The Inherited Metabolic Disorders News

Children's Hospital
London Health Sciences Centre

Summer 2010 Volume 7 Issue 2

In this Issue

From the Editor

I hope everyone's summer is going well. The current newsletter issue has all the information about our recently held 7th Metabolic Family Workshop. It was very successful thanks to all of you, our metabolic team, planning committee, sponsors, Children's Health Foundation and others.

We encourage families to send their information and news. Enjoy the latest "Inherited Metabolic Disorders News"!

Janice Little

From Dr Chitra Prasad

Dear Friends,

Hope you're having a wonderful summer. I am delighted to introduce Veronica Kokavec who has joined our team as the new metabolic counsellor. We were very privileged to have Samantha Smith (Sam) (Parent) on our interview panel. I would also like to thank the entire metabolic team who has helped out when we were short staffed.

In this issue you will also read a wonderful family story by Lisa on MELAS- (a mitochondrial disorder). Lisa and family remain very optimistic despite all the challenges. As part of understanding these disorders better, our team is working on a web based learning tool for mitochondrial disorders for patient families and professionals.

In this journey of caring for patients and families, I have always wondered about the "care of the caregivers". When a family is faced with a child/family member with acute or chronic illness, sleep usually is affected for the patient and his/her family. We all know that sleep is a very important determinant for good health. I have requested Dr. Erica Gold (Psychologist) and my husband Dr. Narayan Prasad (Child Neurologist) to share light on some of the common neurological/psychological issues for families. In the current newsletter they have each discussed about "common sleep problems". Hope you will find their column useful.

Thank you Erica and Narayan!

I would also encourage the families to submit questions via Janice Little (our editor) if you would like some other neurological/psychological issues discussed.

Wishing you and your family all the best for the summer!

Your friend
Chitra Prasad

"Courage doesn't always roar. Sometimes courage is the quiet voice at the end of the day saying, "I will try again tomorrow".

Mary Anne Radmacher

Personal Stories

MELAS

Our lives changed forever when on a cold snowy night in December,2008, our oldest daughter, Leanna, fifteen at the time, suffered from what we later learned was a cluster of grand mal seizures. From our local hospital she was sedated, put on a ventilator and transported two hours south to London's Children's Hospital for further tests and care. With CT scans, MRI's, EEG's, X-rays (as a mass was detected in her lung, later we learned it was pneumonia), lumbar puncture and blood tests ordered to help determine what was going on. When Leanna was more alert, the neurologist, Dr. Narayan Prasad, discovered she had no eye muscle movement and droopy eyelids. The only consistency in the blood tests was high lactate levels, yet no sign of bacteria or infection. Why?

Leanna with Kye, the dolphin at Discovery Cove

With many doctors going over the different test results, I dealt with a teenager that wasn't my teenage daughter. She was very confused, tired, easily agitated, couldn't handle much stimulation, was like Jekyll and Hyde, never knowing what I was dealing with when she'd open her eyes. It was frightening. I later learned that the frontal lobe area of the brain was affected with lesions and scarring, which affects moods and emotions.

Dr. Chitra Prasad ordered a muscle biopsy and explained what they believed Leanna was suffering from, a mitochondrial disease. As her eyes were affected, she believed Leanna had Mitochondrial Encephalomyopathy . Leanna was prescribed a mito cocktail, which is a high dose of vitamins to provide the body with energy that the body is unable to produce on its own due to mitochondria in the cell not working properly.

Leanna & I returned home after nearly three weeks in hospital, to continue to recuperate and build up her strength again. Time paced and we were all learning a new normal. I quit my job to care for Leanna fulltime, doing my best to balance her care and caring for the rest of my family, a husband who works shifts and two younger siblings of Leanna. It was hard, keeping things quiet, stress-free and relaxed as possible, helping Leanna in day to day activities, organizing healthcare people who came to help Leanna, a tutor to keep up with school work, learning Leanna's limitations.

Leanna & mom, Lisa in our wet suits at Discovery Cove

The results from the biopsy came back summer of 2009, indicating MELAS Syndrome, a genetically inherited rare disease, affected due to mitochondrial point mutation 3291 (T>C). MELAS is a rare neurological syndrome belonging to group of Mitochondrial Encephalomyopathies. MELAS is an acronym for; Mitochondrial, Myopathy- sore muscles, Encephalomyopathy – affecting the eyes, brain and central nervous system, Lactate

Personal Stories - continued

Leanna all ready for Winter Semi Formal dance at high school, December 2009

Acidosis- build up of waste product in the blood stream, causing vomiting, seizures and stroke-like episodes. Leanna suffered from more seizures throughout the summer months, due to dehydration, fatigue and overheating. Dr. Nayaran Prasad took Doug & me aside, explaining "the disease is progressing, there is no cure, you need to be brave and strong, and it is inevitable that Leanna would be back in hospital". Not exactly comforting news you want to hear from your doctor. Along with seizures and strokes, different areas of Leanna's brain have been affected, affecting her cognitively. Our last stay in hospital, the doctors felt it was time to have a G-tube put in, knowing symptoms that would arise. After a month in hospital, home again to recuperate and regain strength and weight.

This has changed our lives. Leanna has gone from an award winning student, to being home full time, only handling an hour of tutoring twice a week. She was upset to learn, due to her anti seizure medication; she is unable to get her driver's license, a milestone for every sixteen year old. I've grieved the future Leanna has lost. It's hard seeing Leanna maintaining, yet seeing her younger brother catch up to her, knowing it's a matter of time, before he will pass her, and her younger sister will too. Leanna is unable to be left alone, putting extra responsibility on all of us. We now have different equipment to aid in Leanna's health, like her wheelchair that we use to conserve energy if we go to the hospital for appointments or to the mall.

Leanna & mom, Lisa at the seventh annual Family Metabolic Workshop in London

We are new to this mitochondrial world, but I'm doing all I can to learn more, and advocate on Leanna's behalf, attending the Family Metabolic Workshops, hosted through London's Children's Hospital and the first annual MitoCanada lecture, held at MacMaster Hospital in Hamilton, and meeting others affected by mitochondrial disease through facebook. This has taught us how precious life is and how quickly life can change, to take things as they come and enjoy each moment.

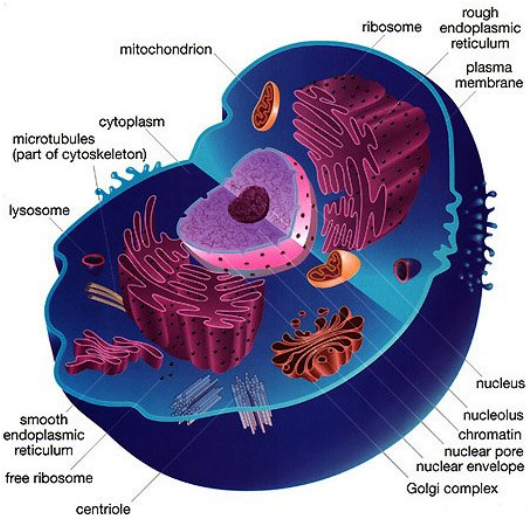
We were blessed to have a family vacation through Make-A-Wish, where Leanna had the opportunity to swim with a dolphin at Discovery Cove in Orlando, Florida, the highlight of the trip for her, this past February. As Leanna continues to do well, we are thankful for knowledgeable doctors, excellent, caring nurses and the many specialists in Leanna's care.

Lisa Glasbergen, ~ a mighty Mito Mom, doing what I can to spread awareness, offer support and raise funds for further research for hope of a cure to be found.

www.mitocanada.org / email - lisaglasbergen@yahoo.ca / on facebook – Lisa Helder Glasbergen

Featured This Issue

MELAS



MELAS is acronym for Mitochondrial Encephalomyopathy Lactic Acidosis and Stroke-like Episodes. MELAS is a rare neurological disease. It is an inherited metabolic disorder and belongs to the family of mitochondrial DNA diseases. It is extremely rare, with prevalence being less than 1 in 10,000. Early symptoms such as stroke and seizures usually begin in childhood, before ten years of age and progressively get worse. Symptoms persist throughout adolescence as day to day functioning becomes very difficult. Many vital organs of the body such as the brain, heart and muscles are victims of MELAS.

Mitochondria are the energy supplying powerhouses of the cell. These organelles convert the food we eat into ATP. ATP molecules are the only type of energy understood and used in the body. MELAS begins to destroy mitochondria, which are vital for cell life, and the effects can be severe for patients. Mitochondria are found in nearly all body cells and therefore patients with MELAS present a wide spectrum of different symptoms. In particular, energy demanding organs of the body such as the brain, muscles, heart, kidneys and eyes, are the most severely affected. Seizures, stroke, partial paralysis, loss of intellectual ability, muscle weakness, vision loss, cardiac and kidney problems are only a few of the most common symptoms of MELAS.

The figures below show the cross section of a cell and an enlarged mitochondrion. The nucleus in the centre of the cell contains DNA organized in genes, which is the blueprint for our bodies. However, a mitochondrion also contains its own DNA and genes and hence its own blueprint. MELAS is caused by a mutation to the $tRNA^{Leu}$ gene of the mitochondria's DNA. The tRNA molecules play a very important role in bringing amino acids together to make proteins from the information coded in genes. However a mutation in the tRNA gene results in dysfunctional proteins and thus dysfunctional mitochondria.

Featured This Issue - continued

Mitochondrial disorders such as MELAS are extremely variable even with in the family due to heteroplasmy (proportion of normal and mutant mitochondria within the cell which determines the clinical presentation). Although prognosis can be poor for some of the patients, many treatment options are available to improve the daily lifestyle of MELAS patients. Nutrition plays a vital role in the management of metabolic disorders. Vitamin and mineral supplements are often prescribed with variable success from patient to patient. The important components of this prescribed "vitamin cocktail" include riboflavin, Coenzyme Q and vitamins E, C, etc. Vitamins help reduce tissue damage caused by the faulty proteins of the mitochondria. Precautions during stressful periods such as surgical procedures or infections are important. Families need to get formal genetic counselling. Newer research on use of arginine as therapy for acute strokes and prevention of strokes is showing some promising results. There are strong mitochondrial support groups available in the USA and now also in Canada.

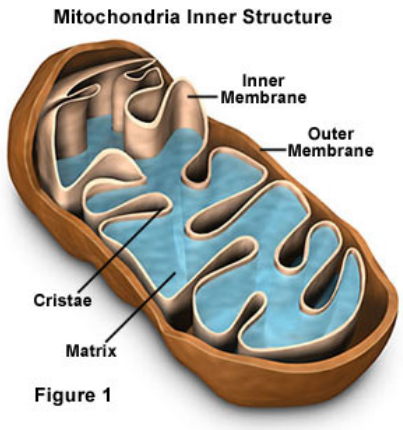


Figure 1

by Nachiket Deshpande BSc 2nd year and Dr. Chitra Prasad MD FRCPC
Nachiket is working on the web based teaching tool for mitochondrial disorders.

INFORMATION ON RESOURCES

Image of mitochondria:
http://www.cartage.org.lb/en/themes/sciences/zoology/animalphysiology/anatomy/animalcellstructure/Mitochondria/mitochondria.jpg

Image of cell:
www.uvm.edu/.../fa06/mvogenbe/Animal-Cell.jpg
http://emedicine.medscape.com/article/946864-overview

MELAS Syndrome by Author: Fernando Scaglia, MD, FACMG, Associate Professor of Genetics, Department of Molecular and Human Genetics, Baylor College of Medicine

Suzanne's Corner

Grilled Onion, Colored Peppers and Mushroom Quesadillas

Ingredients

- 1 Tbs vegetable oil
- 1/4 cup onion strips
- 1/4 cup colored bell peppers, julienne cut
- 2 Tbs sliced mushrooms
- 1 small clove garlic, chopped
- 1/4 tsp chili powder
- 1/4 tsp cumin
- 1/2 tsp salt
- 1/2 Tbs chopped fresh cilantro
- 2 CBF Tortilla Wraps
- 2 Tbs shredded cheddar cheese
- Oil for cooking the quesadillas

Directions

- Heat oil in a large sauté pan; add strips of onion and cook for 3 to 5 minutes or until softened.
- Add mushrooms and garlic and sauté on medium-high heat for another 3 to 5 minutes, or until the mushrooms have softened.
- Sprinkle mixture with chili powder, cumin, salt, and cilantro and mix well; remove from heat.
- Lay out 1 tortilla and evenly spread cooked mixture onto the tortilla.
- Sprinkle the cheese on top if using shreds or evenly spread Cheese Wizard on top of remaining tortilla and cover. Brush the top lightly with vegetable oil.
- Heat a clean nonstick sauté pan and place the quesadilla, oiled side down, into the heated pan. Brush oil on the dry side of the quesadilla.
- Cook for 3 minutes, or until browned. Flip and cook the other side.
- Cut quesadilla into 4 segments and serve.
- SUGGESTIONS: Try serving with salsa and a dollop of guacamole.

Serving size: 2 quarters (106 g) (Makes 2 servings)

	Per Recipe	Per Serving
PHE:	104 mg	52 mg
LEU:	122 mg	61 mg
Pro:	2.4 g	1.2 g
Calories:	460	230

Nutrition Facts

Serving Size (106g)

Amount Per Serving

Calories 230Calories from Fat 130

	% Daily Value*
Total Fat 14g	**22%**
Saturated Fat 2g	**9%**
Trans Fat 0g	
Polyunsaturated Fat 4g	
Monounsaturated Fat 8g	
Cholesterol 0mg	**0%**
Sodium 530mg	**22%**
Potassium 130mg	**4%**
Total Carbohydrate 26g	**9%**
Dietary Fiber 2g	**7%**
Sugars 2g	
Protein 1g	

Vitamin A 10% • Vitamin C 35%

Calcium 10% • Iron 2%

Phosphorus 8%

*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	65g	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

Source: www.cambrookefoods.com

What's New

7th Annual Metabolic Family Day a Success!

The 7th annual Metabolic Family Day held on May 14th, 2010 provided an excellent opportunity to share information on metabolic disorders and hope among families and health care providers. 175 individuals attended the event with their families.

Families were invited to interact with speakers, learn about various metabolic formulas and foods, see what is new with treatment and research, visit displays of metabolic food products and learn about the resources available in their community. The day also provided an excellent opportunity for families to talk with each other, share their experiences and make a few friends along the way.

The Metabolic Team and Jo-Gee the Clown- (Joanne Psiuk-Rogers)

The day began with a warm welcome from Dr. Chitra Prasad, Director of the Metabolic Clinic and Medical Geneticist at LHSC and opening remarks from Debbie Comuzzi, President and CEO of the Children's Health Foundation.

Speakers included Jim Mundy, Canadian Organization for Rare Disorders (CORD), Dr. Murray Potter, Associate Professor Pathology and Molecular Medicine Head, Biochemical Genetics McMaster University Hamilton Health Sciences Centre and keynote speaker Susan Minns, who shared her life challenges with multiple sclerosis and cancer and how she chose to deal with her circumstances in a positive manner that has enriched her life.

The day also included four group sessions: a diet group led by Dr. Rupar and Suzanne Ratko discussed diet-related independence strategies; a neurological group led by Dr Hema Gangham and Dr. Sharon Goobie as well as the team from the Thames Valley Children's Centre reviewed a multi-disciplinary approach to children with developmental delay; a lysosomal storage disorders group discussed enzyme replacement therapies and other newer therapies led by Dr Raiman, HSC Toronto; and a teen and young adult group led by Jill Toswill and Dr. Erica Gold focused on motivational strategies for taking responsibility of their health to lead a more independent lifestyle.

Suzanne Ratko, Registered Dietitian, once again ran the annual "low protein" cooking demonstration, which featured food and recipe ideas by Stephanie Lamay, Nutricia.

Submitted By Jennifer DiRaimo, Genetic Counsellor

What's New- continued

Welcome to our new Metabolic Genetic Counsellor!

Hi Everyone!

My name is Veronica Kokavec and I'm the new metabolic genetic counsellor working with Dr. Chitra Prasad and the Metabolic Team. My educational background includes a B.Sc. in Behaviour, Cognition and Neuroscience from the University of Windsor in 2006. In 2008 I completed a Master's degree in Basic Medical Science at Wayne State University in Detroit Michigan. Just this past May I graduated from Wayne State University with a Master's degree in Genetic Counselling. I am so pleased to be working at the London Health Sciences Centre and am very happy to be part of the team here in Medical Genetics! I look forward to meeting you all.

Sincerely,

~Veronica

News/conferences/papers/projects

1. C. Prasad, S. Venance A. N Prasad, S. Levin, C. Campbell, H. Rosenberg, M. Geraghty E. McCready, and C. A Rupar. Spectrum of Pompe Disease in South Western Ontario: Role of Enzyme Replacement Therapy: Presented at Garrod Meeting June 2010

2. Prasad AN, Rupar CA, and Chitra Prasad. MTHFR deficiency and Infantile Epilepsy.

3. Chitra Prasad, C. Anthony Rupar and Asuri N. Prasad. Pyruvate Dehydrogenase Deficiency and Epilepsy.

4. Prasad AN, Rupar CA, Levin S and Prasad C . Menkes Disease and epilepsy

(2-4) were presented at International Symposium on Epilepsy in Neurometabolic Diseases (ISENMD) & The 13th Annual Meeting of the Infantile Seizure Society March 26-28, 2010 in Taipei Taiwan.

5. Ratko, S, Prasad C and Rupar, C. A .PKU & Acute Lymphoblastic Leukemia (ALL): Challenges in Management! Poster presentation at international PKU conference in Munich.

6. C. Prasad, S. Goobie, J. DiRaimo G. Moran, B. Potter, P. Chakraborty, and K. O'Connor, T. Morley and C. A Rupar. Emotional Impact of Expanded Newborn Screening: A Pilot Project in South Western Ontario (research project to be started by fall 2010). (Funding provided by Children's Hospital of Eastern Ontario Ottawa newborn screening program).

Continued on page 9

What's New - continued

7. Deshpande N, Prasad C, and Prasad AN, Chevendra V and Rupar CA. Developing a web based teaching tool to aid parents, caregivers and professionals about mitochondrial disorders. (research project-ongoing). ($19,227.80) Funding provided by Chris and Donna Stickles in memory of their son Dean Stickles).

8. C Prasad and CA Rupar. Inborn Errors of Metabolism in Infancy and Childhood Presenting with Metabolic Acidosis. Indian Journal of Practical Pediatrics. 2010 (Apr-June); 12(2) 155: 53-62.

9. Siu VM, Ratko S, Prasad AN, Prasad C, Rupar CA. Amish microcephaly: Long-term survival and biochemical characterization. Am J Med Genet A. 2010 Jul;152A(7):1747-51.

10. C. Prasad, J. DiRaimo, P. Chakraborty, S. Goobie, and C. A. Rupar. Positive Newborn Screening for Carnitine Transporter Deficiency: A Marker for Maternal Genetic/ Metabolic Diseases? Treatment Centre Symposium, April 16 2010, Children's Hospital of Eastern Ontario, Ottawa .

Psychology and Neurology Point of View

How to help your child get to sleep

How to address sleep problems

Erica Gold, Ph.D.
Psychologist
Children's Hospital
London Health Sciences Centre

Give the child a clear signal that it is bedtime; for example, tell him/her it is time to get ready for bed. If your child has trouble changing activities you may want to give them a 5 or 10 minute warning that it will soon be bedtime. Have a predictable bedtime routine and try to stick to it

The routine might include one or all of the following:

- turning the television or other electronics off
- if appropriate, offering a bedtime snack
- having a bath, putting on pyjamas, brushing teeth
- having the child use the toilet
- getting into bed
- a parent reading the child one story the child listening to quiet music
- Some children do not like to be alone or are afraid of the dark. In that case a night light might help.

continued on page 10

Psychology and Neurology Point of View - continued

Children who keep getting out of bed need to be firmly and quietly returned there. Lying down with the child may help settle them, but only stay a few minutes because the child will want you to stay longer every night and this is a difficult habit to break.

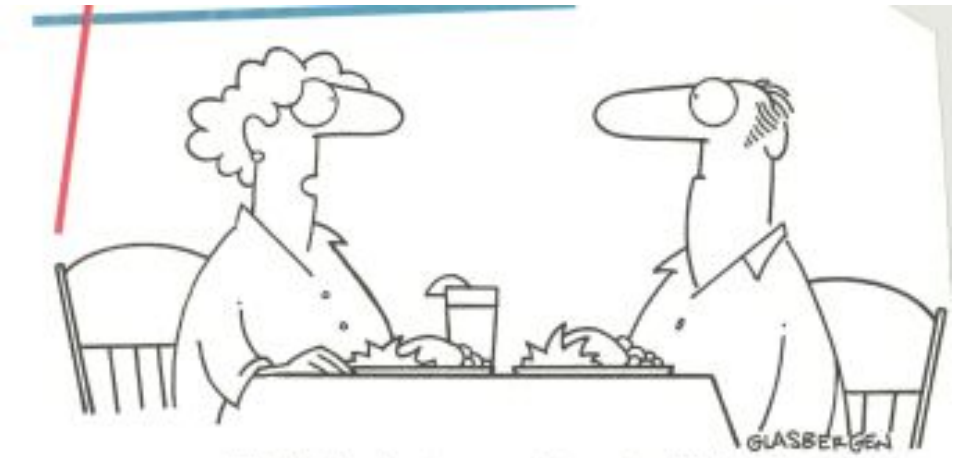
Asuri (Narayan) Prasad, MBBS, MD, FRCPC, FRCPE

Associate Professor in Pediatrics & Clinical Neurosciences, Schulich School of Medicine & Dentistry, Univ. of Western Ontario
Children's Hospital, London Health Sciences Centre

Sleep disorders in children with developmental disabilities

A common thread running through the lives of children pertains to the development of sleep and its regulation. Sleep disturbances even in the "normal" child impacts adversely on the family. In children with developmental disabilities sleep disorders are being evaluated systematically. It is important to understand the basics of the phenomenology of sleep, its development and disorders resulting from dysregulation. Sleep disturbances are reported in a significant proportion of children with developmental disabilities that include (genetic and metabolic disorders). These include "benign" events like night terrors, periodic leg movements of sleep, sleep myoclonus, and rhythmic movement disorders and other REM sleep behaviors. There is increasing recognition that nocturnal sleep related events can be mistaken for seizures and inappropriately treated. Sleep disturbances can also be closely linked to the presence of epileptic seizures and the use of antiepileptic medications. Day time attention problems, sleepiness, irritability, memory problems aggressive behaviors can sometimes be related sleep related problem called Obstructive Sleep Apnea. Identification of sleep related disorder can sometimes be extremely helpful in leading to appropriate treatments with either medications such as melatonin, or clonazepam. In other situations use of appropriate dental appliances, and surgery (removal of enlarged adenoids and or tonsils) can lead to a resolution of symptoms. Please consult your family physician, pediatrician or health provider for further information.

Laughter is still the Best Medicine



"This is the nicest conversation we've had in weeks. Let's not spoil it by talking."

22 STITCHES AUGUST 2004

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!

" Great News !!!"

We are getting a **new dietary tool** to do a more accurate calculation of dietary records. This is a web based nutrient analysis software program for metabolic nutritionists. The funding will be obtained from the "PKU Metabolism Fund" to which some of our families have very kindly contributed. If you would like to contribute to these funds please see the information above for more details.

Charis, Age 5

Contact Information

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Yahoo Online Chat: health.groups.yahoo.com/group/metabolic_disorders
Post Message: metabolic_disorders@yahoogroups.com

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