wanted to do the same things her older sister did, so a lot of her sports were influenced by her sister. We love living in London where Madeline has so many opportunities to participate in many sports and activities.

When I look back on the early years with CDG I don't know how we made it through. Those long nights with a sick little girl where you never knew how sick she could get and just praying that you would avoid that hospital stay that so many of these children experience. We have been told that Madeline has a milder case of CDG, but nobody can figure out why. Today there are about 30 patients with CDG in Canada, and the metabolic disorder has grown to include almost 100 types, with PMM2-1A being about 80% of the cases.

Today Madeline is 21 years old, and one of the most amazing young ladies you will meet. She is bright, funny, and compassionate, and there isn't a day that she doesn't surprise me with her determination and passion for living a normal life. Madeline graduated High School with a full diploma, and currently works at GoodLife Fitness 1 day a week, and Michael's Craft Store for the Christmas season. She is working hard with Hutton House to find employment that is closer to full time, and gives her purpose. Madeline still uses a walker but has learned to walk independently for short distances around the house. Madeline still gets colds that knock her out for 7-10 days, and the risks of stoke like episodes, coagulopathy, deep vein thrombosis, and retinitis pigmentosis are always on our minds.

Madeline's passion is all of her sports; sledge hockey, SARI horseback riding, Track 3 skiing, Special Olympic soccer and golf, wheelchair basketball and curling, and swimming. She is involved with social programs like Best Buddies, and Cliff Gliders. Madeline is fiercely independent and really just wants a regular life like everyone else. I'm proud to say I think she is on her way.

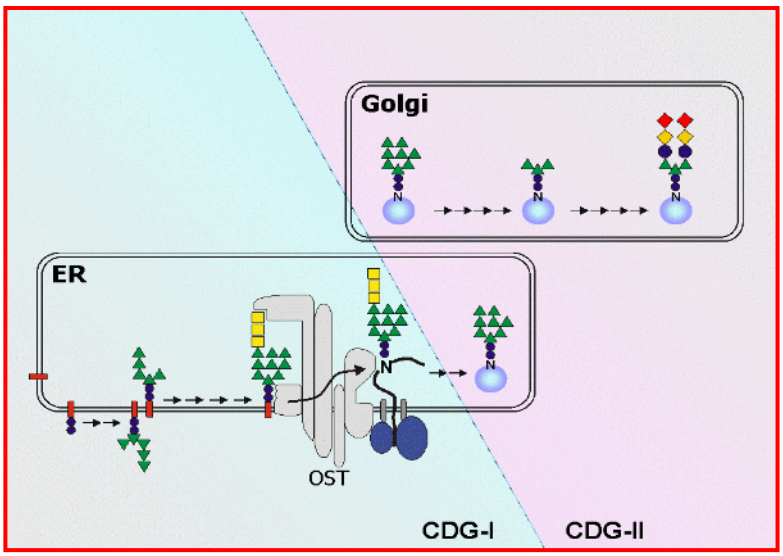
Written by Madeline's mother, Jody

Featured This Issue

Congenital Disorders of Glycosylation (CDG)

Compiled by Dr. Chitra Prasad

Congenital disorders of glycosylation (CDG), also known as carbohydrate deficient glycoprotein syndromes, are multi systemic disorders in which many glycoproteins are deficient or have reduced carbohydrate side chains. Dr. Jaak Jaeken was the first one to describe these disorders. The clinical features include failure to thrive, hypotonia, inverted nipples, unusual fat deposits, mental and psychomotor retardation, stroke-like episodes, protein losing enteropathy, hypoglycemia, and generalized dysmyelinization. Many subtypes of congenital disorders of glycosylation have been described based on the isoelectric focusing patterns of transferrin and on clinical features. Type Ia phosphomannomutase, is the most common deficiency. Sialic acid is the terminal sugar residue of the two carbohydrate side chains of transferrin. Any block in the synthesis of these side chains will result in an undersialylated transferrin molecule. Because it is a major serum protein and is easily detectable, transferrin is utilized as a marker in screening for congenital disorders of glycosylation. Although many congenital disorders of glycosylation are yet to be described, CDG should be suspected in patients with clinical features mentioned above. The inheritance is autosomal recessive for most subtypes of CDG. Unfortunately there is no treatment, except for type 1b where mannose is supplemented. Active research is ongoing in a number of different centers around the world to find a cure for this group of disorders.



Glycosylation Pathway

References:
http://www.ggc.org/Diagnostics/Biochemical/glycosylation.htm
http://www.euroglycanet.org/
http://www.cafamily.org.uk/Direct/c64.html
http://www.euroglycanet.org/home.html

Dr. Jaak Jaeken, first to describe CDG

2005 Throwback

Madeline and her parents (right) had the opportunity to meet Dr. Jaak Jaeken (left) after his presentation on CDG at London Health Sciences Centre.

Publications

Outcomes in pediatric studies of medium-chain acyl-coA dehydrogenase (MCAD) deficiency and phenylketonuria (PKU): a review. Orphanet J Rare Dis. 2020 Jan 14;15(1):12 Pugliese M, Tingley K, Chow A, Pallone N, Smith M, Rahman A, Chakraborty P, Geraghty MT, Irwin J, Tessier L, Nicholls SG, Offringa M, Butcher NJ, Iverson R, Clifford TJ, Stockler S, Hutton B, Paik K, **Tao J**, Skidmore B, Coyle D, Duddy K, Dyack S, Greenberg CR, Ghai SJ, **Karp N**, Korngut L, Kronick J, MacKenzie A, MacKenzie J, Maranda B Mitchell JJ ,Potter M, **Prasad C**, Schulze A, Sparkes R, Taljaard M, Trakadis Y, Walia J, Potter BK; Canadian Inherited Metabolic Diseases Research Network.

Growth hormone deficiency in megalencephaly-capillary malformation syndrome: An association with activating mutations in PIK3CA. Am J Med Genet A. 2020 Jan;182(1):162-168. Davis S, Ware MA, Zeiger J, Deardorff MA, Grand K, Grimberg A, Hsu S, Kelsey M, Majidi S, Matthew RP, **Napier M,** Nokoff N, **Prasad C**, Riggs AC, McKinnon ML, Mirzaa G.

High diagnostic yield of direct Sanger sequencing in the diagnosis of neuronal ceroid lipofuscinoses. JIMD Rep. 2019 Sep 3;50(1):20-30. Jilani A, Matviychuk D, Blaser S, Dyack S, Mathieu J, **Prasad AN, Prasad C** ,Kyriakopoulou L, Mercimek-Andrews S.

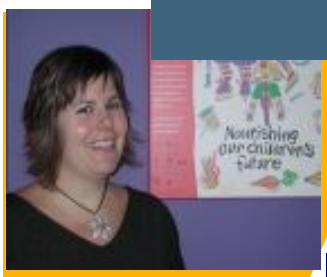
Cohesin complex-associated holoprosencephaly. Brain. 2019 Sep 1;142(9):2631-2643 Kruszka P, Berger SI, Casa V, Dekker MR, Gaesser J, Weiss K, Martinez AF, Murdock DR, Louie RJ, Prijoles EJ, Lichty AW, Brouwer OF, Zonneveld-Huijssoon E, Stephan MJ, Hogue J, Hu P, Tanima-Nagai M, Everson JL, **Prasad C**, Cereda A, Iascone M, Schreiber A, Zurcher V, Corsten-Janssen N, Escobar L, Clegg NJ, Delgado MR, Hajirnis O, Balasubramanian M, Kayserili H, Deardorff M, Poot RA, Wendt KS , Lipinski RJ, Muenke M.

Five-month-old male with chronic diarrhea. Paediatr. Child Health. 2019 Nov 30. pxz155, https://doi.org/10.1093/pch/pxz155. Barootes HC, Ashok D, **Ratko S, Yu, AC.**

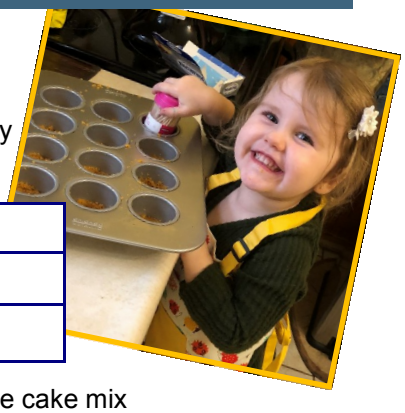
Presentations

Garrod Presentation: May 2019– Toronto

The many faces of Glucose Transporter 1 (GLUT1) deficiency (Poster). **Natalya Karp**, **Asuri N Prasad**, Craig Campbell, **Tony Rupar**, **Sarah Denomme**, **Samantha Colaiacovo**, and **Chitra Prasad**



Suzanne's Corner



Kaitlynn's Celebration Cupcakes

This is a very simple and delicious recipe that Kaitlynn and her family love to make.

Ingredients	Amount
Betty Crocker Super Moist Cherry Chip cake mix	1 box (432 g)
Sprite	1 can (355 mL)

- Instead of adding the water, egg and oil, simply add 1 can of sprite to the cake mix
- Follow the instructions on the box for mixing

How to calculate protein content

1. The protein content on the box is only for the cake mix powder (I checked with General Mills that it does not include the eggs)
2. Each series of cake mix production may have a different protein content, so it is important to look at the box each time you buy it. For example, the box at Walmart (series 103C) had 1/10 packet containing 2 g protein and the one from Sobey's (series 102C) had 1 g protein.

3. Protein counting

Nutrition Facts
Per 1/10 pkg (43 g)

Amount	% DV*
Calories 160	
Fat 1.5 g	2 %
Saturated 1 g + Trans 0 g	4 %
Cholesterol 0 mg	
Sodium 310 mg	13 %
Carbohydrate 35 g	12 %
Fibre 0 g	0 %
Sugars 19 g	
Protein 1 g	

If using the mix from series 102C

	Amount of protein
10 cupcakes	1 g
20 mini cupcakes	0.5 g
1/10 cake (slice)	1 g

Baking

- Use the cooking time on the box as a guideline. It may take a little longer depending on the number of cupcakes made
- To make sure that the cake or cupcakes are done, insert a toothpick in the centre. If it comes out clean, then they are baked

Decorating

- Use low protein options such as Cool Whip (3 tablespoons has 0.1 g protein)
- Decorate with sprinkles

There are so many benefits to including all children in planning and preparing meals:

- great learning opportunities
- interacting with parents, sisters, brothers and grandparents in a fun way
- trying foods which they have prepared

A special diet should not prevent this from happening.

We love seeing that our families know the importance of getting children involved with their food preparation.

Look at all of these tasty creations!

Helen (below), LCHAD deficiency, and sister, Claire (above)

Kaitlynn, PKU

Emmitt, PKU

Karson (right), PKU
Preparing formula

Jonny, OTC deficiency, and brother, Charlie

Save the Date!

16th Annual Low Protein Cooking Demonstration

Real Canadian Superstore
825 Oxford Street East
London, Ontario

Date: Saturday, July 18th, 2020

We are thrilled to have Chef Neil from England come back to lead us in some fun and delicious cooking.

Thank you to Vitaflo for sponsoring our event!

Please contact Suzanne Ratko to secure your spot. Include names of those attending.

519 685 8500, ext 52469

suzanne.ratko@lhsc.on.ca

Metabolic Family Workshop Coming May 14, 2021!

Keep an eye out for details in the upcoming issues of The Inherited Metabolic Disorders News!

Our Stars

Jasper, MPS VI, receiving gene therapy in Italy, and his family

Evelyn, hypophosphatasia, and her parents

Anik, carbonic anhydrase VA deficiency, and his parents

Our Talented Artists

"Every great dream begins with a dreamer. Always remember, you have within you the strength, the patience, and the passion to reach for the stars to change the world."
– Harriet Tubman

Madeline, congenital disorder of glycosylation type 1a

"Creativity is intelligence having fun"
– Albert Einstein

Martin, hypophosphatasia

Evelyn, hypophosphatasia

Abilene, PKU

Inspirations

Tips for Starting the New Year Off Right

With a the New Year having just begun, there is no better time to refresh your life and to try to incorporate some new habits into your daily routine.

1.) **Keep a gratitude journal–** try to write down two or three things you are thankful for each day, even if they're simple things. This practice can help you appreciate all of the wonderful things in your life, no matter how small.

2.) **Try to incorporate more exercise into your daily routine–** try to choose activities that will get you more active and that you will actually enjoy doing. Not everyone can afford to spend hours at the gym every week, so try something more manageable that fits your lifestyle, like going for a walk around your neighbourhood. Exercise is not only good for your body but also helps us cope with anxiety and stress.

3.) **Drink plenty of water–** making a conscious effort to drink more water throughout the day will help keep your mind and body working optimally.

4.) **Tidy up–** take some time to go through your closet and home and donate items you no longer use. Getting rid of clutter helps create a space that feels more welcoming and relaxing and also makes our homes more functional.

5.) **Try new recipes–** it's easy to get in a rut rotating through the same meals each week. Try making a point of introducing a new recipe every week. This will help make meals more exciting and is something the whole family can get involved with.

6.) **Take up a new hobby–** if there's been something you've been meaning to try, just do it! Sometimes we stop ourselves from trying new things because we are worried we won't be good at them. Try pushing these fears aside and allow yourself to explore something new!

7.) **Put time into building up relationships–** it's easy to get caught up in our day-to-day lives and forget to set aside time to catch up with those we care about. Even if it is just meeting up for a tea or coffee for half an hour, setting aside time to reconnect with loved ones will help build the relationship and also leaves us feeling content.

8.) **Try volunteering–** if you find you have some extra time, try volunteering somewhere new. Volunteering is a fulfilling way to give back to your community and you might even develop new skills and relationships.

9.) **Do good for others–** it is important to remember that everyone is dealing with things we may know nothing about. Be kind to others and even go out of your way to do something nice for someone; it might just make their day and yours!

10) **Take personal time–** especially as the craziness of the holidays winds down, take the time you need to re-center yourself. Even just stealing a couple of minutes away for yourself at a time can make a huge difference.

Compiled by Meghan Zadorsky

Natasha Frohlich

Natasha became the Coordinator of The Fertility Clinic and Medical Genetics in October 2019. Natasha's educational background is in nursing, having graduated from the University of Western Ontario with Distinction in 2007. Natasha has worked at LHSC for over 12 years. She began her career as a registered nurse on Acute Medicine at University Hospital. She then progressively took on more leadership roles: first as a charge nurse on Acute Medicine, then as a member of the Accreditation team where she helped the organization to obtain Accreditation with Exemplary Standing. Natasha also graduated from the Emerging Leader Program in 2018.

"Try to be a rainbow in someone else's cloud "

—Maya Angelou

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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 for donations of $20 or more.
Thank you!