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From the Editor

I hope everyone is having a wonderful summer!

Our Metabolic Family Day and Low Protein Cooking Demonstration were once again a huge success. See the section "What's New" for a full report of the events, as well as pictures.

As always, your suggestions and stories are welcome. Please contact me by email or telephone (see page 14 for contact details) if you wish to contribute to the newsletter. I hope everyone has a safe and happy summer!

Janice Little

From Dr Chitra Prasad

Dear Friends,

Greetings!

I really appreciate the wonderful write up about "Marlo" in this newsletter. Debbie (her mom) has shared with us the trials and triumphs of dealing with this rare disorder "Pyruvate dehydrogenase deficiency".

This metabolic family day was very special for me as Dr Mark Korson (from New England Medical Centre Boston) was the chief guest speaker. As some of you know he was instrumental in my choosing a career in metabolic medicine. His talk was inspiring in many ways as he focused on the parents and caregivers and their role in the management of patients. This is so true!



Drs. Prasad and Korson

Hope you and your families will enjoy the newsletter. With sincere thanks to all for their help at the metabolic family day.

Your friend,
Chitra Prasad

"Far away there in the sunshine are my highest aspirations. I may not reach them, but I can look up and see their beauty, believe in them, and try to follow where they lead."

Personal Stories

Marlo's Story

by Debbie (Mom)

My third pregnancy seemed to be very normal right up until my 25th week. My second child, Jaiden, was born at 30 weeks with a rare chromosome abnormality. She struggled for 3 months in the NICU before coming home and has many physical and neurological issues. With this pregnancy my doctor wanted to make sure the baby was doing well so I had an ultrasound in my 25th week. It was at this time we realized that the baby was developing fluid in her brain known as *ventriculomegaly*. I was devastated. I remember barely making it out to the parking lot before I broke down crying. We already had two other children; a healthy 3 year old boy and a 2 year old daughter with severe disabilities. I was not prepared to go through this again. The rest of my pregnancy was very rough. I started having ultrasounds every week. At the 27th week ultrasound it was discovered that the baby now had fluid in her lungs known as *plural effusions*. At this point our doctors were not sure she would even live until delivery. My husband and I had multiple blood tests done to try and determine what the baby may have. I also had an amniocentesis, which ruled out most genetic and chromosome issues. We did find out that she had a rare blood disorder and may need a transfusion at birth.

When I was 28 weeks and 5 days I went into preterm labour. The labour was stopped but I was admitted to the hospital for observation. I spent a total of 3 weeks with two more incidents of preterm labour. The third round of preterm labour they were unable to stop and it was agreed that I would be flown to another hospital to have the baby's lungs drained and her delivery would be imminent. I was only 29 weeks 5 days. Before leaving I had a final ultrasound and the fluid on her lungs was gone and my labour had also subsided. Finally, we received some positive news. I stayed in the hospital on bed rest until I was 32 weeks and then came home on bed rest for the remainder of my pregnancy. I was monitored very closely and was required to come to the hospital every day for non stress test. Because of the baby's possible need for a blood transfusion at birth it was agreed that I would deliver via c-section at 38 weeks.

Of course, this baby had other ideas. While I was at the hospital for my daily non stress test I notice I was having very regular contractions on the monitor. I was not feeling them yet but the nurse was concerned enough to find a doctor. By that time I was starting to

Personal Stories - continued

feel mild contractions. The nurse checked to see if I was dilated and I was already at 4 cm.

Marlo was born by c-section at 3:15 pm on August 15, 2005 at 37 weeks 1 day. She weighed 6 lbs 3 ozs. She was checked by the NICU team and they felt she was doing fine and they let me hold her. Marlo was very sleepy and would not latch on. She didn't seem to have a desire to eat. When she was one hour old her nurse felt she was not breathing appropriately and a Neonatologist came and re-examined her. She also agreed that her breathing was not right and Marlo needed to go to the NICU for observation. I remember that moment vividly. Up until that point I could tell myself that everything was going to be all right but then I knew something was very wrong.

About an hour after Marlo was taken to the NICU I was wheeled in on a stretcher to see her. While I was holding her she stopped breathing for the first time and she had to be bagged. From this point on she struggled with bradycardia, tachypnea, and apnea spells. She would not suck either so she needed to be fed with a nasal gastric feeding tube. When Marlo was 5 days old she had an MRI that showed she had severe Dandy-Walker variant. Her neurologist felt that it was unlikely Marlo would live long enough to come home. It was another hard blow. We arranged to have Marlo baptized at the hospital. All of our family and friends showed up with only a few days notice. It was so nice to see that much support from our family and friends. After her baptism we agreed to a "do not resuscitate" order. We did not want to see her suffer. We loved her too much for that. She had a few bradycardia spells in the hospital but was able to recover on her own. At 15 days old we brought Marlo home. This was a huge milestone, as we never thought that it would happen. She was still having major bradycardia, tachypnea and apnea spells but she recovered each time without intervention. She was so tired and was only awake maybe 1 – 2 hours a day and we were feeding her with a feeding tube still.

When Marlo was about 6 weeks old her respiratory issues started to resolve. She was awake more and more and she started feeding with a bottle. By the time she was 3 months old she was strictly breastfeeding. This was something I thought would never happen. We removed the "do not resuscitate" order. Her first major illness was when she was 5 months old. Jaiden had bacterial pneumonia and was hospitalized. Marlo was breastfeeding so she stayed in the hospital with us. While she was there, Marlo

Personal Stories - continued

contracted RSV. She took it well and we were able to manage her at home. She continued to have respiratory issues through the winter. She dealt with several rounds of bronchiolitis, bronchial spasms and aspiration pneumonias. In May we noticed that Marlo had not gained any weight since her last check in February. This started her down another path with failing to thrive. We struggled to get every calorie into her. I fought her getting a g-tube. Jaiden already had one and I could not handle the idea of having 2 children with feeding tubes. In April 2006 Marlo had a skin biopsy done. Her doctor felt there was a good chance that Marlo had Mitochondrial disease.

The Fall brought more respiratory issues. Her first admission was in December 2006. Marlo was admitted with bronchiolitis and she refused to eat. She needed an NG tube again. I was finally ready to accept that she needed a feeding tube. A surgery date was set for Friday January 12, 2007. She was also going to have a muscle biopsy done in hopes of getting a diagnosis. On Wednesday January 10, 2007 Marlo's doctor called to tell me that there was a diagnosis of Pyruvate Dehydrogenase deficiency. Our world came crashing down. We no longer had a little girl with severe disabilities we now had a little girl who we knew was going to die. Her diagnosis was a death sentence. She of course had the worst form of it since she started showing signs in utero. The average life expectancy for a child with this disease as severe as her is between 3 – 4 years. Marlo started taking a mito cocktail to help reduce symptoms and give her more energy. We changed her diet to a modified ketogenic diet since she was not able to break down the carbohydrates in her food. She struggled with respiratory infections and pneumonias and seemed to be in the hospital more than she was home.

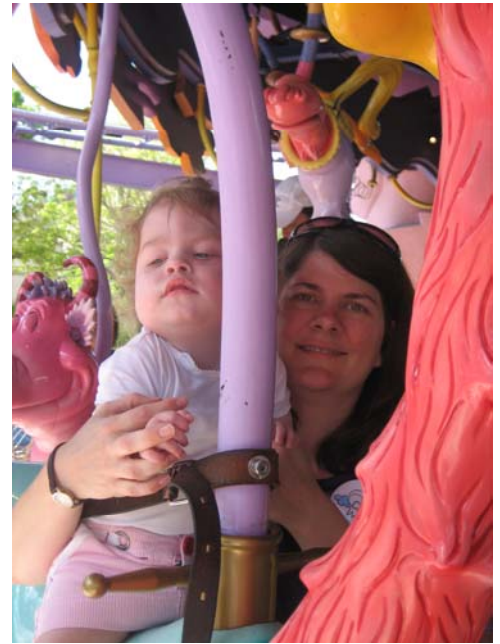
In January 2008 Marlo had spent most of the month in the hospital struggling with pneumonia and respiratory infections. Even after she would clear the infection she would still struggle just to breathe. She was working so hard and her respirations were in the 40's even when she slept. Her doctors felt there was nothing left to do. For the second time we took our beautiful little girl home with a "do not resuscitate" order. A few weeks after she was home her pulmonologist prescribe a high dose of steroids. She responded well to them but as soon as they were stopped she would deteriorate again. She could not stay on the steroids for long term so we tried a few other options. The last thing we tried in the late spring was Alvesco, which is a corticosteroid. It was

Personal Stories - continued

her wonder drug. Since started this drug Marlo has only dealt with two hospitalizations. Although Marlo suffers from neurological and physical disabilities she is stronger every day and enjoys life. We know that her quantity of life is limited but our goal for Marlo is to provide her with what she needs to have the best quality life we can give her.



Marlo



Marlo



Jaiden and Marlo

Featured This Issue

Pyruvate Dehydrogenase Complex Deficiency (PDCD)

By Chitra Prasad MD FRCPC

PDCD is a rare disorder. Pyruvate dehydrogenase (PDH) is an essential and important enzyme in the mitochondrial metabolism. The effects of this deficiency are serious as there is a lack of energy production and build up of lactic acid. PDH catalyzes the oxidation of pyruvate to acetyl CoA (Fig 1). When this step is blocked, then pyruvate is converted to lactate and alanine. Acetyl Co A is one of the two essential substrates needed to produce citrate. Because citrate is the first substrate in the citric acid cycle, the cycle cannot proceed. The citric acid cycle is essential for the metabolism of carbohydrates. Individuals with severe disease have prenatal onset with structural brain abnormalities. Other clinical features include distinctive facial features (in some patients), developmental delay, seizures, growth retardation, ataxia, and occasionally breathing abnormalities. Eye examination may reveal poor visual development. The most common form of PDH deficiency is caused by mutations in the X-linked E1 alpha gene. The females can be severely affected. All other types are due to alterations in recessive genes. Investigations include elevated lactate and pyruvate levels in the blood (although ratio is normal) and high alanine levels on plasma amino acids. For confirmatory diagnosis skin biopsy is required for PDH measurement in the fibroblasts. Cranial MRI is very useful to detect the brain anomalies seen in PDH deficiency particularly ventricular dilation, cerebral atrophy, partial or complete absence of the corpus callosum. Magnetic resonance spectroscopy is another technique used to demonstrate high lactate levels in the brain.

Treatment is mostly supportive with use of anti-seizure medications, cofactors such as thiamin, carnitine, and lipoic acid, (mitochondrial cocktail) and correction of acidosis. Dichloroacetate reduces the inhibitory phosphorylation of PDH and can decrease the lactate levels however prolonged use can cause side effects. Ketogenic diet (with restricted carbohydrate intake) has been used to control lactic acidosis with minimal success. The ketogenic diet bypasses the defect by providing the product of the PDHC reaction directly as acetyl CoA from the metabolism of fat.

References:

Pyruvate Dehydrogenase Complex Deficiency:

Author: Richard E Frye, MD, PhD, Assistant Professor, Departments of Pediatrics and Neurology, University of Texas Health Science Center at Houston

Coauthor(s): Paul J Benke, MD, PhD, Director of Clinical Genetics, Associate Professor, Department of Pediatrics, University of Miami

<http://emedicine.medscape.com/article/948360-media>

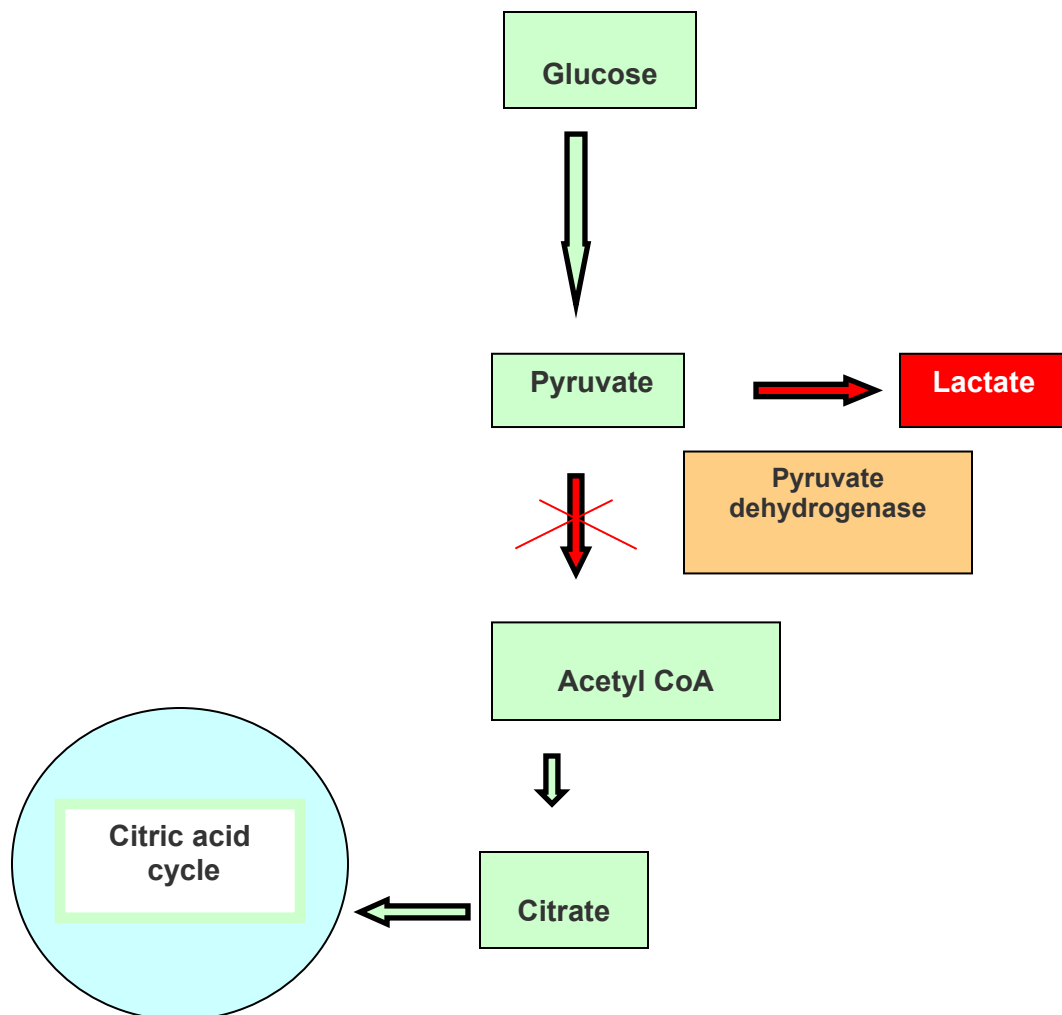
Featured This Issue - continued

Atlas of Metabolic Diseases by William L Nyhan and Pinar T Ozand (Chapman Hall Medical)

Robinson BH. Lactic Acidemia and Mitochondrial Disease.

http://rarediseases.info.nih.gov/GARD/Condition/7513/Pyruvate_dehydrogenase_deficiency.aspx

Fig 1



Announcements

Congratulations to Megan Marcy, Metabolic Dietitian and her husband Ryan, on the birth of their first child, Benjamin who was born July 16, 2009 and weighed 5 lbs15 oz.



Recent Publications

Abstract 1. Presented at Canadian Pediatric Society meeting June 2009

THE EXPANDING SPECTRUM OF MEDIUM CHAIN ACYL-COENZYME A DEHYDROGENASE DEFICIENCY (MCADD) FROM TRAIT TO LETHALITY: MCADD EXPERIENCE USING THE CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM (CPSP) (SEPTEMBER 2005-AUGUST 2008).

By C Prasad, KN Speechley, S Dyack, CA Rupar, P Chakraborty and JB Kronick.

Abstract 2. Poster presentation International congress of metabolic disorders in San Diego August 2009

AICARDI-GOUTIERES syndrome may masquerade as a metabolic disease.

By Faghfoury H, Feigenbaum A, Blaser S, Prasad C, Donner E, Hahn A, Rupar CA, Crow Y.

Abstract 3. Poster presentation for American Society of Human genetics meeting October 2009

Positive Newborn Screening for Carnitine Transporter Deficiency: A Marker for Maternal Genetic/ Metabolic Diseases?

By C. Prasad, J. DiRaimo, P. Chakraborty, S. Goobie and C.A Rupar

Resources

Mitochondrial Disorder Resources:

United Mitochondrial Disease Foundation (UMDF): www.umdf.org

Mito First Handbook from UMDF: www.umdf.org/atf/cf/%7B28038C4C-02EE-4AD0-9DB5-D23E9D9F4D45%7D/MITO%20FIRST.pdf

Metabolic Camp:

The Specialty Food Shop in Toronto, Ontario is hosting a Metabolic Camp October 14-17th, 2010 for ages 7 - 18 years.

Check out future newsletters for more information and Specialty Food Shop's website: <http://www.specialtyfoodshop.ca/SFSWhatsNew/section.asp?s=Metabolic+Information&SID=20300>

Suzanne's Corner



Vegetable Rice Soup



Ingredients

- 1 cup CBF Short Grain Rice or CBF Imitation Rice, cooked
- 1 medium potato peeled and diced into cubes
- 2 green onions, chopped
- 3 carrots halved lengthwise and cut crosswise into 1/2-inch slices
- 2 ribs celery cut into 1/2-inch slices
- 1 15 oz can of crushed tomatoes (with juice), diced
- 2 Tbs cooking oil
- 1 1/2 quarts water
- 2 tsp CBF Chicken-Flavored Consommé and Seasoning
- 1/3 cup fresh parsley, chopped (optional)

Directions

- Prepare Cambrooke's rice according to the instructions.
- In a large saucepan, heat the oil over moderately low heat. Add the onions, carrots and celery and cook, stirring occasionally, until the vegetables start to soften (about ten minutes).
- Stir in the water, consommé, tomatoes, potatoes. Bring to a boil. Reduce the heat and simmer, partially covered, until the vegetables are almost tender (about 20 minutes).
- Stir in the cooked rice. Bring the soup back to a simmer and cook until the vegetables are tender (about five minutes). Stir in the parsley (optional). Note: Optional food not calculated in nutritional profile.

Serving size: 1 276g bowl (Makes 6 servings)

Nutrition Facts	
Serving Size 1 bowl (276g)	
Amount Per Serving	
Calories 100	Calories from Fat 35
% Daily Value*	
Total Fat 3.5g	6%
Saturated Fat 0g	0%
Trans Fat 0g	
Polyunsaturated Fat 1g	
Monounsaturated Fat 2g	
Cholesterol 0mg	0%
Sodium 60mg	3%
Potassium 280mg	8%
Total Carbohydrate 16g	5%
Dietary Fiber 2g	8%
Sugars 1g	
Protein 1g	
Vitamin A 50%	• Vitamin C 15%
Calcium 4%	• Iron 4%
Phosphorus 4%	
*Percent Daily Values are based on a 2,000 calorie diet. Your daily values may be higher or lower depending on your calorie needs:	
	Calories: 2,000 2,500
Total Fat	Less than 85g 80g
Saturated Fat	Less than 20g 25g
Cholesterol	Less than 300mg 300mg
Sodium	Less than 2,400mg 2,400mg
Potassium	3,500mg 3,500mg
Total Carbohydrate	300g 375g
Dietary Fiber	25g 30g
Calories per gram:	
Fat 9 • Carbohydrate 4 • Protein 4	

Per Serving

PHE:	47 mg
LEU:	mg
Pro:	1.3 g
Calories:	100



What's New

6th Metabolic Family Workshop 29th May 2009

Metabolic disorders, or inborn errors of metabolism, are usually the result of a lack of, or dysfunctional enzyme required for cell metabolism. The 6th Metabolic Family Day provided an excellent opportunity to share this information among families and professionals. Attendance has doubled in the last six years to over 153 family and guest participants.



Families were invited to interact with speakers, learn about different metabolic formulas and foods, see what's new with treatment and research, visit displays of metabolic food products and learn about the resources available in their community.

The day began with a welcome from Dr Guido Filler, Chair and Chief of Pediatrics at LHSC. The day included four group sessions: Diet Group (Dr Erica Gold and Dr, Mark Korson discussed diet related independence strategies), Neurological Aspects of muscle tone in Metabolic Disorders (Dr. Craig Campbell and Janet Cormier physiotherapist led the discussions in this group), Lysosomal Storage Disorders (Group leader Kathy Corley) and Teenage group (Group leaders Jill Tosswill - Social Worker and Karen Weishuhn - Registered Dietitian in Toronto).

This year's keynote speaker Dr. Mark Korson, Chief of Metabolism at Tuft Medical Centre Boston spoke about empowering patient families to help them cope with their children's metabolic illnesses. The title of his talk was "P stands for Patient, and Parent and Power". He gave us many examples in which parents and families have formed partnerships with the medical professionals to optimize the care of their child.

What's New - continued

Bruce Wray from Children's Foundation introduced the highlight of this Workshop, which was a special session where the mothers of children (Debbie Lawrence, Samantha Smith, Jennifer Culp and Lindsay Erb) with metabolic disorders shared their coping strategies. These mothers shared feelings of courage and optimism despite their many daily challenges.



Low protein Cooking demonstrations have also become an integral part of Metabolic Family Day, under the leadership of Dietitian Suzanne Ratko. This year's 5th annual Low Protein Cooking Demonstration was held on the 30th of May and was sponsored by Vitaflo. It was held at the Loblaw on Wonderland Road. Malathy Ramanajum from Taste Connections gave a low protein cooking demonstration to the participants and showed them how to prepare innovative recipes.



Grateful acknowledgements are extended to Children's Health Foundation, our sponsors, Genzyme, Ross Metabolics, Cambrooke Foods, Mead Johnson Nutritionals, Applied Nutrition, Vitaflo, Nutricia North America (SHS), PKU Perspectives, BARD and National Food Distribution Centre as well as speakers, members of the planning committee, patients, families and many volunteers. Our

sincerest thanks go to Jennifer Culp who once again organized the room for children's care.

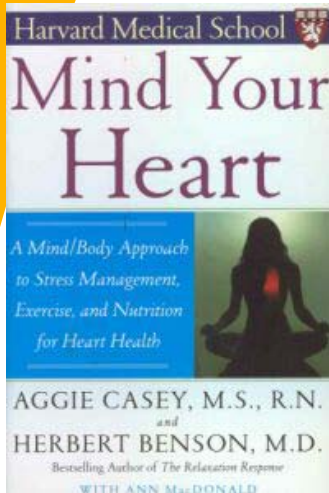
Our metabolic team includes Suzanne Ratko, Kathy Corley, Joanne Psiuk-Rogers, Joanne Weir, Janice Little, Megan Marcy, Dr. Chitra Prasad, Dr. Tony Rupar, Dr. Sharan Goobie, Dr. Narayan Prasad, Jill Tosswill, Jennifer DiRaimo and CPRI Staff.

The Inherited Metabolic Disorders News



2009 Metabolic Family Workshop

Mind Your Heart



Here are a few helpful tips to keep your heart healthy from the book “Mind Your Heart”

- ◆ **Become a less aggressive driver.**
- ◆ **Create helping rituals. They make you feel good. Open the door for someone, pick up litter, etc.**
- ◆ **When feeling stress, ask yourself, “Is this really important? Will it really matter a week, month, or year from now?”**
- ◆ **Resist the urge to judge or criticize.**
- ◆ **Become a better listener.**

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, you may send a cheque to:

The Children's Health Foundation C/O Medical Genetics Program of Southwestern Ontario

Attention: Janice Little

800 Commissioners Road East

London, Ontario, N6A 4G5

Charity # 118852482 RR0001

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

Thank you!



Zane, age 9

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