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MSUD NEWSLETTER

Published by the MSUD Family Support Group • Volume 29, Number 1 • SPRING 2011

OXIDATIVE STRESS IN INBORN ERRORS OF METABOLISM

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In the paper "Profiling of oxidative stress in patients with inborn errors of metabolism" (Molecular Genetics and Metabolism. vol.98), Mc Guire and coworkers explored the accumulation of marker of oxidative stress in patients with a variety of inherited disorders of metabolism. Oxidative stress refers to the accumulation in cells of molecules that are in a highly reactive state. These molecules (free radicals) are produced as a by-product of normally occurring processes in cells and are usually mopped up by antioxidant defenses. Free radicals that are not neutralized by cellular antioxidants can damage cellular components including DNA or proteins. Free radical damage has been implicated in the disease process

(*OxidativeStress* cont. on page 2)

Meet the Director, Sandy Bulcher

For the past 10 years or so, I have been the Director of the MSUD Family Support Group. Staying involved with the organization and working with families, professionals, and related organizations is very rewarding. My husband, Dave, is involved with the support group also, as the treasurer. We have two sons, Tyler and Jordan. Tyler is 24 years old and will soon graduate from pharmacy school. Jordan is 21 years old and has Classic MSUD. He is a junior at The Ohio State University majoring in molecular genetics. We live in Powell, Ohio, a suburb of Columbus. The headquarters for the MSUD Family Support Group is located in our home, our spare bedroom, to be exact. In my other life outside of MSUD, I work full time as a RN in the Endoscopy Department at Ohio State University Medical Center.

My Role: As director of the support group, my main role is contact person for new families, existing families, professionals, and other organizations. When a new child is diagnosed with MSUD, I add the family to the database, send out a "welcome package" of MSUD literature, and call them to offer support and encouragement.

(*MSUDDirector* cont. on page 2)

Inside This Issue:

MSUD Symposium 2012

***Save the date:* June 28-30**

Embassy Suites- Airport, Philadelphia. PA.

The hotel is conveniently located 1 mile from Philadelphia International Airport and offers free shuttle service to and from the airport. In addition, all hotel rooms are suites and include a living room and bedroom, plenty of space for the whole family. During your stay in Philadelphia, check out historic sights such as the Liberty Bell and Independence Hall. *Hope to see you there!*

Sandy Bulcher, Director-MSUD Family Support

(*OxidativeStress* cont. from page 1)

in a number of common disorders such as Alzheimer's disease and heart disease. An imbalance resulting in increased levels of oxidative stress can result from excessive production of free radicals or deficiencies in the availability of cellular antioxidants.

Based on work done in cell models, oxidative stress has been proposed to potentially contribute to the disease state in several inborn errors of metabolism including organic acidurias, phenylketonuria (PKU) and MSUD. The work in the paper by Mc Guire and coworkers assessed a marker of protein oxidation, a marker of fat oxidation, and the abundance of antioxidants in urine samples from patients with inborn errors of metabolism in comparison to the values observed in a group of patients of similar ages unaffected by inborn errors of metabolism. The results of the analysis showed that markers of oxidative stress were significantly elevated in a subset of inborn error of metabolism patients. With regard to MSUD, there was evidence for increased levels of oxidative stress markers in aggregate for the nine patients who enrolled in the study. In addition, in two out of three patients from whom multiple samples were collected over time, oxidative stress markers rose during episodes of mild upper respiratory infection during which branched chain amino acid levels also rose. Overall, these preliminary studies suggested that elevations in oxidative stress are a feature of multiple inborn errors of metabolism and that these elevations might occur during periods of clinical illness or poor disease control. Additional studies will be necessary to determine if the elevations in oxidative stress markers observed in this study can be replicated in larger numbers of patients, if these elevations are chronic or limited to periods of illness, and the mechanism by which increased oxidative stress may contribute to the development of symptoms in patients with inborn errors of metabolism. ■

(*MSUDDirector* cont. from page 1)

I am also in contact with professionals, including physicians and researchers, involved in MSUD. Dr. Brendan Lee from Baylor University in Texas and I have been communicating periodically over the last few years regarding the potential use of phenylbutyrate in MSUD. I'll continue to work closely with him as he moves forward with this exciting study.

In addition to working with families and professionals, I interact with members of other organizations. Building relationships with organizations such as the National PKU Alliance, Genetic Metabolic Dieticians International, and National Organizations of Rare Diseases (NORD) to name a few, is important, as there is strength in numbers. I'll be working with these and other organizations during the coming year to push forward national legislation for coverage of special medical formulas and foods. Senator Kerry from MA has agreed to sponsor the legislation again and I am hopeful that 2011 is the year to get the bill passed.

Staying Connected: Existing MSUD families can stay connected to the organization through biannual newsletters, our support group website (www.msud-support.org) and egroups. MSUD is now on Facebook, too. To join, sign up for a Facebook account and search "MSUD". We also offer a medical symposium every two years. Symposium 2012 will be held in Philadelphia June 28-30th at the Embassy Suites- Airport. I hope to meet new families and reconnect with old friends at the next symposium.

What Can You Do?

■ Notify me of changes in your contact information. To keep the database current, please notify me of any changes, especially changes in your mailing address. Each time Dave and I mail out the newsletter, some are returned to us due to incorrect address information. We don't want you to miss out on receiving valuable information.

■ Consider hosting a fundraising event. If you are reluctant to get involved in fundraising, I can assist you in finding resources to make your event successful.

■ Contribute financially to the support group. The yearly membership dues are $15 and the majority of our families and professionals do not contribute. These funds are vital for the organization to function and continue our goal of helping families and professionals involved with MSUD.

■ Consider designating funds to the MSUD Family Support Group in memory of a loved one. If a loved one passes away, contributions to the support group can be made in their honor and memory. Please contact Dave (contact information below) for details.

■ Contribute to our newsletter. We all love to hear everyone's stories!

■ Consider becoming involved in the support group. I can assist you in finding a role that best fits your time and talent.

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Phenylbutyrate Therapy for Maple Syrup Urine Disease

Brendan Lee, M.D., Ph.D.
Howard Hughes Medical Institute
Department of Molecular and Human Genetics,
Baylor College of Medicine

We have recently published our preliminary studies on the use of phenylbutyrate in MSUD. In 3 unaffected control subjects and in 3 of 5 patients with MSUD, we found that an already FDA approved drug phenylbutyrate can decrease branched chain amino acid levels (BCAA). The decreased levels were in the average range of about 30% though some had more and others less. Our studies suggest that the drug acts to turn on any residual activity in the branched chain ketoacid decarboxylase (BCKD) enzyme.

At this time, while these data are encouraging for developing a drug treatment for MSUD, it is important to remember that there are many questions that need to be answered before trying this therapy. To do so, we have submitted a study to the National Institutes of Health to perform a definite clinical trial of phenylbutyrate in MSUD. We have been fortunate to receive a grant from the Scott C. Foster Fund in support of this project. With the support of the MSUD Family Support Group and the NIH, we hope to begin to recruit for this study by the end of 2011. The study will address several important questions before this drug can be recommended for use:

1) How many MSUD patients respond to phenylbutyrate vs. placebo when neither the doctor or the patient knows what they are taking? This is termed a double blind placebo controlled trial.
2) What is the magnitude of the drop in BCAA on phenylbutyrate?
3) Can mutation status predict who may or may not respond?
4) Can we develop a predictive test on blood cells to help determine the basis of response?

Our hope if these studies are successful is that we can use phenylbutyrate adjunctive therapy to increase protein intake in patients on restricted diets, prevent frequency and/or severity of decompensations, and/or help treat decompensations when they do occur.

Please stay tuned to the MSUD Family Support Group website and newsletter to learn more about the study and for information about participation. The study will be performed at Baylor College of Medicine and will involve several trips to Houston. All significant costs of the trial including travel would be covered by the study. ■

Porter started Kindergarten this fall, and he likes school a lot. He spends the day reading, doing activities, and running around at recess. He brings his lunch every day (his favorite is lo-pro macaroni and cheese!). He is a healthy and active kid, and loves teaching his little brother, Jameson, to build forts and play with trains.

We went to Family Camp this year, organized by the PKU Organization of Illinois. Porter had a terrific time trying new food, playing in the woods, and meeting more families.

Porter Roth, Age 6(Classic)and his brother Jameson

Special Thanks to

Herb Foster and the Scott C. Foster Fund

for their generous donation of $35,000 for Dr. Brendan Lee's Buphenyl research project.

The money will assist Dr. Lee in developing a test to better predict which individuals with MSUD will respond to the medication.

FUNDRAISING IN CHICAGO

Things are happening in the Windy City!

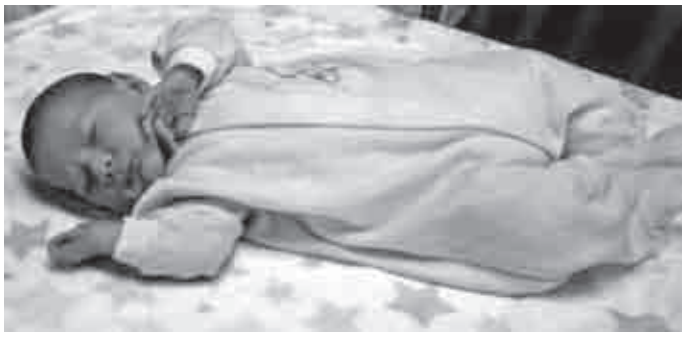
The 2nd not-quite-annual fundraiser will be held on Saturday March 12 from 6 - 10 pm at the Dana Hotel and Spa in downtown Chicago.

The event will feature live music, great food, exciting raffle items, and a gathering of terrific people as we unite to raise funds for our support group.

For those wanting to stay overnight at the Dana, a special group rate is available.

Please contact Barbara Mudrick
barbmud@yahoo.com
224.944.1282 or
Karen Dolins
karen.dolins@gmail.com
914 7235458
for further information.

Lester and Ruth Nolt are happy to announce the birth of our healthy son!



Randall was born on January 1, 2011. He weighed 7 pounds 14 ounces and measured 20 inches. Randall did not need to be tested for MSD because Lester is not a carrier.

Everyone was pleased with how well the pregnancy went. Everything was normal and there were no problems. Many thanks to Sandy Vancalcar and Dr. Greg Rice and his partner of Waisman Center, Madison Wisconsin for their dedicated help. They worked very closely with the perinatal doctors at Meriter Hospital and our family doctor.

We had prenatal check-ups monthly and further along every two weeks. We did weekly blood tests for amino acids or more often if needed. From the beginning of the pregnancy to the end my leucine levels ranged from 491 _moles/L (6.9 mg/dL) at the highest to 49 _moles/L (0.6 mg/dL) at the lowest. My leucine intake from food increased steadily. At the beginning I was able to tolerate 550 mg of leucine and at the most I tolerated 3,000 mg of leucine. I was able to do my regular chores up to the week before Randall was born. He was in breech position, so that changed our plans and he was delivered by a non-emergency C-section. Everything went well. Recovery time at the hospital was 11 days. Five weeks later I feel well and am almost back to my normal schedule.

Ruth and Lester Nolt

Research at Hershey: How MSUD and Liver Transplant Therapy Affect the Brain

Emilie Muelly, Graduate Student
at Penn State Hershey Medical Center

All parents fear the metabolic crises of MSUD, particularly the risks associated with brain swelling. However, other serious problems such as inattention, depression, and anxiety chronically burden some MSUD patients. The risk for these conditions may be related to the long-term quality of metabolic control rather than the number or severity of acute metabolic crises. As all families who struggle with classical MSUD know, perfect metabolic control is impossible to achieve, even under the best of circumstances.

Mechanisms of inattention, depression and anxiety among MSUD patients are not well understood. In collaboration with the Clinic for Special Children, researchers at Penn State Hershey Medical Center are examining this problem more closely. We plan to study how MSUD chronically alters the structure and chemistry of the brain, how such changes relate to symptoms, and whether or not these chronic conditions can be modified by liver transplantation.

Using Magnetic Resonance Imaging (MRI) we can capture different types of information about the brain, such as the size and structure of different regions, connectivity pathways between different brain areas, and the concentration of specific chemicals involved in nerve signaling and energy metabolism. We can compare imaging results of MSUD patients to their siblings and also correlate these results with blood amino acid levels, medical history, and neurological symptoms. This will allow us to better understand how the chemical disturbances in MSUD chronically affect the brain.

The ability of liver transplantation to eliminate protein restriction and the risk of acute crises is now well established. But can liver transplantation alter brain structure and function in ways that reduce the risk for chronic symptoms? If so, is this effect dependent on age at transplantation? We hope that our research will provide answers to these questions and thereby help families afflicted with MSUD to gain a deeper understanding of the disease and take a more informed approach to its treatment.

We thank those who have volunteered for the study! Once we have analyzed the data, we hope to have a picnic with all the participants to share the results. If you are interested in finding out more about the study, contact one of the doctors at the Clinic for Special Children (717.687.9407) for more information. ■

Join us June 20-25, 2011 for the
17th Annual Metabolic Camp
at Emory University in Atlanta, GA!

This is a model, research-based camp for young women 12 years age and older with PKU and MSUD, which focuses on building social support through a variety of activities including nutrition education, cooking classes, discussion groups, and local field trips.
The camp typically accepts 30 attendees on a first-come, first-served basis.
Registered dietitians from across the nation and around the world volunteer their time to serve as camp counselors, and nutrition students provide support as assistant counselors.

The cost of the camp is $325 per person, which includes all sponsored meals, lodging, group activities, field trips, and closing banquet.

Partial scholarships are available for certain financial circumstances. Check with your local RD and clinic to see if local sponsorship is available.

For more information, visit ***www.metcamp.org*** and contact Rosalynn Borlaza, Camp Coordinator, at 404.778.8521 or rborlaz@emory.edu

Lemon Bars

3/4 cup butter
2 1/4 cups Low-Protein Baking Mix
1/2 cup powdered sugar
1 tablespoon powdered coffee creamer
Mix well and pat firmly into a 9-13 baking pan. Bake at 350 degrees for 15 minutes.

Topping:
1/3 cup water
2 cups sugar
6 tablespoons lemon juice
3 tablespoons cornstarch
3 tablespoons water
1 drop yellow food coloring
Combine water, sugar and lemon juice on a small saucepan. Bring to a boil. Mix cornstarch with 3 tablespoons water. Slowly add to boiling lemon mixture and stir until thickened. Remove from heat and add food coloring. Pour over baked crust.

Crumbs:
2 tablespoons butter
3/4 cup Low-Protein baking mix
1/4 cup brown sugar
Mix well and spread over filling. Bake at 350 degrees for 20 minutes.

	Protein	Leucine	Calories
Per recipe	3.0 g	265 mg	4396
Per serving	0.1 g	7 mg	110

Please send recipes to
Food News Editor

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Quick and Easy Potato Pancake

150 grams raw potato finely grated
Salt and pepper to taste
3 tablespoons oil

Place frying pan on stovetop and add 2 tablespoons oil and heat. When pan is hot add potatoes. Fry on medium heat until bottom of pancake is golden brown. Turn potato and add remaining oil. Fry till brown. Makes 2 servings

	Protein	Leucine	Calories
Per serving	1.25g	82.5mg	200

Onion Patties

1/2 cup MixQuik
1/2 teaspoon salt
1 1/2 cups finely chopped onions
3/4 cup water
Mix all together adding more water to make a thin batter. Drop by tablespoon into a greased skillet and fry turning once.

	Protein	Leucine	Calories
Per recipe	2.9g	121mg	325

To calculate the Leucine per patties divide the total amount by the number of patties you make.

Peppermint Crunch Cookies

1 package white almond bark (1pound 8ounces)
Red or green food coloring
4 Rice Crispy Cereal
4 cups miniature marshmallows
1 cup crushed peppermint candy

Melt almond bark in microwave and stir in a drop or two of food coloring. Mix in rice crispies, marshmallows and peppermint candy. Spoon on wax paper making 60 cookies and refrigerate till harden. Makes 60 cookies.

	Protein	Leucine	Calories
Per recipe	12.8g	734mg	5212
Per serving	.2g	12mg	87

Cheese Ball

5 oz Low-Protein shredded Cheddar cheese
5 oz Low-Protein shredded Mozzarella
1/3 cup onions, chopped
1/3 cup Miracle Whip
1 packet Washington's Golden Seasoning

Mix cheeses with onions, Miracle Whip and Golden Seasoning. Shape into a ball on wax paper. Chill in freezer for 30 minutes. Roll in minced parsley or chives. This is very soft but will hold together rather well. Keep refrigerated until ready to serve. 20 - 2 tablespoons servings.

	Protein	Leucine	Calories
Per recipe	8.8 g	773 mg	1175
Per serving	0.4 g	38 mg	59

Cambrooke Foods

has completed their move to a manufacturing facility that will better accommodate their needs and expand production capabilities.

Versatile Pita Pockets are the first of a series of new products that have been introduced using the new equipment that has been acquired. These pocket breads are great for vegetarian sandwiches because they are easy to fill and hold. Try cutting them horizontally in half and then into triangular pieces before baking into pita chips for dipping and snacking.
An addition to their ready-to-eat dessert line is **Pumpkin Raisin Cookies**. These are golden brown homemade cookies - with a pumpkin-spice taste. They are a perfect snack with a hot drink or an after-school treat. If you haven't had the **Tweekz** (imitation chicken nuggets) in a while, try them again because they now have 32 mg of DHA Omega 3 fatty acids per serving.

Cambrooke will launch their Social Media sites this winter. Join your friends and the Cambrooke team on Facebook and Twitter for some friendly and informative dialogue sharing, plus tips and ideas for managing your disorder.

The **Camino pro**® formula line of ready-to-use drinks now have an enhanced vitamin and mineral blend. If you have not had the opportunity to try them or need updated information, contact Cambrooke Foods.

Request your free Camino pro® samples or place your order today. Call toll-free, (866) 4 LOW PRO / (866) 456-9776 or visit our website at www.cambrookefoods.com. If this is not convenient, you can mail (4 Copeland Drive, Ayer, MA 01432), e-mail (orders@cambrookefoods.com) or fax at (978) 443 -1318.

Oven Baked Fries

2 baking potatoes
1/4 cup Italian Dressing
Cut potatoes into 1/2 inch strips. Place in a bowl and pour dressing over potatoes. Toss to coat. Place on a baking sheet and bake at 425 degrees for 25-30 minutes. 4 servings

	Protein	Leucine	Calories
Per serving	2.35g	127mg	158

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This Newsletter does not attempt to provide medical advice for individuals.
Consult your specialist before making any changes in treatment.

NUTRICIA North America
formerly SHS North America

This publication is supported by a grant from Nutricia North America