Medical Therapy for Maple Syrup Urine Disease

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Maple syrup urine disease (MSUD) is a rare genetic disease named for the distinctive, sweet odor of the urine and sweat. It is caused by deficient activity of the branched chain a-ketoacid dehydrogenase complex, which is involved in the breakdown of leucine, isoleucine, and valine. Although MSUD is a life-threatening disorder, it can be well-managed with prompt, careful, and thorough treatment for life. Successful medical therapy is highly contingent on accessibility to a medical team that is experienced in the care of infants, children, adolescents, and adults with MSUD.

MSUD is characterized by episodes of metabolic decompensation, usually caused by infection, excessive protein intake, or fasting. Early signs that are usually apparent to parents include poor feeding and excessive sleepiness in infants, and ataxia (“wobbly” gait), slurred speech, and vomiting in older children. During decompensations, the concentrations of the branched chain amino acids in the body are elevated. Leucine in particular is associated with neurotoxicity. High concentrations of isoleucine and valine are not associated with any obvious toxicity, although elevated concentrations of isoleucine and its metabolites are not associated with any obvious toxicity, although elevated concentrations of isoleucine and its metabolites

(Wasserstein, M.D. cont. on page 3)

MSUD Research Update

Catherine McKeon, Ph.D.
Senior Advisor for Genetic Research
National Institute of Diabetes and Digestive and Kidney Diseases

The National Institutes of Health (NIH) under the Department of Health and Human Services (DHHS) is the major funder of scientific research in the United States. The NIH funds studies in many aspects of medical research at universities and research organizations across the country. Several components of the NIH support research on MSUD including the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Child Health and Human Development. NIH-funded researchers have contributed to our knowledge of MSUD by identifying the enzyme defect in the branch-chain alpha-ketoacid dehydrogenase complex (BCKD) and the underlying genetic defects in MSUD. These discoveries have led to the development of a test for MSUD that can detect the disease in newborns so that dietary treatment can begin prior to the development of serious consequences. Although some states have adopted this newborn screening test, many have not. The DHHS Secretary’s Advisory Committee on Genetics, Health and Society has recommended that all states include MSUD in their newborn screening programs.

Dietary treatment, especially when instituted from birth, has

(McKeon, Ph.D. cont. on page 13)
Plans are underway for Symposium 2006. I am excited to see old friends, meet new families, and learn more about MSUD. We expect a large number of attendees for this symposium, as our numbers have increased by 25-50 with each symposium. When I hosted the symposium in Columbus, Ohio in 1996, 175 people attended. Nearly 375 people attended the symposium in Decatur, GA in July 2004. Due to this growth, we have made some changes in the structure/format of the conference. Watch for the symposium registration form which will include details about speakers and topics, in early spring 2006.

WHERE:
Dublin Embassy Suites, 5100 Upper Metro Place, Dublin, Ohio 43017
614.790.9000 • www.embassysuitescolumbusdublin.com
Each suite has a private bedroom with 1 king or 2 double beds and a separate living area with a sofa bed, dining table, microwave, and refrigerator. The hotel also has an indoor pool, whirlpool and fitness center.

WHO: MSUD families and professionals

COST:
No registration cost to attend the symposium for MSUD families or professionals.
Hotel rate-$104.00 per night, includes free parking. Buffet breakfasts, lunch on Friday and Saturday and evening snacks are included. Low protein foods will be provided for these meals. Dinners are on your own.

TRANSPORTATION:
The hotel is located off Interstate 270 and SR 161 on the northwest side of Columbus. Port Columbus, the nearest airport (airport code is CMH), is a 30 minute drive from the airport.

SCHEDULE:
Thursday June 15th: Registration/Reception 7-9pm
Friday June 16th: Meeting Time 9am-5pm
Saturday June 17th: Meeting Time 9am-12noon,
Family Gathering 2-5pm

TRAVEL ASSISTANCE:
We have received another generous donation from the United Services Foundation. This money is designated to help with travel expenses for those who do not have other financial resources available. Those who have never attended an MSUD Symposium will have top priority for assistance to attend Symposium 2006. However, anyone from the U.S. or other countries may submit a request to Wayne Brubacher. We want to make it possible for everyone to be there who wish to attend. Don’t hesitate to call Wayne Brubacher, contact person, at 574.862.2992 or send an e-mail to: wjbrubacher@characterlink.net.

I am looking forward to the symposium and hope that many families and professionals will attend. If you have any questions feel free to email or call. Sandy Bulcher: dbulcher@aol.com or 740.548.4475
cause the characteristic smell.

It is clear that outcome correlates with the age of onset of therapy, the quality of metabolic control over time, and the number and severity of metabolic decompensations. Successful medical treatment of MSUD has three components:

1) early identification and rapid institution of therapy within the first week of life;
2) a daily medical regimen, or “maintenance therapy,”
3) an aggressive treatment protocol that is used during metabolic decompensations.

The first component of therapy, early identification, is achievable in states that include MSUD in their Newborn Screening Panel. MSUD is currently on the Newborn Screening Panel in 36 states and the District of Columbia, and is slated to be included in a few more states in the future. In New York, positive results are typically available by about 5 days of age. Confirmation of diagnosis and institution of therapy are performed within hours of notification.

The second component, maintenance therapy, is mainly dietary. Success requires close collaboration and excellent communication between the family and the medical team, particularly the metabolic nutritionist. The goal of maintenance therapy for patients of all ages is to keep plasma concentrations of leucine, isoleucine, and valine (the branched chain amino acids, or BCAA) within normal limits, while providing adequate protein, carbohydrates, fat, and other nutrients to allow the body to grow and function normally. Maintenance therapy involves restricting the intake of the BCAA using specialized metabolic formulas. In addition to carbohydrates, fats, vitamins, and minerals, these formulas provide the essential amino acids other than the BCAA, and therefore are the main source of protein for MSUD patients. Small amounts of natural protein are also included in the diet. The amount of natural protein is prescribed on an individual basis, depending on how much each patient can tolerate while maintaining satisfactory plasma concentrations of leucine, isoleucine, and valine. Our practice is to measure BCAA concentrations weekly for the first six months of life, bi-weekly from six to 12 months of life, and then at least monthly thereafter. Leucine levels that remain chronically elevated can cause mental retardation. Deficiencies of any of the BCAAs are also dangerous, and if not corrected rapidly can cause failure to gain weight, anemia, hair loss, and skin rashes. Many patients take solutions of pure isoleucine, leucine, or valine. These are prescribed in order to carefully and precisely quantify the intake and plasma concentration of each amino acid. Infants and young children undergoing rapid growth face frequent adjustments in their dietary prescription. Older children, adolescents and adults may face difficulties with compliance with the diet, so regular measurements of BCAA concentrations are essential.

In contrast, the goal of decompensation therapy is to rapidly reduce elevated plasma leucine levels to a non-toxic level. We use a combination of branched-chain amino acid free hyperalimentation, intravenous glucose, insulin, and intralipids. Mannitol may be given if cerebral edema is suspected. Close observation in an intensive care unit to monitor neurological signs and symptoms, fluid status, and vital signs is essential. Occasionally, hemodialysis is needed to rapidly lower the leucine level. Hemodialysis can often normalize the plasma leucine within several hours, and if performed by experienced physicians, is safe and extremely effective.

Liver transplantation is another option for treatment. It works by replacing the defective enzyme with a functioning one. A successful liver transplant can obviate the need for the severe dietary restrictions and minimize the risk of metabolic decompensation. There are many factors that must be weighed for each patient when considering liver transplantation. These factors include, but are not limited to: the risk of surgery, the possibility of organ rejection, the need for anti-rejection medications, accessibility to medical therapy, dietary compliance, and overall metabolic control.

With early detection, excellent dietary control, and rapid reversal of metabolic decompensation, we have seen remarkable outcomes in our patients. Aside from eating different food for lunch, our younger patients are indistinguishable from the other children at school. Our older patients, many of whom are college graduates, are independent, self-sufficient adults. Thus, with early diagnosis, meticulous medical therapy, and close collaboration between the family and the medical team, MSUD is a manageable disease with a favorable outcome.

THE SEA MOLDS ITS INHABITANTS
By Nikolai Rudd

The sea molds its inhabitants
The air gives life to us.

Tradition, marked with carved crafts,
A thousand words proclaim
That unspoken touch.
A smile, the glimmer in the eye.

So--share my thoughts
As you share my heart.

And smile with tremendous beam,
For, your gleam--will never fade.
Update on the MSUD Gene Therapy Project
Harbhajan S. Paul, Ph.D.

During the past few months, several critical and positive events have taken place for the MSUD research project.

We hope to obtain funding from the National Institutes of Health (NIH) to support this project on a long-term basis. After discussion with several very experienced researchers at the University of Pittsburgh, we arrived at the consensus that we should broaden the scope of the MSUD project. We feel that doing so will improve our chance of getting funding from the NIH, and ultimately developing an effective treatment for this disease. In addition to gene therapy, it was suggested that we should consider other approaches to cure MSUD. Accordingly, our revised approach for the treatment of MSUD in the mouse model now includes:

   a) Gene therapy  
   b) Liver cell transplantation  
   c) Embryonic cell (ES) transplantation

In light of these developments, we had to push back the gene therapy experiment that we had planned for the Summer of 2005. Since the submission of a major research grant application is planned, we need to obtain additional data to include in the grant application. Additionally, we are in the process of preparing our results to date for peer-reviewed publication in the scientific literature and need additional data on the characterization of these mice for this publication. We have limited availability of MSUD mice to perform all the studies. Most of the mice were used for gathering additional data in support of the NIH grant application and the manuscript. As soon as we gather the critical data, and sufficient mice become available, we will start the gene therapy experiment. The gene delivery vector for the gene therapy experiment has already been prepared and we hope to start this experiment soon.

Another positive development is that a graduate student (Kristen Skvorak) in the Department of Molecular Genetics and Biochemistry at the University of Pittsburgh has chosen to work on the MSUD project for her Ph.D. thesis research. She has already completed several important steps and is now engaged on a full-time basis on the MSUD project. She is very excited about the gene therapy for MSUD. It is very encouraging to see the interest of young persons in the MSUD project.

Researchers at other universities have recently contacted us about our MSUD mouse model. These investigators would like to study other approaches to cure the disease. We are very pleased and are looking forward to our collaboration with these scientists.

Dr. Gerard Vockley has recently joined the Children’s Hospital of Pittsburgh as head of Medical Genetics. We had meetings with him and he has agreed to advise us on several aspects of MSUD project. We believe his input will be very beneficial for the success of the MSUD project. Dr. Steve Strom, a professor at the University of Pittsburgh and an expert on liver cell transplantation, is also going to collaborate with us on the MSUD project.

The use of mouse embryonic stem cell to treat MSUD is being actively planned. This approach has recently been used to cure another genetic disease in mice. We are very encouraged with that study and are eager to try this approach with our MSUD mice.

In summary, although slowly, the MSUD project continues to make progress.
**Spanish MSUD Chat Group**

When my son Marlon was born four years ago and diagnosed with MSUD, I felt alone. He was the only person in the state of Alaska diagnosed with this metabolic disease. I was recommended to join the MSUD support group, and thanks to this group I learned very valuable information about this disease from the parents and guardians of children suffering from MSUD. I cannot imagine our lives in these last four years without the support of all of the wonderful families that participate in this group. They became our second family.

Later on messages were posted in this group. There were families from Spanish speaking countries that were hoping to find some support and help. The language was in many cases an impediment. Being born and raised in Spain, I felt for those in my country and other parts of the Spanish speaking world who had no way to communicate with other families that were living with MSUD. One day I thought I could form a Spanish MSUD chat group. The MSUD support group agreed to post my name and information on their website. I now receive phone calls and e-messages from countries such as Spain, Mexico, Honduras, Argentina, Peru and Chile. Some of these families are very desperate to obtain some help, and others just seek to meet someone that would share their situation. I feel great joy whenever I can help these families to connect with those of us living similar situations. Several families from Spain and South America have now joined.

If you would like to join the Spanish MSUD chat group, please send an e-mail to the following address:

**monicazf@yahoo.com**

**Grupo de charla sobre MSUD en español**

Cuando mi hijo Marlon nació hace cuatro años y le diagnosticaron con MSUD me sentí muy sola. El era el único en todo el estado de Alaska diagnosticado con esta enfermedad metabólica. Me recomendaron unirse al grupo de apoyo de MSUD, y gracias a éste, logré información increíblemente valiosa sobre esta enfermedad, la cual venía directamente de padres de niños y adolescentes que sufrían la misma enfermedad. No puedo ni siquiera imaginarme nuestra vida en estos últimos cuatro años sin el apoyo de todas las maravillosas familias que participan en este grupo. Llegaron a ser nuestra segunda familia.

Al cabo de algún tiempo llegaron mensajes al grupo. Estos venían de familias de países hispanohablantes que tenían la esperanza de encontrar apoyo y ayuda. Frequentemente el idioma se convertía en un impedimento. Al haber nacido y sido criada en España, me consternaba el saber que había familias con necesidad de apoyo en mi lugar de origen y otros países, quienes no tenían forma de comunicarse con otras familias que estuviesen viviendo con MSUD. Fue entonces cuando se me ocurrió la idea de formar un grupo de charla sobre MSUD en español. El grupo de apoyo de MSUD en los Estados Unidos aceptó a anunciar mi nombre e información en su página web. Hoy en día recibo llamadas telefónicas y mensajes electrónicos de países como España, México, Honduras, Argentina, Perú , Chile, etc. Algunas de estas familias se encontraban en situaciones desesperadas para obtener algún tipo de ayuda relativa a esta enfermedad. Otras, sin embargo sólo deseaban conocer a alguien más viviendo su misma situación. Varias familias de España, México y América del Sur, forman ahora el grupo de charla sobre MSUD en español.

Si desea unirse al grupo de charla sobre MSUD en español, por favor envíe un e-mail a la siguiente dirección:

**monicazf@yahoo.com**

Mónica Falconer  
Anchorage, Alaska

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**Pen Pals**

Any kids out there interested in talking with other MSUD kids?  
A new on-line group has been formed.  
Sign on, introduce yourself, compare experiences, and talk about whatever is on your mind.  
The address is: MSUDkids@yahooogroups.com.
Editor’s comment: The following is Mary Ann Peters perspective on her daughter Leanna’s pregnancy. It was reviewed by Leanna who gave her permission to submit it to the MSUD Newsletter. While pregnancy presents a metabolic challenge, we do not mean to infer that pregnancy is unsafe for all women with MSUD. This is a matter to be decided upon individually between each woman and her medical team. For another perspective on MSUD and Pregnancy, see the article about Sue Ann McKnight’s (MSUD adult) pregnancy in Vol 15, #2 Fall/Winter 97-98. The article can also be viewed online at www.msud-support.org

My name is Leanna Peters and this is my personal experience with giving birth to my son Almon on October 11, 2004 as told by my mother. My pregnancy was a horrible experience. I survived and gave birth to a beautiful baby boy.

LEANNA PETERS 9-MONTH PREGNANCY DIARY
By Mary Ann Peters

In January 2004, my daughter Leanna took a pregnancy test and learned she was pregnant with her first child. Here is a chronicle of the events.

Leanna was not strict with her diet before becoming pregnant, and all the foods she liked and would eat before now made her sick. She vomited every day.

She went to a regular OB/GYN physician at the beginning of her pregnancy, but in her fourth month was referred to a Maternal Fetal Medicine group of physicians at Yale New Haven Hospital. They monitored her very closely with many, many Level 2 ultrasounds and the baby progressed with no medical intervention. She was also referred to Dr. Margaret Seashore, MSUD specialist at Yale New Haven Hospital at this time. Dr. Seashore and her nutritionist met with Leanna monthly and monitored her leucine intake. They tried to convince her to eat properly and keep track of her leucine. Her leucine levels remained a bit elevated as she didn’t follow her diet, but luckily they never became dangerously high. She also caught several colds throughout her pregnancy, and eventually developed bronchitis because she was smoking off and on against her physician’s orders.

On October 8, 2004, three days before her due date, Leanna started having mild labor pains. As the hospital was an hour away I took her to Yale New Haven Hospital. The doctor examined her and found her to be one centimeter dilated. As she was a high risk, she stayed at the hospital and the doctors decided to induce her. She became very itchy, which the doctors said was a side effect from the epidural. She was given a sedative to help her sleep and keep her calm. By the 3rd day, she still hadn’t delivered. The doctors asked her if she wanted to have a cesarean section and she said she wanted the baby out now. She was prepped for surgery and at 11:40 a.m. on Monday, October 11, 2004, Almon Richard Barylski, III was born, weighing 6 lbs., 7oz, and measuring 19 inches long. He was a beautiful baby boy with a head full of blonde hair and blue eyes.

Leanna was in and out of consciousness as a result of the drugs she was given and could not hold her new baby boy. Her son spent less than a day in the maternity ward before being transferred to the neonatal unit because they could not stabilize his blood sugar, which caused him to vomit often. Because Leanna received high doses of dextrose during labor, the doctors think the baby became too dependent on the dextrose and was born with very low blood sugar. As a result, he was administered an IV and spent 3 days in ICU before being discharged.

After the delivery Leanne remained weak. She was frustrated with all the IVs that she received and the limitation of food as the medical staff tried to maintain her leucine levels in a normal range. After 4 days the doctors felt her metabolic condition was stable and she was discharged.

Two days later, Leanna started experiencing dizziness and vomiting. I told her to go the local hospital and I also called her MSUD specialist at Yale New Haven Hospital. She refused the IV the doctors advised because she had just been released from the hospital and remembered the many days with an IV. She went home that night, but the next morning I took her to Yale New Haven Hospital because she was still vomiting.

During the drive to the hospital, Leanna started hallucinating and screaming at me to put my brakes on. She did not know who I was or where she was. I immediately called 911 because she was getting more serious by the moment. The police sent an ambulance which took her first to the local hospital, and then to Yale New Haven.

Leanne’s leucine levels were at 9 and she was transferred to ICU for the night to stabilize her metabolic condition. She complained of seeing everything upside down and it really scared her. By the next morning her leucine levels started to drop and she was transferred to one step below ICU.

(Leanna cont. on page 7)
Leanna’s appetite returned and she was asking for food. Because her levels were so high, the dietitians would not give her the foods she desired. She became very angry and insisted on eating what she wanted. I explained to the dietitian that it was okay for her to eat the foods that she normally ate but in smaller portions. As a result, they made her happy and she started eating again and drinking her MSUD II. Her levels continued to drop, and she was discharged from the hospital. Her blood was monitored after discharge, and her levels continued to drop.

Leanna was very sick during those 3 days and we almost lost her, but she is strong willed and pulled through. As a mother, I worry every day that Leanna can go into metabolic crisis again and with no warning. I try to remind her everyday to drink her MSUD II drink and eat 3 meals a day.

She was lucky to survive this pregnancy, and I am very concerned about her getting pregnant again. Despite my concerns, she still insists on having another baby but agrees to wait until she is much older.

News from SHS North America

MySpecialDiet.com
SHS North America announces the launch of MySpecialDiet.com, a revolutionary metabolic diet management Web site dedicated to improving the lives of the metabolic community.

MySpecialDiet.com provides:
- Current and relevant information and research on metabolics
- A dynamic online diet management tool and helpful tips to help with diet compliance
- A community encouraging interaction among patients, families and healthcare professionals
- Best of all, membership is FREE!

Join this exciting online metabolic community by visiting MySpecialDiet.com!

SHS Becomes Exclusive Distributor of Milupa Products
SHS North America and Milupa North America are pleased to announce that effective November 1, 2005, SHS North America will become the exclusive distributor of the Milupa range of metabolic products. SHS and Milupa have teamed up to provide the best in clinical nutrition to the benefit of the metabolic community. SHS North America now offers the most comprehensive family of metabolic products to help improve diet management and diet satisfaction. Discuss with your healthcare professional which SHS or Milupa product is right for you.

SHS North America will distribute the following Milupa products: MSUD 2 • PKU 2 • PKU 3 • HOM 2 • OS 2 • TYR 2 and UCD 2. Please note that infant “1” formulations will be distributed until current inventories are depleted (expected in March 2006). Discuss with your dietitian or healthcare professional about transitioning to an SHS Analog infant formula or a Milupa stage 2 product.

New and Improved Maxamaids and Maxamums
SHS North America announces the availability of its improved Maxamaid and Maxamum range of products. Features include better tasting formulas and an updated vitamin and mineral profile, based on the new Dietary Reference Intakes (DRIs), published by the Food and Nutrition Board of the Institute of Medicine. To ease adaptation to these new formulations, SHS North America is proving a sample pack along with a transition guide. Contact your dietitian or healthcare professional to discuss transitioning or switching to the new formulations. Old formulations will be available for a limited time.
Jenna (14) and Jesse (12) Kiel are siblings with MSUD. Many of you have read their history in earlier Newsletters. So now as we are heading into the teen years, I’ve been asked to update you on their life. Carl & I have four children in our family, the two oldest Adam and Sara do not have MSUD. They are now both in college, at Michigan Tech and the University of Michigan respectively. Jenna was the first baby in Michigan to be diagnosed by Newborn Screening, so she was treated for MSUD at 5 days of age. Jesse has been treated as of birth, as we had an amniocentesis done. I could not even imagine life for them when I first heard the news. But 14 years later, we are doing much better than I had anticipated in those early days.

Jenna started high school this fall. This is a big change, as our kids go to a small school near our house, and high school is a blending of 6 schools with a class of 200 kids. She has loved it so far! Jenna drinks 20 ounces of formula throughout the day. She has formula before school, after school, and at night - so the diet is not really an issue at school. Her levels have been very low since school started. We did have a scare this summer. After a 2 week vacation, she started menstruation and her levels rose dramatically. She vomited twice, and we thought she was recovering at home, but her levels kept rising instead of falling. After a week, we checked into our metabolic clinic at Detroit Children’s Hospital and she went on IV fluids with saline, but never needed TPN. She was eating well, and we were back home in 4 days. I believe she was just completely run down, and then the hormones on top of everything else. This was her first hospitalization in 10 years – since she was in preschool.

Aside from MSUD, Jenna lives a normal teenage life. She loves to read, knit (she’s working on Christmas presents now), IM her friends on the computer, and she shares a weekly newspaper route with Jesse. People usually say they cannot believe she has MSUD. I spent parent teacher conferences at the high school educating her teachers about MSUD and Jenna. They were all surprised, Jenna does pretty well in school – she gets A’s in English and reading, but math and science……well, let’s just say they are not her favorites. Jenna will be taking Driver’s Training in the spring. We’ve already set parameters for driving - she must do more frequent DNPH tests and it must be clear for her to drive. She also wants to go to our church’s Youth Convention this summer in Arizona. So that will take a bit of planning for her diet and accountability.

Jesse is in 7th grade. He enjoys playing percussion in band, takes piano lessons and plays keyboard, and shares the newspaper route with Jenna. He recently bought a drum set and has now started a garage band with his friends. It’s a little noisy at our house during their practice!! Jesse is an excellent student, having been involved in Jenison’s Gifted & Talented learning program. He also was 4th runner up in the Regional Spelling Bee. He’s hoping this year will be his year to win. Jesse also drinks 20 oz of formula per day, but does not take it to school anymore. This is an agreement we made when the kids started middle school.

Both kids have spent a week at camp while in 6th grade. We coordinated the menu with the kitchen help, and it really worked out great! Jenna was voted “Best Camper” for being so responsible about her formula and diet. I believe our biggest challenges right now are: weight gain and hormones. Both kids have put on more weight since hitting puberty. I think all the calories from the formula plus the calories from the food they are eating are just too much. I know this is a common problem in the MSUD population. We have been working with our dietitian to make changes in their formula to lower calorie intake. Also, for Jenna the problem of monthly hormone fluctuations have caused elevated levels. We have adjusted her diet (lowered her protein just before her period) to anticipate for that, and things have been much better the last few months.

I am not trying to over-simplify life with MSUD. We have definitely been blessed that Jenna & Jesse’s defect allows them to eat more protein than many MSUD kids – they normally eat 10+ grams of protein per day. They also have been quite resilient to illness and high levels. We have had only 2 hospitalizations in the past 10 years. Until this summer, Jenna had not been in the hospital since she was 4 (over 10 years), and Jesse has had only 1 serious hospitalization which was 5 years ago. I believe life with MSUD has gotten easier past the toddler years. But I am like that rest of you. You always worry, you always wonder, and God gives you the grace and courage to allow them to live their lives. I think the hardest challenge for me as an MSUD parent is to let go. This requires a lot of training and educating of my children, and yet is SO rewarding when you see them making good decisions and choices on their own. Both kids want to go to college like their brother and sister. Oh boy…..more letting go!!!
**Root Beer Cookies**

1/3 cup Crisco shortening  
1/3 cup margarine (Blue Bonnet works best)  
2 tablespoons sugar  
1/4 cup brown sugar  
1 pkg (4 serving) instant pudding  
1 teaspoon root beer extract  
1/3 cup water  
2 cups wheatstarch  
1.5 teaspoons baking powder  
1/2 teaspoon salt  
1 teaspoon guar gum

Preheat oven to 350 degrees. In mixing bowl, cream shortening and margarine with sugars. Add pudding mix and root beer extract, mixing well. Bake cookies for 8-10 minutes. Test bake a cookie first to be sure you do not need to add wheatstarch if your cookie is too flat or more water if it is too thick. Makes 36 cookies.

**Frosting**

1/4 cup Crisco shortening  
2 cups powdered sugar  
2-3 tablespoons water  
1/2 teaspoon root beer extract  
Mix powdered sugar, Crisco and extract together. Add water till frosting is the right spreading consistency. Ice cookies.

**Protein** | **Leucine** | **Calories**  
--- | --- | ---  
Per cookie: | .1gm | 4mg | 120  
(with 1 tablespoon frosting)

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**Pumpkin Cookies**

1/2 cup Crisco shortening  
1/3 cup margarine  
(Blue Bonnet works best)  
2 tablespoons sugar  
1/4 cup brown sugar  
1 pkg (4 serving) instant pudding  
1 teaspoon vanilla  
2/3 cup canned pumpkin  
2 cups wheatstarch  
1.5 teaspoons baking powder  
1/2 teaspoon salt  
1 teaspoon guar gum

Preheat oven to 350 degrees. In mixing bowl, cream shortening and margarine with sugars. Add pudding mix and vanilla mixing well. Add pumpkin, wheatstarch, baking powder, salt and guar gum, mixing well. Test bake 1 cookie to make sure you do not need more wheatstarch or water. Makes 36 cookies.

**Maple Frosting**

1/4 cup Crisco  
2 cups powdered sugar  
1/2 teaspoon maple flavoring

Mix Crisco, powdered sugar and maple flavoring. Gradually add water till spreading consistency. Ice cookies.

**Protein** | **Leucine** | **Calories**  
--- | --- | ---  
Per cookie: | .1gm | 4mg | 120  
(with 1 tablespoon frosting)

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**Raisin Filled Cookies**

Raisin Filling  
3/4 cup raisins  
3/4 cup brown sugar  
3/4 cup water  
1.5 tablespoons wheatstarch  
Cook all together till thick.  
Cool.

Cookie  
1/2 cup Crisco  
1/3 cup margarine (Blue Bonnet works best)  
2 tablespoons sugar  
1/4 cup packed brown sugar  
1 pkg (4 serving) vanilla instant pudding  
1 teaspoon vanilla  
1/4 cup water  
2 cups wheatstarch  
1.5 teaspoons baking powder  
1 teaspoon guar gum  
1/2 teaspoon salt

In a mixing bowl, cream shortening and margarine with sugars. Add pudding mix and vanilla, mixing well. Add water, wheatstarch, baking powder, guar gum and salt, mixing well. On Saran wrap, shape into a log and chill for 2 hours. Preheat oven to 350 degrees. Remove dough from refrigerator and cut into 1/4 inch slices. Place slices on cookie sheet and add a teaspoon of filling on top of slices. Carefully place the remaining slices of dough on top of the filling, pressing the edges together. If the top slice of dough does not stick to the bottom piece, use a pastry brush and wet the edge of the top piece with water, then press together. Makes 24 cookies.

**Frosting**

1/4 cup Crisco shortening  
2 cups powdered sugar  
2-3 tablespoons water  
1/2 teaspoon root beer extract

Mix powdered sugar, Crisco and extract together. Add water till frosting is the right spreading consistency. Ice cookies.

**Protein** | **Leucine** | **Calories**  
--- | --- | ---  
Per cookie: | .2gm | 7mg | 145

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**Pumpkin Pudding**

1 cup canned pumpkin  
4 tablespoons cornstarch  
1/2 cup brown sugar  
1 cup Rich’s Coffee Rich  
1 teaspoon cinnamon

Combine all ingredients in blender until smooth. Bake at 350 degrees in baking dish until set. Serve with cool whip sprinkled with cinnamon.

Makes 4 servings.

**Protein** | **Leucine** | **Calories**  
--- | --- | ---  
Per serving: | .7gm | 43mg | 199
**Shake & Bake**

For breading vegetables for deep frying

- 3 cups wheatstarch
- 2 tablespoons salt
- 2 tablespoons brown sugar
- 2 tablespoons chili powder
- 2 tablespoons ground cumin
- 2 tablespoons black pepper
- 4 tablespoons paprika

Mix together and store in a tight container in the freezer. Dip vegetables in water and then shake in a plastic bag using the amount you need to coat your vegetables. Deep fry vegetables in oil heated to 375 degrees. Drain on paper towel.

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<th>Protein (g)</th>
<th>Leucine (mg)</th>
<th>Calories</th>
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<tbody>
<tr>
<td>Per recipe</td>
<td>1.2</td>
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<td>1640</td>
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<tr>
<td>Per 1/4 cup mix</td>
<td>0.1</td>
<td>7</td>
<td>102</td>
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<tr>
<td>Broccoli (2 Tbs raw)</td>
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<td>27</td>
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<tr>
<td>Cauliflower (4 Tbs raw)</td>
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<tr>
<td>Mushrooms quartered (1/3 cup) raw</td>
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<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Onion (1 ring) raw</td>
<td>0.1</td>
<td>10</td>
<td>12</td>
</tr>
</tbody>
</table>

**Apple Salad**

5 apples red and green diced
1 27 oz. crushed pineapple
2 cups Cool Whip
2 cups miniature marshmallows
1/3 cup sugar

Combine diced apples with drained pineapples, cook whip and marshmallows. Chill. When ready to serve, remove serving for low protein person and add 1/2 cup chopped pecans or walnuts to remaining salad. Makes 10 servings.

<table>
<thead>
<tr>
<th></th>
<th>Per recipe</th>
<th>Per serving</th>
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<tr>
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<tr>
<td>570 mg leucine</td>
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<tr>
<td>1780 calories</td>
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**Great New Snack Product**

By Sarah Foster

Over the last several years, great strides have been made in both the quality and variety of low protein foods. I can remember as a kid growing up with PKU having only two modified low protein food choices available: Aproten Spaghetti and wheat starch. Thankfully, those days are long behind us!

However, even with the advances and improvements to low protein foods in recent years, there was still no low protein food that satisfied my desire for a salty/savory snack and wouldn’t "break the bank" when it came to my protein allotment for the day.

As many of you know, I am a sales representative for Applied Nutrition Corp., the makers of Complex MSUD® & Energy Option®. I was lucky to have the ear of Rick Finkel, the owner and president of Applied Nutrition. Rick is a great person and always willing to help when he is able. He and Sandra Maltzman, the registered dietitian for Applied Nutrition Corp., went to work in the lab developing the first ever commercially available savory snack food specially formulated to have less than 1 gram of protein per serving.

I’m happy to be able to let the MSUD community know that Rick and Sandy’s work has resulted in a new product called Tangles®, by Maddy’s®. Tangles® are the little puff with the big crunch. They have the crispy texture and zesty taste we’ve been looking for And are available in three delicious flavors: Smokin’ Bar-B-Q, Salt & Vinegar and Original. They are packaged in a convenient 1 ounce Jumbo Grab bag with only 0.4g of protein and 25 mg of Leucine per bag, and look just like a snack grabbed off the shelf at your local convenience store!

If you’d like more information about Tangles® simply visit www.DietForLife.com or call 1-800-605-0410 and Nichole or Sonja will be happy to help you. I look forward to seeing all of you again in Dublin at the Symposium.
A Seat at the Dinner Table for Ethan
By John Jackson

On Thursday May 6th 2004 our lives were given yet another gift from God in the form of the birth of our second son Ethan Paul. It was in the early morning when we first saw his face. He was just as beautiful as we imagined him to be and so much more. Our family has now grown to two boys and a girl. My eyes fill with tears of joy even now just thinking of how much love my heart can hold.

We brought Ethan home on Saturday May 8th and he was a perfect baby. He was quiet, didn't cry much and slept really well. We thought, how lucky we were, his personality was so laid back we thought we just had a low-key baby. By the time he was six days old we started to feel that Ethan was just too quiet, slept too much, and just a bit too laid back. When he did cry it was more like a scream rather than a cry. Ethan just didn't seem right, he slept the night away with no interest in eating. We called our doctor with our concerns and even though their response was simply "that it was normal and he most likely had colic," we insisted that they see him.

That evening we took Ethan in and the next thing we knew we were heading back to the place he was born. So we arranged for someone to watch our three-year-old son and drove to the hospital. During the first four days he endured all kinds of test and we were given many different theories of why Ethan was not getting better and only getting worse, but no answers came.

A first-year doctor appeared to have a greater interest in showing how much knowledge of the medical textbook he had rather then making us feel confident that he would help our son. Also during these four days while yet another doctor was looking at him she witnessed Ethan have a seizure. Again our hearts continued to be ripped apart as we learned that we were not getting closer (so we thought) to bringing Ethan home.

Next came even more tests including an MRI and EEG. At this point Ethan was now nine days old and we hadn't even had the joy of being able to look into his eyes and allow him to look at ours because his eyes had been closed for about seven days now. By that time Ethan had lost his ability to suck so we had to place a feeding tube in him. One of the hardest things we have ever had to do was to accept that fact that this little tube was the thing, at this point that was keeping him alive. Later we would find out that was the thing that was also killing him. In retrospect that is a hard pill to swallow.

On the 10th day Ethan was moved to the PICU and we awaited the results for the MRI. The wait was hard and gave us little hope that we would get anything other than bad news. Sure enough Dr Fain explained to us that Ethan had something called Luco Dystrophy and was given just two weeks at the most to live. Our lives were shattered; the family that we thought we had, would now once again leave us a vacant seat at the dinner table. My wife and I said for the first time a prayer together out loud. We prayed for strength and to ease the suffering for Ethan, but at the same time we asked God if he could grant us a miracle for more time with Ethan. Then the miracle happened! Dr. Fain looking for a better answer had given us hope for the first time. He asked us if we noticed a sweet smell with Ethan and right away we both said yes. Three hours later, Dr. Fain spending all that time on the phone, said he thinks Ethan has MSUD (Maple Syrup Urine Disease). Next thing we knew we were following an ambulance carrying Ethan to Ann Arbor.

The next day after arriving at Mott's Children's Hospital our world and faith again would be put to the test when Ethan stopped breathing and was put on a respirator.

At that point we thought we were going to lose our son, but the miracles kept on coming. Ethan was taken off the breathing machine the next day. After meeting with Dr. Carlson the metabolic Neurologist on the 11th day we finally had the answer that Ethan has MSUD and Dr. Carlson knew just how to make him better.

While still having a feeding tube and in a coma, Dr. Carlson gave Ethan a special formula called Kenotex. A day or two later he opened his eyes for the first time, then the next day he moved around and soon started to take a bottle by mouth. This may sound strange, but my wife and I were fighting for who gets to feed him in the middle of the night, so we both did it together. And loved every minute of it. Then Ethan did something that we didn't even realize that had never done before. We heard his voice for the first time. A beautiful coo! We cried tears of joy for the first time since he was born.

Now we are home and without the feeding tube. Our quiet, low-key baby is now not so low-key and not so quiet. Ethan smiles all the time, he loves to play with his bother and sister and talks to anyone who is around to listen. It is still unknown what the long-term effects will be with Ethan but he is growing like a weed. He rolled over at 3 months and is meeting or exceeding each milestone with flying colors. Ethan also started walking at 1 year. There is no greater joy to know our Family is now complete. There will always be a seat at the dinner table filled by Ethan.

Ethan is home, for the first time he is where he belongs and is still that perfect baby we first fell in love with on that early Thursday morning May 6th 2004.
Our MSUD Family Scrapbook

Jordan Bulcher, 16 years old with Classic MSUD, participated in the state marching band finals with the Olentangy Liberty High School Marching Band. The band received the highest rating, Superior!

Elan Geffen has fulfilled a lifelong dream of becoming a Volunteer Fireman! He is part of a special Rehab Unit that responds to fires and “Serves Those Who Serve” by seeing to it that firefighters stay hydrated and fed in order to perform their duties. Deer Park Unit 8 in Cherry Hill, NJ responds at all hours, day or night with their well equipped vehicle shown above. Elan is 21 years old with Classic MSUD.

Oliver Patterson, 12 years old, holds a trophy he earned as being first in his class chosen this semester as Student of the Week, for “determination to progress in all areas”! Oliver, a Variant MSUD, attends school in Qatar while living there with his family.

The Patterson Family, Bernie, Gabriele, Oliver and Eric, are presently living in the Middle East- very far from their Canadian homeland!
Their travels have taken them to Austria, Sri Lanka, India... just to name a few!
See article on page 14.

To share accomplishments (large and small) with your MSUD Family, send photos with caption to: agcreative1@aol.com or Adrienne Geffen, 1025 Red Oak Drive, Cherry Hill, NJ 08003
dramatically improved the quality of life for patients with MSUD, but it is far from a cure. Researchers are looking at many different ways to improve therapies for patients with MSUD. Some of this research is focused on gene therapy and liver transplantation, therapies that might be useful for many diseases. Others are more specific to MSUD itself.

Many NIDDK-funded Investigators are working to try to improve gene delivery to the liver. This approach, once perfected, should be applicable for delivering the genes for many genetic conditions including the genes responsible for MSUD. Two vector systems are currently showing promise in animal models. One vector is based on a modification of an adenovirus vector. This vector, called a helper-dependent adenovirus, has all of the adenovirus genes removed. In an animal model, genes delivered with this vector were expressed for over a year. Another promising vector is a new form of adenovirus associated virus, AAV type 8. This form of AAV has been shown to be more efficient in transducing liver cells than other forms of AAV. Both of these vector systems are undergoing toxicity testing in preparation for trials in patients.

Several recent advances have expanded our knowledge on MSUD and may provide new avenues for treatments. There are 6 genes that encode subunits of the BCKD complex. By studying the mutations that cause MSUD, investigators hope to gain a better understanding of the interactions between these proteins. Recently, NIDDK-supported investigator Dr. David Chuang at the University of Texas investigated the mutations that cause MSUD in an Israeli population that has a relatively high incidence of MSUD. They were able to define the mutations in 8 patients. Although some mutations totally disrupt the function of the protein, others prevent proper folding and assembly of this enzyme complex. In cases where the protein is made but not properly folded, it may be possible to increase the amount of functioning protein. In these patients, a mutation was described that could be treated with high doses of the cofactor thiamine, which helps the complex to assemble and become active, reducing the severity of the disease. By comparing these patients with other patients with the thiamine-responsive form of the disease, Dr. Chuang has determined that the presence of one E2 expressing allele is diagnostic for the thiamine-responsive form of the disease. This discovery identifies one group that can benefit from a method to increase protein folding and assembly. Other molecules that increase folding are currently being studied as potential treatments.

Another possible lead for treating MSUD was found by an NIDDK-supported investigator, Dr. Brendan Lee, at Baylor College of Medicine when studying another rare disease. Dr. Lee was studying the effect of the drug, Buphenyl on the metabolism of patients with urea cycle defects. Dr. Lee found that this drug therapy reduced serum branched chain amino acids in these patients. Since the branch chain amino acids accumulate in MSUD, this drug may also be useful in the treatment of MSUD. Dr. Lee is beginning a clinical trial with this drug for MSUD. Anyone interested in more information regarding this project can contact Sandy Bulcher.

These are two specific examples of research that could lead to improved treatments for MSUD. You can find more details on these studies in the references below:


April 12, 2002 was a wonderful day for my husband, Dean and I. We were welcoming our first child, a little boy into the world. Derek Lawrence Jones was born that night and to us, seemed to be the perfect baby we had waited so long to meet.

At about 5 days old, we were convinced that we had a baby with colic or one of those other “normal” newborn issues. He would only sleep for around 10 minutes at a time and he eventually stopped feeding. We were called by our doctors’ office and told that the newborn screen had come back and would need to be re-tested because there seemed to be a “lab error” showing that Derek had a very rare condition called Maple Syrup Urine Disease (MSUD).

After being re-tested, we were called again on April 24th and were told to take him to Children’s Hospital Medical Center of Akron where he was going to be directly admitted for treatment. Naturally we were in a state of denial and disbelief. After about four hours, we were called and told that Derek was now in a comatose state and needed to be life-flighted to Rainbow Babies and Children’s Hospital in Cleveland, Ohio. Derek was admitted to the NICU at 1:00am on April 25, 2002. This is where we met the doctor who we believe saved our son’s life, Dr. Douglas Kerr.

Dr. Kerr, along with his many wonderful colleagues and Derek’s dietician, Judy McConnell who have become a constant and wonderful part of our lives. Derek is now 3 and a half. He enjoys playing with his younger brother, Adam, who will be 2 on February 1st. Derek just recently started going to Sunday school and will be playing his first year of soccer coming up in the Spring of 2006.

We, as a family are dealing with the everyday questions and concerns of raising a child with MSUD. However, just this past September 22, 2005 we held our first fundraiser to help the search for the cure. We held a reverse raffle and raised $4,650.00. As an extra added bonus we were able to meet Dave and Sandy Bulcher, who were kind enough to drive 2 hours to our town of Barbenton, Ohio for our fundraiser.

We plan on continuing to help raise money each year to help improve the quality of Derek’s life and all of those affected by MSUD.

The Jones Family, Dean, Amy, Derek and Adam

Oliver in the Middle East  By Gabriele Patterson

How do you travel across the world to a vastly different country with a child that has MSUD? With VERY careful planning and the help of many people. It was a big decision to move to Qatar as we did 2 years ago. It was a lifestyle decision. We wanted to show our then 9 1/2 year old twins Oliver (Variant MSUD), and Eric that there is a big world out there, and from small town Canada, this was not always easy.

The planning was a nightmare, and without the good people from The Calgary Children’s Hospital, the move would not have been possible at all. Our dietitian sat down with me and gave me a crash course in calculating formula. Oliver takes his formula via a G-tube, and the little crate that we shipped was full of his supplies: 3 pumps, 100 feeding bags for the pump, syringes, a year’s worth of low protein flour, formula and the usual paraphernalia. I also contacted a physician in Saudi Arabia before the move to make sure that sufficient expertise is available in this part of the world should Oliver get sick.

Living and traveling here is interesting, and we have also traveled extensively since our move. As a family, we have visited Sri Lanka, Kenya, Tanzania, India (that trip gave me some concern) and Egypt. Two summers were spent traveling 7 weeks each through Germany and Austrian and one week in Paris. No problems so far (other than I got REALLY, REALLY sick in India. Oliver was fine!). Everywhere we go, there are french fries or some sort of other potatoes and rice. I pre-bake the bread and brownies and take them from hotel freezer to hotel freezer.

The hotel and kitchen staff has been always exceptionally accommodating. In Tanzania, the young waiter and the dining room supervisor were absolutely aghast at the sight of the g-tube and his dietary limitations and took it upon themselves to come up with the best alternatives to what we were eating. They really rose to this challenge.

Oliver’s level of control has been good. We do not get very many blood tests done as they come 4 weeks late or not at all, so I have to judge a lot by his actions. I am very careful with his diet. Another difference is the expense. In Canada, the Government paid the aid for Oliver. Here, we foot the bill. (See photos on page 12)
My name is Bernardo Villela. I am twenty-four years old and I have Classic MSD. My daily routine is rather simple. I have my formula three times a day: breakfast, lunch and dinner. I watch my protein intake never consuming more than twelve grams per day. MSD is not something I think of that much because I don’t feel it really impedes me. I haven’t really felt that MSD has complicated my life since I was very young. I haven’t been hospitalized in eleven years, and the last time was due in part to the fact that I had chicken pox. The way I look at it, and what I usually tell people, is that I have a special diet because that’s all it feels like most of the time.

I recently graduated from C.W. Post- Long Island University with a BFA in Film. During my two years there I was on the honor roll three out of four semesters and made the Deans List in my senior year. I had previously attended Fairleigh Dickinson University- Madison for four years where I became well versed in film theory and screenwriting before transferring to C.W. Post to focus on the production aspects of film.

This summer I wrote and directed Suffer the Little Children a non-commercial, non-exclusive adaptation of the Stephen King short story by the same name. I acquired the rights over a year ago and lead the film from casting all the way through to the final edit. The film will be going on the festival circuit in 2006 (www.sufferproductions.com). I am currently employed at Stonestreet Studios in New York, as a director, editor and instructor. Stonestreet is a conservatory which teaches film acting to theater students and works in conjunction with New York University- Tisch School of the Performing Arts.

The older I’ve gotten the less I’ve thought about MSD. Sometimes I go for days without even thinking about the fact that I have it. I take good care of myself and am very aware of what I need to do to keep my levels down. All in all I haven’t let MSD get in the way of what I want to accomplish. I’ve set goals for myself and I’m determined to achieve them.

My daughter Hannah Dolins is 11 years old and has Classic MSUD. This year she began Middle School. When she was younger, she was hospitalized due to infections that raised her leucine levels once or twice a year. Treated with IV's including BCAA-free amino acid solutions, she always recovered well. She has not been hospitalized for almost 2 years now. She followed the growth curve at about the 50th percentile for weight and 25th percentile for height. In the past couple of years her rate of growth increased, and she is now at the 50th percentile for both height and weight.

With the pre-teen years has come an impulse to experiment. From time to time she asks for foods that she knows she can not have. She says she wants “just a taste,” but we worry that she would try to test her limits by having more. We try to explain to her that she’s better off not tasting these foods.

Hannah does not have a large appetite. Perhaps this is why we have not found it necessary to use special low protein products. She eats a small frozen waffle for breakfast. Lunch is often 20 grams of whole wheat bread, and for dinner she will have a little rice, pasta or potato. Fruits and vegetables are added to this. She currently has an allotment of 550 mg leucine, which she gets from these foods. She has a small scale which she can carry with her to school and to restaurants.

Hannah loves to read. She taught herself to read before kindergarten. As she has gotten older and schoolwork has become more complex, she has had more difficulties. Her biggest challenge, and the area in which she needs the most help, is remaining organized. Her locker needs to be cleaned out regularly. I often receive papers long after I should have.

Hannah has participated in team sports including softball, basketball, and soccer. While she enjoys these sports, she took the last year off and now has been taking horseback riding lessons. She also enjoys theater, and has spent the last 2 summers in a theater program at a local college. Hannah dreams of being able to go to sleep-away camp like her brother and sister. At this point, we don’t see how this would be possible.

She is a member of the MSUD kids email group, and would love to hear from other MSUD kids. (See Page 5 to learn how)