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MSUD NEWSLETTER

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SAVE THE DATE!

MSUD Symposium 2008

will be held on **June 26-28,2008** at the Columbus Embassy Suites in Columbus, Ohio

Plan ahead to join us!

Editor's Message

Karen Dolins, EdD, RD, CDN

Mom to Hannah, Age 13

All of you who read this newsletter twice a year probably do so for a variety of reasons. Some get comfort from knowing that they're not alone in dealing with MSUD, and enjoy reading stories written by individuals describing how they or their loved ones live with the disease, while others look for practical advice such as recipes and products. Many of us are eager for news about advances that will allow us to put MSUD behind us. Two such advances are in the areas of liver transplantation and genetic engineering.

This issue of the newsletter includes an update on medical therapy and encouraging news on genetic research. Past issues have explored liver transplant as an option (see Summer 2006 for the article written by Dr. George Mazareigos for more information on liver transplantation). Our organization does not take a position on whether liver transplantation or genetic engineering is in the best interest of our population. This is a very emotional issue for most of us, and a personal one, and we must continue to respect one another's opinions regardless of whether we agree with them.

(Editor's Message *cont. on page 2***)**

TOPIC: Genetic Research & Medical Therapy

New Treatments for Metabolic Disorders: What about MSUD?

Paul M. Fernhoff, MD, FAAP, FACMG

Medical Director, Emory Medical Genetics

During the past several years, new treatments for some metabolic disorders have become available that eventually might be used to treat MSUD. This is a brief overview of two of these new treatments. One is called "Enzyme Replacement Therapy" [ERT] which is now used to treat several lysosomal storage disorders [LSDs]. LSDs include disorders such as Gaucher and Fabry Syndromes. Another technology called "Chemical Chaperone Therapy" [CCT] is in the early stages of trial for use in LSDs and other metabolic disorders.

Would either ERT or CCT work in MSUD? First a very brief reminder of what happens when someone has MSUD. You have heard many times that a person with MSUD lacks an enzyme called branched chain alpha-ketoacid dehydrogenase [BCKAD]. This enzyme is found in large amounts in the cells of our liver and kidneys. BCKAD helps our bodies break down leucine, isoleucine and valine, amino acids found in nearly all natural sources of protein.

What is an enzyme? An enzyme is a large protein made up of many different amino acids. The amino acids are carefully assembled in a certain order to make an enzyme.

(Fernhoff, MD *cont. on page 2***)**

Inside This Issue:

(Fernhoff, MD *cont. from page 1***)**

This assembly occurs in a part of our cells called the endoplasmic reticulum [ER]. Think of the ER as an assembly room where enzymes and other proteins are made. Thousands of different enzymes are assembled in the ER. It's a very busy part of the cell. After assembly, BCKAD leaves the ER, and goes into other compartments of the cell called the mitochondria, the power plants of the cell. Once inside, and in its proper place in the mitochondria, BCKAD breaks down leucine, isoleucine and valine to other chemicals and to energy that is needed by our body.

The main current treatment of MSUD is to limit the amount of leucine, isoleucine and valine in the diet of an MSUD affected individual. This prevents the build up of these amino acids and their toxic byproducts. It's a treatment, but not a cure.

Why can't we just give someone with MSUD the missing BCKAD enzyme? Several problems. First you need to make large amounts of purified BCKAD. That's difficult, but not impossible. Second how would you give it? If given by mouth, most of the BCKAD protein would break down in the acid of the stomach. Any BCKAD not broken down, still would not be absorbed intact from the intestines into the body.

What about injecting BCKAD directly into the blood stream? This is how ERT works to treat those individuals LSDs. The critical difference is that the enzymes that are used to treat people with LSDs are modified to be taken up directly by the certain cells and organs of their body that are most affected in the LSDs. If ERT is to work in MSUD, the BCKAD would need to first be modified so it could be taken up by cells in the liver and kidney, and also modified so that the BCKAD goes into the mitochondria, the cell's power plants. It's possible, but probably years away.

Of course liver transplantation has been successful in a number of patients with MSUD. A new liver, with normal BCKAD activity, effectively "cures" MSUD, although genetically they still have the disease. However given the risks of liver transplantation and the need for long-term immunosuppressant drugs, it is still being debated as to which MSUD patients are the best candidates for a liver transplant.

What about "CCT? This works differently. Many individuals who are affected with an LSDs or with MSUD do not actually lack the enzyme. They make an imperfect, but still workable enzyme, that is trapped inside the ER, the cell's assembly room. Taken by mouth a drug, called a chemical chaperon, combines with the trapped enzyme and allows the trapped enzyme to escape the ER and get to another part of the cell where it can work. Would CCT work in MSUD? We know in some patients with MSUD, taking large doses of thiamine [Vitamin B1], helps to increase the activity of their imperfect BCKAD. This is a similar concept to CCT and it just might work in MSUD. Currently chemical chaperons are being studied in laboratories and animal models to determine their safety and how well they will work in different genetic/metabolic disorders. Once proven safe and effective, hopefully we may have another way to treat some patients with MSUD. Stay tuned! ■

(Editor's Message *cont. from page 1***)**

Putting together this newsletter requires a great deal of effort from a number of people. I rely heavily on the guidance and assistance of Joyce Brubacher, my predecessor, Adrienne Geffen who prepares the layout, and Sandy Bulcher who helps with content.

As editor, it is my job to solicit writers. We generally include a medical update, recipes which are supplied regularly by Glenda Groff, and MSUD family news which comes from all of you. Some newsletters have a theme. After a symposium, of course, we always summarize the presentations for those of you who were not able to attend. In our Winter 2007 issue, we presented a look at "MSUD Treatment Around the World."

In my role as editor, I have become aware of issues which face us all, and feel motivated to make a difference. Our hearts all break when we hear of children whose health is impaired due to the inability to access metabolic formula. Our support group tries to do what it can. We are committed to providing formula to those in need, although we can only do so on a short-term basis as a stop-gap until the family is able to make more permanent arrangements. This task is made more difficult by the rules and regulations regarding the import of metabolic food in individual countries. Kay Larsen has been selflessly giving a great deal of her time and energy to making this happen.

We would like to do more. We would like to work with formula companies more closely, and apply for grants that would ensure that no child with MSUD anywhere in the world suffers from lack of formula. We would like to be a resource for parents struggling to ensure that their children's educational needs are met in school, and for those dealing with emotional issues related to chronic disease. But to accomplish these goals would require a commitment from more of you.

Just as this newsletter is more powerful when we hear from more of you, so will be our support group. Please volunteer: to contribute to the newsletter, to work on access to formula, to serve as a member of the board, to identify a need and fill it. After all, the more we give the more we get.

Finally, I am incredibly proud of my daughter Hannah, who became a Bat Mitzvah this year at the age of 13. In the Jewish religion, once a child becomes a Bar (boys) or Bat (girls) Mitzvah, they are responsible for their own actions, both good and bad. Hannah raised funds for our MSUD formula fund as part of a Temple social action project, and has also pledged to donate 1/3 of the money she received as gifts to the fund. Perhaps this is one of the benefits of volunteerism: we model social consciousness for our children.

Volunteering brings us closer to each other. I hope to get to know more of you as you do what you can to keep our organization, and our support for each other, strong. ■

MSUD Board Members Visit Dr. Susan Hutson

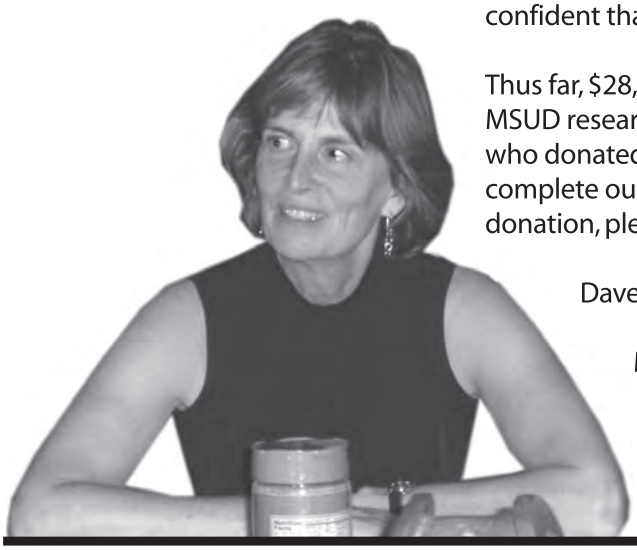
Several MSUD board members traveled to Winston-Salem, NC in March 2007 to meet with Dr. Susan Hutson and her staff. The purpose of our visit was to learn more about her MSUD research. Those present were Wayne, Joyce, and Shayla (MSUD) Brubacher from IN, Ivan and Mary Kathryn Martin from PA, and Dave, Sandy, and Jordan (MSUD) Bulcher from Ohio.

▲ *First row: (from left to right) 2 of Dr. Hutson's staff, Mary Kathryn, Joyce, Shayla, Jordan and Dave. Second Row: (from left to right) 1 of her staff, Ivan, Dr. Hutson, another staff member, Wayne and Sandy.*

We met Sunday afternoon March 25th at a local hotel. From there we went to Dr. Hutson's home for a social evening complete with spaghetti dinner, regular and low protein. We enjoyed getting to know Dr. Hutson and appreciated her hospitality.

The following morning, Monday March 26th, we met Dr. Hutson at Wake Forest University. Dr. Hutson and her staff presented their plans for developing MSUD mouse models. (See Dr. Hutson's article in this newsletter for details) Our visit concluded with a question and answer session. Dr. Hutson and her staff were eager to learn more about daily life with MSUD. Shayla Brubacher and Jordan Bulcher answered questions such as, what can you eat?, does your formula taste good?, and what do you feel like when your leucine is elevated?. The professionals seemed genuinely interested in understanding life with MSUD.

We want to thank Dr. Hutson and her staff for sharing their research plan with us. We are excited that several teams of researchers in the US are interested in developing better treatment options for MSUD and feel confident that breakthroughs are on the horizon.



Thus far, $28,884 has been donated to Dr.Hutson's research from those interested in MSUD research. A special thanks to Dean and Amy Jones, MSUD parents from Ohio, who donated $4,800 through fundraisers. A remaining balance of $6,116 exists to complete our commitment to Dr. Hutson. If you would like to make a tax deductible donation, please send check by December 2007 to:

Dave Bulcher, MSUD Treasurer, 82 Ravine Rd, Powell, Ohio 43065

Make check out to: *MSUD Family Support Group*
(write Dr. Hutson's research in the memo area)

As always, thanks for your support,
Sandy Bulcher, Director MSUD Family Support Group

When Things Go Wrong (*Author Unknown)*

When things go wrong, as they sometimes will,
When the road you're trudging seems all uphill,
When the funds are low and the debts are high,
And you want to smile, but you have to sigh,
When care is pressing you down a bit-
Rest if you must, but don't you quit.

Success is failure turned inside out -
The silver tint in the clouds of doubt,
And you never can tell how close you are,
It might be near when it seems afar;
So stick to the fight when you're hardest hit -
It's when things seem worst that you must not quit.

MSUD IN RUSSIA

By Anna Kursaeva
Translated by Irene Yusim

Russia is a very big country, but there are very few confirmed cases of MSUD. I am convinced that this is because children died undiagnosed rather than that few children with this disease are born. When my daughter **Nadya** was born 6 years ago, I was told that she was the first child with MSUD in Russia.


Nadya


Nikita

Nadya was born in February 2001. She appeared a healthy girl with good weight of 3900grams (8.5 pounds). She was actively breastfeeding. A few days later she stopped to breastfeed, cried non-stop and by the tenth day she was in a coma. Doctors in my local hospital suspected internal bleeding. The closest intensive care unit for babies was in Moscow (over 1 hour away) and Nadya was transferred there. She ended up in one of the best children's hospitals in Russia. But even there, it took 2 months to get the right diagnosis of classic MSUD. (As a side note, health care, as everything else, is centralized in Russia. That means that the better hospitals are in bigger cities and the best hospitals and best services are in Moscow, the capital of Russia). Nadya spent 3 weeks in a coma and 2 weeks on a ventilator.

After the diagnosis, it took 4 weeks to receive MSUD formula ordered from the UK. Only by 6 months did Nadya regain her birth weight of 3900g. She was in the hospital for 9 months. When I brought Nadya home, doctors were pessimistic about her prognosis. I put all my energy into Nadya's rehabilitation. She received massage therapy, physical and speech therapies along with other therapies. We went to special in-patient rehab centers several times a year for intensive therapies. Nadya was followed by a whole team of doctors including a specialist in genetics, specialist in kidneys, neurologist and a dietician. Unfortunately, late diagnosis and the prolonged period without formula left Nadya with a severely damaged nervous system, kidneys and liver. By the time Nadya was 5, we had to stop massage and other intensive therapies because of her severe seizures. She is now doing a very mild regimen of exercises at home. Problems with her kidneys and digestion lead to constant toxic levels, vomiting and very poor appetite.

Looking back, I realize that there was no chance for things to turn out any better. At the best children's hospital, doctors knew nothing about MSUD. I did find out later that there was one diagnosed case of MSUD in 1994. Due to the financial crisis in our country at that time, neither parents nor the government were able to provide the baby with the formula. The child stayed on IV and died at 6 months.

There have been two more cases of MSUD in Russia since Nadya's.

In 2002, in St. Petersburg (second largest city in Russia), was born a boy, named **Egor**. He was diagnosed at 1 month and received formula a week later. Scared of the financial responsibilities, his parents gave him up to an orphanage. I personally was in contact with his doctors and he received pretty good care. In 2006, the frequency of his crisis increased. He was in a coma several times, and during the last episode he passed away. Egor lived only 4 years.

In 2005, in Siberia, another boy, **Nikita**, was diagnosed with MSUD when he was almost 6 months old. He spent 6 months in a hospital, 1 month in a coma and on a ventilator. Formula was immediately delivered to him from Moscow by plane. He likely has

(MSUD in Russia *cont. on page* **5)**

Member Stories

Amanda Andraos

My name is Amanda Andraos; I am 19 years old and have MSUD (Maple Syrup Urine Disease). I was diagnosed at 9 days old by doctors at the University of North Carolina hospital, and have been closely monitored since then. My early years in school, weren't very difficult; I would take my formula in a container and just add water and drink it with my lunch. As for the food, kids used to ask why. I would simply say its how God made me. Dealing with my diet as I got older became a lot easier, simply because I became more dependent on myself instead of on my parents. I would love to say that from my experience my parents were very helpful while I was younger and now that I'm depending on myself I have learned so much. I graduated high school in 2005, and then I went straight to college. I started out at a community college to get my electives out of the way and now I'm attending the University of North Carolina at Greensboro and plan to major in nutrition. I chose nutrition due to the fact that my nutritionist Dr. Diane Frazier has been a great help with keeping up with my records and helping me learn how to take care of my own dietary needs. She has been there for me when I needed her for a simple recipe or even to ask why I am limited to only a certain amount of protein a day. Her motivation and understanding has changed my view on life and I would love to help younger children that suffer from any metabolic issues to become independent like she helped me. Another dream of mine is to help younger children with MSUD or PKU understand that it's not a disorder, it's life. You are able to do what you want if you put your mind to it. I attended the metabolic camp last year and saw that some of the girls were down about having their disorders, but the counselors set the bar high and showed the girls it's not a burden to life it's a gift from God and we need to take it and make it our own. By making it our own I mean to make something of oneself. Be who you want to be. ■

(MSUD in Russia *cont. from page 4***)**

a milder form of MSUD with Leu tolerance of 700mg/day. That is why he was able to survive such a late diagnosis. He is very lucky with his parents – his mom is a doctor and has knowledge of German. She is able to communicate with German doctors through email.

The reality is that children with rare genetic disorders in Russia will remain at a disadvantage, far behind other countries, for awhile. Diagnosis is only possible in the few largest cities where lab equipment is up to the standard. Long-term care that includes amino acid tests and follow-up with specialists is practically not available anywhere but Moscow. Even in St. Petersburg, the second largest city in Russia, BCAA was only available with combined values for Leu and Ile. A blood sample of the boy born in Siberia was delivered to Moscow by plane to figure out his BCAA levels. Fortunately, DNPG tests and keto-stix are available for purchase through the Moscow lab.

Luckily, we live not too far from Moscow, so that we are able to track Nadya's BCAA levels. Nadya is followed by a geneticist who is familiar with metabolic disorders and a dietician who works with children with PKU. Nikita is also followed by a geneticist in his town, however, there are no highly specialized doctors there. His mom develops his diet plan and consults the German doctors for difficult questions.

Government help and protection for our children is also minimal. A law adopted in 1994 gives federal financial help to people with genetic disorders such as PKU and diabetes. However, MSUD is not one of the diseases listed and our hope of changing the law for the very few children is very, very slim.

The federal government leaves it up to the city to help out children with MSUD. The available help varies widely, depending on the city. My small town pays for about 10-12 cans of formula a year. Nikita is getting all of his supply paid for by his city. I rely on charitable funds. It is a real life savior for Nadya. Another problem with the city help is that they are only allowed to buy formula produced by SHS, since only that formula is approved for sale in Russia (that approval took me a lot of work in the first year of Nadya's life). However, now Nadya is doing better on Ketonex, the city is not able to purchase it for me.

The fact that the MSUD formula is available for sale in Russia is a big step forward. In 2001, it took me 4 priceless weeks to get the formula from the UK. By comparison, both Egor and Nikita had the formula available to them within days. Other small changes have taken place over the last 6 years. More information about MSUD is available. Nadya's case is described on the internet. We are known by doctors, dieticians as well as the SHS employees in Russia. I was able to offer help with information (a lot of it from the egroup and MSUD website) to Egor's doctors and Nikita's mother. My mother and I have translated many articles on treatment of MSUD from English to Russian. Our hope is to one day creating a website with these articles and other information on MSUD in Russian.

In conclusion, I would like to express my most sincere thanks for all the help and support to all members of the e-group. A special thank you to Joyce Brubacher who did so much for us in the most difficult first years of Nadya's life.

Egor's Short Life in Russia

By Mrs. Wayne (Joyce) Brubacher

Anna, the mother of a little Russian girl with MSUD, with whom I had been in contact (see article by Anna, MSUD in Russia, in this issue), sent me an urgent request for help on March 31, 2002. She was deeply concerned about a one month old baby boy in St. Petersburg, Russia who had just been diagnosed with MSUD. Egor's parents felt unable to take on the responsibility of a child who would require a lot of intensive and expensive care, and they were giving him up. The doctors were not well acquainted with MSUD, and Egor's future looked bleak.

My heart was touched with the plight of this child. I wrote about the need for a home for Egor in the Vol. 21 No. 2 issue of the MSUD Newsletter and put a notice on the MSUD Family Support Group website. Irene Yusim, a friend of Anna's in the United States, spent many hours communicating with adoption agencies and potential families. Several families showed interest in adopting Egor but eventually gave up. Families adopting from Russia are not allowed to meet the children until all the paperwork is done. This, along with the high cost of international adoption, Egor's delayed development, and the need to learn how to care for a child with MSUD, discouraged families from adopting him.

After spending 6 months in a hospital, Egor lived in one of the best orphanages in Russia until the age of four. He was then transferred to a specialized facility for handicapped children. A Russian family in Finland, through a Christian charitable organization, purchased formula for Egor and delivered it to the orphanage.

Although Anna lived a long distance from Egor, she was very instrumental in his care. She supplied some of her own formula immediately after his diagnosis and sent the first supplements of isoleucine and valine. Throughout Egor's life, Anna stayed in contact with his doctors providing them with information she had learned from her own research and from contacts with doctors and dietitians in other countries. These doctors highly respected her opinion. She eventually took a long train ride to visit Egor and took pictures of him to show potential adoptive families.

Egor passed away near the end of last year (2006). It is so sad that no family could be found to adopt him. As Anna wrote to me, "All the qualified care Egor received cannot substitute for the personal attention any child needs. In Russia, handicapped children do not get adopted. A lot of healthy children live in orphanages. Egor's only chance was to find someone through the MSUD group." We failed to find a home for him, but his life was not in vain. Russian doctors in St. Petersburg now have more knowledge of MSUD which may benefit others in the future. May God bless Anna and Irene for all they are doing for the cause of MSUD in Russia. ■

On the subject of VOLUNTEERING:

We get to make a living; we give to make a life. - Winston Churchill

The best way to find yourself, is to lose yourself in the service of others. - Ghandi

The unselfish effort to bring cheer to others will be the beginning of a happier life for ourselves. - Helen Keller

Nothing liberates our greatness like the desire to help, the desire to serve. - Marianne Williamson, Author/Lecturer

A person's true wealth is the good he or she does in the world. - Mohammed

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DON'T BE LEFT OUT!

Become a member of the MSUD egroup. The only requirement is that you are a member of the MSUD Family Support Group. To join the MSUD eGroup, send an email to the moderator, Emily Talley at **emilytalley@mindspring.com** requesting to join the egroup.

To become a member of the MSUD Transplant eGroup go to the link **http://health.groups.yahoo.com/group/msudtransplant/** and search for msud and liver transplant. You can also email Oula Haddad at **jhaddad1@yahoo.com** requesting to join the group.

SPANISH MSUD CHAT AND SUPPORT GROUP - A MULTINATIONAL FORUM

By Monica Falconer
Mother to Marlon, 6 years old, transplanted on 3/31/06
Coordinator of the Spanish MSUD Chat & Support Group

It has been four years since I decided to form a Spanish MSUD chat and support group. Two years after the diagnosis of my son Marlon with this disease, and with the support of the MSUD English group, I came to the conclusion that many Spanish speaking families living with this metabolic disease would benefit from a forum in their native language.

Nowadays we are thirty families in our chat group. We all communicate in Spanish and we have families from countries such as Spain, Mexico, Honduras, Argentina, Chile, Colombia , Costa Rica, and also some that reside in the US and Germany.

When the group was first formed, there were only a few families who exchanged valuable information, some low protein recipes and experiences living with the disease. We were bound by living with MSUD, but our experiences varied very much with the country where the families resided. Our group has grown, and the stories we share are still moving and unique in many cases. The treatment for a metabolic crisis does not always follow a standard protocol. The means to get formula for these children also varies. The approach to a cure is not always an option. But parents in our forum always manage to make the most of our means with the same goal in mind: keeping our MSUD children as healthy as possible.

We have shared happy occasions in which our children would finally get the right treatment or a happy end to a metabolic crisis. Times when some children would finally obtain the formula they need to survive, the hope for a cure, the achievement of leaving MSUD behind through a liver transplant… but we also had some sad occasions in which we all grieved the loss of some of our member's children. Through happy and sad times, we have learned to communicate and share all of our knowledge, hoping that new families would always receive the most accurate information related to MSUD.

Our goal is to reach as many families as possible in Spanish speaking countries who might find themselves alone and living with MSUD. We hope to share our experiences with them, and provide them with reliable information and support.

We would appreciate it if the families that read this newsletter would pass information about the MSUD Spanish Group to their metabolic clinics.
On many occasions we have found that families have gone for years without communication with other families due to the language barrier.
By getting the word out, we can prevent this from happening.

Our thanks to the MSUD Support Group for promoting our forum on their website and for allowing us to participate in this newsletter. ■

GRUPO DE CHARLA Y APOYO SOBRE MSUD– UN FORO MULTINACIONAL

Mónica Falconer
Madre de Marlon, 6 años, MSUD, transplantado 31/01/06
Coordinadora del Grupo de Charla y Apoyo en Español
monicazf@yahoo.com

Ya han pasado cuatro años desde que decidí formar un grupo de apoyo y charla sobre MSUD en español. Dos años después del diagnóstico de mi hijo con esta enfermedad, y con la ayuda del grupo de apoyo de MSUD en inglés, llegué a la conclusión de que muchas familias de habla hispana podrían beneficiarse de un foro en su propia lengua.

Hoy en día somos treinta familias en nuestro grupo de charla. Nos comunicamos en español y los components somos residentes en diversos países como España, México, Honduras, Argentina, Chile, Colombia, Costa Rica, Alemania y los Estados Unidos.

Cuando el grupo se formó, había tan sólo unas pocas familias que intercambiaban información, algunas recetas aproteícas y experiencias vividas con esta enfermedad. Todos compartíamos nuestras vidas con MSUD, pero nuestras experiencias variaban mucho dependiendo del país en que residían las familias. Nuestro grupo ha crecido y las historias que ahora compartimos siguen siendo únicas y extremecedoras en algunos casos. El tratamiento de una enfermedad metabólica no siemrpe sigue un protocolo. Los medios para obtener fórmula para estos niños también varían. La cura de MSUD no siempre es una opción. Pero los padres en nuestro foro se las arreglan para aprovechar los medios a nuestro alcance siempre con la misma meta en mente: mantener a nuestros hijos con MSUD lo más saludables posible.

Hemos compartido muchas ocasiones felices en las que nuestros niños al fin conseguían el tratamiento adecuado o se recuperaban de una crisis metabólica. Hubo ocasiones cuando algunos niños al fin conseguían la fórmula que necesitaban para sobrevivir, recibían la esperanza de una cura, dejaban atrás la enfermedad de MSUD debido a un transplante de hígado… pero también hemos compartido momentos muy difíciles en los que todos sentimos la tragedia que fue la pérdida de las hijas de dos de nuestras familias. Pero durante momentos de felicidad y tristeza, hemos aprendido a comunicarnos y compartir nuestros conocimientos con la esperanza de que nuevas familias reciban información adecuada sobre la enfermedad de MSUD.

Nuestra meta es alcanzar a la mayor cantidad de familias posible que residen en diferentes países de habla hispana, quienes podrían encontrarse solos o aislados con esta enfermedad. Esperamos poder compartir nuestras experiencias con estas familias y proveerles con información adecuada y nuestro apoyo.

Apreciaríamos si las familias que tengan acceso a este artículo comentasen sobre la existencia de nuestro foro en sus clínicas de metabolopatías. En varias ocasiones hemos descubierto que algunas familias habían vivido aisladas con MSUD debido a la barrera del idioma, sin poder comunicarse con familias en su misma situación. Por favor, anuncien nuestra existencia en sus clínicas y a los equipos médicos que atienden a sus hijos. Entre todos podemos hacer llegar la noticia de nuestro foro a más familias.

Nuestro agradecimiento al Grupo de Apoyo de MSUD en inglés por haber promovido nuestro foro en su página web y por permitirnos participar en esta revista.

Rachel and Seth Webb – Pinetops, North Carolina

By Sonya Webb

Rachel & sister Sarah

As of Saturday July the 14th, this will be a 15 year journey for our family. What a ride it has been. Our first child, **Sarah**, was born 8-13-90, healthy and without MSUD (not that we cared at that point). On 7-14-92, after a normal pregnancy, Rachel was born, a healthy beautiful baby girl. She quickly became ill, fed poorly, cried all the time and was very irritable. At 10 days old, she quit breathing and I had to do rescue breathing at home. She was hospitalized at out local hospital and soon after discharged with a diagnosis of apnea and poor feeding.

Rachel came home on an apnea monitor; it alarmed all the time. She continued to eat poorly and cried almost non-stop. At 3 months old, she took a turn for the worse. She became quiet, was having focal seizures and would not eat at all. She was taken back to the hospital and from there was sent to a bigger medical facility where she stayed for about a month. She was there for 2 weeks before they knew what was wrong with her. They then gave us the grave diagnosis of MSUD.

Sarah, the cheerleader!

We were like all of you I'm sure, totally stunned by this weird sounding disease. Because of the late diagnosis (our state did not test at that time) Rachel suffered irreversible brain damage. She is physically handicapped. She was delayed in all areas of gross and fine motor development. She finally started crawling after her little brother came along and he started to crawl. She soon followed suit with the walking as well. Today she uses crutches to walk and a wheelchair for long distances.

In kindergarten she was taken out of regular classes for remediation, but it was soon found that she did not need this. She has been in regular classes in school ever since. She is not an academic achiever but she does well and usually brings home B's and C's, with occasional A's and D's. We're proud of her! She has a gift for socialization, she is almost always happy in spite of her situation. She takes on new challenges without hesitation. She tried out for cheerleading in the 7th grade but didn't make it. That didn't stop her from trying out the next year, and she did make it. She went on to be voted as the cheerleading rep for the squad. She has already tried out for high school this fall and will be on the JV squad. Rachel still doesn't like her formula but drinks it without any problem. She follows her diet well. She has had very few hospitalizations due to crisis. Last year was the first time in about 4 1/2 years.

On 1/19/94, **Seth** was born. When I became pregnant, I had an amniocentesis done to test for MSUD. It came back positive. We were devastated. To think that you could possibly have 2 of these children and afford the formula was a dilemma in and of itself. The pregnancy was completely normal as well as the delivery, (all except everyone was freaking out at the little local hospital because they knew he had MSUD. I had to beg to hold him.) The next day he was transferred to Duke where he was stuck and examined over and over. Oh, if I knew then what I know now! We came home after about 10 days. He did well, fed well and had a good appetite. Even though he was started at birth with the formula, to this day he still doesn't like it, but drinks it without being forced.

Seth & sister Sarah

Seth had a few hospitalizations when he would get a virus. He would do crazy things like hallucinate or appear to have gotten into a wine bottle because he couldn't stand up or walk straight. These were usually quickly resolved and we would return home. On 12/26/05, shortly before his 12th birthday, Seth became quite ill. He was vomiting, extremely pale and extremely thirsty. We started our routine, the cake icing, the high calorie fluids etc. We were not going to resolve this at home, so off to the

(Rachel & Seth *cont. on page 10***)**

◀ Hannah Dolins
(classic MSUD, 13 y.o.) was called to the Torah on June 16th, 2007 as a Bat Mitzvah. She has studied Hebrew for several years, and learned to chant a portion from both the Torah and the Haftorah. She also led the congregation in several prayers.

▼ Snow in Argentina

(left - right) Florencia, Augustin, Eduardo & Jimena (transplanted 7/06) Gatica build a snow man. It was the first time it snowed in Buenos Aires since 1918!

(Rachel & Seth *cont. from page 9***)**

hospital we went. In the ER, the usual fluids were started, Lactated Ringers and D10. The staff reported a high blood sugar but was pretty sure it was not correct. They pulled out their glucometer on the floor and checked it again. It registered "HI". The doc had the lab redraw a stat glucose and it was still high, over 900. We had just gotten to our room and then we were off to the ICU. We stayed over a week in ICU. Seth now had diabetes too! Like you, my reaction to the doctor on the way to ICU was "it can't be diabetes, what will he eat?" We were stunned, again! The doctor told us later that she could only find one other case of a both MSUD and diabetes. For the first time Seth ask "why me"? He'd always had such a great attitude about MSUD and dealt with it like an adult…. or better. After the first 2 days in ICU, our nerves began settling a bit, so we could comprehend what was going on and how this would all work out. Seth's attitude totally changed and he was back to his old self with all the confidence that he'd ever had and more. He told me before discharge that this had all happened to him for a reason and that GOD knew what he was doing. Wow, I was thankful.

Since that time it has been quite a journey. It is indeed a daily challenge to keep it all in balance. Basically, Seth continues to follow his MSUD diet and counteracts his carbohydrate intake with insulin. He takes a minimum of 4 shots a day plus any extras for when he wants to snack on protein free (sugar-loaded) candy or other low protein snacks. He does all his glucose testing and injections himself. He has done so remarkably well with it; I can still hardly believe it. He has had more hospitalizations due to his MSUD since this than before. We are still not sure if there is any relation between the 2 that has caused this.

Seth has also been treated for ADD for about 4 years. He is extremely active, plays all the time and has been on the ball team at school and in town. He performs average in school, although he has the ability to be above average. I'm convinced that his imbalances with both MSUD and diabetes have a direct impact on his day to day performance at school. Seth follows his diet well and is keenly aware of what makes him feel bad.

Both Rachel and Seth take 90gms of Ketonex-2 daily and count protein grams for an allotment of 15-19gms everyday. Though they are not classic MSUD, they do not eat any meat or dairy products.

Our oldest daughter, Sarah, deserves the "Best Sibling Ever Award". She has been most supportive and patient with all the extra time and energy that must go into special needs children.

Our health care for the past 13 years has been phenomenal. We have the best Health Care Team in the country. (No bias here). We go to UNC- Chapel Hill in Chapel Hill N.C. From day one they were all on board, quick to respond, always listening to us and made us feel more like family than patient/ doctor. Our doctors are Joseph Muenzer and Mugu Calikoglu. Our dieticians are Dr. Diane Frazier and Dr. Sureka. Without them I dare to think where we might be today.

First and foremost, Christ has been our saving grace. He has led us through these years of uncertainty and given us the strength to carry on. He has blessed us with a wonderfully supportive family and friends. For that we are so thankful. We hope that in some way our story will help someone else to cope or feel encouraged. ■

Understanding the Effects of MSUD and Improving Treatment Options: The Work Continues

TOPIC: Genetic Research & Medical Therapy

By Dr. Susan Hutson

Our work with mouse models is directed towards developing a clearer understanding of the molecular basis for the effects of MSUD on the central nervous system and body metabolism. It is our hope that such an understanding will lead to better treatment options for MSUD.

We are generating an animal that is genetically engineered so that a key part of the E1_ subunit of the E1 decarboxylase enzyme can be deleted when this animal is bred with a line of mice containing an enzyme that clips out a specific piece of DNA in the E1_ gene. The founder mice, which are scheduled for shipment in October, will be bred and the colony expanded here. Once this colony is ready we will breed them with appropriate mice carrying Cre-recombinase, the enzyme that makes the targeted gene deletion, to make the following animals:

1) A mouse animal model of Classic MSUD in which branched chain amino acid (BCAA) breakdown at the branched chain a-keto acid dehydrogenase step is severely impaired in all body tissues (global E1 knock-out). The complete knock out can be generated in utero or after weaning so the animal can be managed and will mimic classic MSUD. The heterozygotes (50% of normal enzyme levels) will provide a model of intermittent MSUD using diet to challenge the animal.

2) An animal where BCAA breakdown is impaired only in the brain (central nervous system only). As the primary effects of MSUD are neurological, this animal will allow us to determine if impaired metabolism of BCAAs in the brain is sufficient to manifest the neurological pathology, and to test our theory of how BCAAs and their a-keto acid metabolites produce the pathological effects in brain.

3) Animals where BCAA breakdown is impaired in a specific tissue outside the central nervous system. These animals will be used to answer specific questions about the role of BCAAs in body energy metabolism.

In an exciting development, my longtime collaborator Dr. Kathryn LaNoue at Penn State College of Medicine and I at Wake Forest University Health Sciences, have recently established collaboration with Dr. William Zinnanti also at Penn State. We will work together on the E2 animal that was obtained from Dr. Gregg Homanics at the University of Pittsburgh, using the E2 knockout mouse he developed with Dr. Paul. Dr. Zinnanti has found biochemical and pathologic changes that give us immediate targets to look at in the new E1 mice and E2 mice. Additionally, we will be testing a newly developed treatment in these mice based on reducing brain leucine accumulation using non protein amino acid analogs. This treatment concept has been developed in another disorder of essential amino acid metabolism with promising results. We plan to submit an NIH grant to support our project once we have enough data on the new E1_ KO mouse.

Recently, we have generated a mouse containing a global knockout (KO) of the mitochondrial branched chain aminotransferase (BCATm). In this animal BCAA metabolism is blocked at the first step in all tissues outside the central nervous system. The cytosolic BCAT is found in brain neurons whereas BCATm is found in brain astroglia. This BCATm KO has elevated levels of BCAAs in plasma and body tissues. This KO mouse does not exhibit the neurologic symptoms found in MSUD but it does show increased protein turnover, changes in insulin sensitivity, hypermetabolism, and resistance to diet induced obesity. This animal provides evidence that BCAAs have profound effects on body metabolism, independent of their effects in brain and suggests the branched chain keto acids are the primary toxic metabolite in MSUD. Our manuscript describing the animal that we generated has just been published in Cell Metabolism and is also a collaborative project with scientists working in the obesity/diabetes field.

Those of us in the field of branched chain amino acid metabolism are very excited about the future as we work together to understand the molecular basis of MSUD and the role of branched chain amino acids in the body, and to develop improved treatments for people with MSUD. We appreciate the support of the MSUD Family Support Group. ■

Noodle Casserole with Cheese Biscuits

3 Tablespoons margarine
3/4 cup onions
1 cup sliced mushrooms
1 1/2 cups tomatoes with sauce
1/2 cup zucchini
1/2 cup ketchup
1/2 cup water
5 cups cooked low protein pasta (elbows, spaghetti)

Biscuits
1/4 cup tomato sauce
2/3 cup water
2 tablespoons powdered non dairy creamer
2 tablespoons Shake and Cheese (Cambrooke Foods)
2 cups Mix Quik + 2 tablespoons

Sauté onions, peppers and zucchini in margarine. Add tomatoes with sauce, water and ketchup. Add noodles and toss to coat. Measure nine 3/4 cup servings into individual serving dishes. Mix tomato sauce with water. In a mixing bowl combine Mix Quik, cheese powder and non dairy creamer. Add tomato mixture and stir gently till combined. Sprinkle 2 tablespoon Mix Quik in a sheet of wax paper and pat out the biscuit dough until about 1/2 inch thick. Cut with a 2 1/2 inch cookie cutter. Place 1 biscuit on each serving and brush with melted butter. Bake at 350 degrees for about 15 minutes till biscuits are done. 9 servings. These can be frozen and re heated later as needed.

	Leucine	Protein	Calories
Per recipe	651mg	14.5g	3099
Per serving	72mg	1.6g	344

Please send recipes to
Food News Editor

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Mock Clam Fritters

2 Tablespoons chopped onions
1/2 cup Cambrooke Mix Quik
1/3 cup clam juice
1/4 Teaspoon Old Bay Seasoning
oil for frying

Mix onions, Mix Quik, calm juice and seasonings together. Heat cooking oil until 325 degrees and drop clam mixture by tablespoon into the hot oil. Fry till golden brown, turn and fry on the other side. Remove and drain on paper towels. Serve immediately. Makes 8 fritters.

	Leucine	Protein	Calories
Per recipe	10 mg	.75 g	426
Per serving	1.25mg	.09g	53

Baked Zucchini

1/4 cup sliced onions
2 cups sliced zucchini
1/4 cup melted margarine
1/4 cup dry Low Protein bread crumbs
2 Tablespoons Low Protein shredded cheddar cheese

In lightly greased 1 quart casserole dish layer onions and zucchini slices; Drizzle with 2 tablespoons melted margarine. Sprinkle with low protein cheese. Combine remaining margarine and bread crumbs, sprinkle evenly overtop of vegetable mixture. Bake at 350 for 30 minutes. 2 servings.

	Leucine	Protein	Calories
Per recipe	317mg	4.9g	637
Per serving	158mg	2.5g	318

Margarine 404, zucchini 56, bread 100, onions 15, cheese 25 =598 calories

Barbeque Sandwiches

1/3 cup chopped peppers
3 Tablespoons margarine
1/2 cup onions
3 cups (225 grams) shredded Mushrooms
2 Tablespoons Worcestershire Sauce
1 teaspoon chili powder
1/3 cup brown sugar
3/4 cup ketchup
1 Tablespoon Mustard
1 teaspoon garlic salt
1 1/2 tablespoons clear jel or 2 tablespoons cornstarch mixed with 2 tablespoons water

Sauté onions and peppers in margarine. Add mushrooms, Worcestershire sauce, chili powder, brown sugar, ketchup, mustard, and garlic salt. Simmer 5 minutes and then stir in clear jell water mixture. Cook till thickened. Using a 1/3 cup measuring, cup divided into 8 servings. These servings can be frozen on a cookie sheet on mounds and then placed into freezer bags when frozen. Remove from freezer and heat in microwave until hot. Serve on a low protein hamburger bun. 8 servings.

	Leucine	Protein	Calories
Per recipe	555mg	10.9g	822
Per serving	79mg	1.4g	107

Cambrooke Foods invites you to 'Bring it to the Table' with **Camino pro**™ our new line of food-friendly amino acid supplements for PKU and MSUD patients ages five and over. The Camino pro™ line contains drinks, sauces, bars, and sorbet stix that taste great and are designed to be enjoyed at mealtime, snack time, or on-the-go time.

Camino pro™ products will enhance your mealtime experience with their ability to be used in conjunction with low protein food. Mix and match Camino pro™ easy-to-count modules to meet your protein needs. Each single-serve product is also complete with vitamins and minerals, so you never have to worry about getting all the nutrients you need!

Whether you are returning to diet, struggling with your current formula, or just looking for a change, Camino pro™ will help make the low protein diet enjoyable, flexible, and fun – as it should be. Call your physician today and request samples or contact Cambrooke Foods directly for a Sample Request form.

NEW FOODS by Cambrooke Foods

Satisfy your tastes with new low protein **blueberry scones**, a breakfast alternative to the cranberry scones. Experience a taste from the south of the border with our new savory **Southwestern Biscuits**, a lunch or dinner item. New ready-made **Primavera Pizza**, a traditional cheese pizza with a light vegetable topping, is new in our pizza line.

Medley Meals join our expanding line of ready meals and are available in two varieties. Heat and serve convenient, the preservative-free **Vegetable Masala** and **Moroccan Stew** can be eaten as is or served over your favorite low protein pasta or rice. Traveling with a metabolic disorder will never be the same because these new meals are not only delicious, but they are shelf stable and nutritious!

Did you ever wish for spaghetti and meatballs just like everybody else? Now your wish has come true. Cambrooke Foods is pleased to introduce **Veggie Meatballs** which come in a pack of 16. One serving of 2 meatballs has 0.97 grams of protein and 66 mg of leucine. They are ready to heat and serve. Just heat, add sauce and serve with spaghetti. The delicious taste and texture will make you wonder why people eat beef.

Cambrooke Foods also has another new item - **Barbecue Calzones**. Calzones are the fun alternative to pizza. Their oval-shaped barbecue calzones feature a wonderful toasty crust with a savory blend of veggies and sauce. They are an ultimate grab-n-go food that doubles as a sit down dinner. Barbecue Calzones come 2 in a pack. Each calzone has 1.3 grams of protein and 54 mg leucine.

Cambrooke Foods is ALWAYS open to serve you. 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 (2 Central Street, Framingham, MA 01701), e-mail (orders@cambrookefoods.com) or fax at (978) 443 -1318.

A Day of Fun!

On June 30, 2007 we had an **MSUD Picnic** in PA for Dr. Morton's patients. There were 42 MSUD people and 2 transplantees at the picnic. We had Low-Protein spaghetti from Cambrooke Foods topped with Low-protein Meatballs from PKU Perspectives. This made a meal that was very tasty. It was a warm day and the Low-Protein Ice Cream from PKU Perspectives was quite a hit. You sure don't want to miss a day like this. It was great to fellowship and share with each other as caregivers and patients.


1.


2.


3.

1. As you can see on the pictures, we had a happy healthy group.

2. The girls were deciding which of the homemade goodies are the best.

3. Maritsa Larson is immensely enjoying her ice cream cone.

Thank You, Mark & Lorraine Martin

Initial Studies to Cure Maple Syrup Urine Disease (MSUD) in a Mouse Model

By Kristen J. Skvorak, Ph.D. Candidate

TOPIC: Genetic Research & Medical Therapy

For those who did not meet me at the 2006 MSUD Symposium in Ohio, I am a graduate student in Dr. Gregg Homanics' lab in the University of Pittsburgh's Molecular Genetics program. MSUD is the focus of my doctoral dissertation. My goal is to develop new and improved therapies to treat and cure the disease.

For a project as vast and ambitious as developing treatments for a complex disease such as MSUD, much more than just one graduate student is needed to make it happen. Diverse skills are required that no single investigator has. Thus, collaboration is essential to the project's success. Collaborations bring together some of the best and brightest investigators from a variety of fields that are outside of MSUD research. Many of you have met my lab's long time collaborator, Dr. Harry Paul, who has been an essential power in propelling this project forward. In another effort to attract more investigators and increase scientific interest in MSUD, the MSUD mouse model previously made in our lab (BMC Med. Gen. 2006, 7:33) was recently accepted into The Jackson Laboratory's mutant mouse "zoo." The Jackson Lab is a well-known and highly regarded resource for thousands of mouse strains and is used by tens of thousands of researchers in over 60 countries. What this means is that the MSUD mouse model is now publicly available to any qualified investigator who wishes to use it in their research.

There are three things I am currently working on in order to accomplish my goal. The first is further characterizing the MSUD mouse model. For these studies, I am collaborating with Drs. Cheng and Zinnanti at Penn State College of Medicine. The second, in collaboration with Dr. Xiao at the University of North Carolina School of Pharmacy, involves using gene therapy as a novel approach to cure this disease. Dr. Xiao is a leading expert in the field of adeno-associated viral (AAV) vectors, our gene therapy vector of choice. The third method we will investigate, with the help of Dr. Strom at the University of Pittsburgh, is the use of cell based therapies, such as hepatocyte (liver cell) transfer or differentiated embryonic stem cells (ESCs), to cure MSUD. Dr. Strom is an expert in hepatocyte transfer and will be a major asset to this portion of my project.

Additional Characterization of the MSUD Mouse Model.
Characterization of our mouse model is a very important first step. Without a thorough understanding of how the MSUD mouse model is affected by the disease, I would be unable to determine the best and most effective therapy to cure it. For my most recent characterization studies, we found that brain glutamate, glutamine, and GABA levels were significantly reduced in the mouse model. Glutamine, an amino acid, is a substrate for the production of both glutamate and GABA, excitatory and inhibitory neurotransmitters in the brain, respectively. These findings are associated with neuropathology in this model involving the swelling and fluid accumulation in the brain's cerebrum; this is also consistent with human cases of MSUD. This is exciting news because this provides more evidence that the MSUD mouse model is more similar to human MSUD than previously known. Therefore it is an excellent model for testing therapies to be applied to humans with MSUD in the future.

Gene Therapy.
Gene therapy is an attractive and promising avenue to pursue to correct MSUD. Viral vectors used for gene therapy are little more than molecular FedEx trucks to deliver beneficial genes into a living cell, something scientists and doctors cannot do on their own. The viral vector we chose for our studies is adeno-associated virus (AAV). This vector is especially superior for my application compared to other gene therapy vectors since AAV has low to no immune response, is able to infect non-dividing cells such as liver, and has been shown to be efficient at long-term and sustained gene expression. Our AAV vector was engineered by Dr. Xiao to contain the E2 subunit of human BCKDH, a mouse gene expression agent to direct the production of E2 protein exclusively to the mouse liver, and packaged into AAV2 and AAV8 that differ only by the virus' outer protein coat. The viral vector was administered to the mice at 3 weeks of age by simply injecting a small amount of virus containing solution into the abdomen. Some animals were also given a second "booster" injection at 7 weeks of age. Preliminary studies suggested increased BCKDH enzyme activity in AAV8 treated animals and an increase in survival for both AAV2 and AAV8 treated animals compared to saline treated. However, at this study's completion there was no significant difference between saline, AAV2, and AAV8 treated groups. AAV also did not normalize blood branched-chain amino acid levels. In order to determine why AAV gene therapy was not successful in our animal model, in vitro models are currently being tested. Thus far, preliminary results suggest that E2 expression from the AAV vector is lower than

(Mouse Model *cont. on page 17*)

3rd Annual Transplant Conference, June 2007

By Amy R. Zimmerman

I attended a conference about transplant for MSUD which was held at the Netherlands Inn and Spa in Strasburg, PA on June 12, 2007. I had been transplanted in January 2006 and had a fun time sitting with other families for a luncheon of chicken, mashed potatoes, green beans and desserts. After the luncheon, we adjourned to the conference room where Dr. Holmes Morton M.D. started out with a cordial welcome to everyone. Speakers included Drs. George Mazariegos, Rakesh Sindhi M.D., Kevin Strauss and Holmes Morton M.D., and Dr. Hilary Feldman Ph.D. all of Children's Hospital of Pittsburgh. Dr. Mazariegos discussed his perspective on MSUD and transplants. Some of it was a bit hard to understand, even for someone who had gone through transplant. He was explaining that there are pros and cons to every surgery, but in the end he believes that the transplantee will have a better life. He showed various slides of statistics about transplants- for MSUD and other conditions. Dr. Sindhi spoke about genetics and transplant along with a slide show of various graphs pertaining to health of a "normal" person versus an MSUD child. His accent made it difficult to understand at times what he was saying, but he made his points.

Dr. Feldman spoke about the neurological aspects of liver transplant for MSUD. She explained how MSUD affects fine motor skills and more, and how they are discovering that after transplant things become clearer and more defined for that patient. Their team is conducting neurological studies before transplant and then one year after transplant. Sometimes things don't change quite so drastically, but parents of MSUD transplanted children have noticed subtle changes in their children. Dr. Strauss spoke last about the long lasting devastation some MSUD children experience and how more damage is done as the child becomes an adult. He highly recommends that MSUD patients get a transplant before things get worse for them. He was, in my opinion, the best of the speakers because, unlike Drs. Mazariegos and Sindhi, he knew that the people sitting in the audience needed to have the medical "jargon" broken down for them into understandable terms. Participants had an opportunity to engage in discussion and a question-answer session. There were small conversations going on during the question-answer session, but mostly everyone was listening. Some of the questions weren't really questions at all, but confirmation on the benefits of transplant. No one at this conference had anything bad to say about transplants. Afterward, there were various little conversations going on and people talking everywhere. I was standing with my parents while they were talking to Dustin Hahn's parents. Nikolai Rudd and I sat with Elan Geffen, who had to leave before the end of the program. Dustin, Nikolai, and I had our picture taken for everyone to see! We are doing so well! Even Lynn Seward, transplant coordinator, said, "You guys look sooo good! I can't believe you look so healthy!"

Dr. Marc Yudkoff, an MSUD doctor at CHOP was at the symposium too. I was told that he was not in favor of transplant and that he had come to question the doctors from Pittsburgh. That is, until he got to see about 11 other transplant patients and me eating chicken and looking so healthy. He enjoyed seeing his former patients (including myself) doing so well. All in all, the day was a complete success!

My Life, Love of Travel, and Why I Don't Want a Liver Transplant

By Rachael Ennis

My name is Rachael Ennis; I am 23 years old, a former English teacher at Haverhill High School in Haverhill, MA, and a patient living with MSUD. I graduated with a 3.7 GPA from the University of Massachusetts Amherst, and am currently attending graduate school at Simmons College for Library and Information Science. I love hiking, skiing, going to the gym, traveling, and exploring; I've been frustrated by my drink holding me back from the freedom of "real" camping; I can't fish or hunt for myself, but I can for others. I have always wanted to live my life to the fullest, and I have always looked at food as more of a luxury than a necessity; my mother would explain to me that my diet, like many things in life, was a responsibility, and she would tell me that I am the only one who can make decisions about my diet. I have consequently always been health conscious and determined to vary my limited diet as much as possible: I eat everything I can from turnips to red pumellos (a variety of grapefruit). I've also become a very good cook, of foods I can, and cannot eat, with my boyfriend or mother as ready tasters.

I value my health, and that is why I am writing this for the MSUD newsletter. I know the kind of physical condition people need to be in, in order to really appreciate a place like Yellowstone National Park; I am not there yet; I am in training. I would love to visit Africa, and China, and the Polynesian Islands in the future, but the more susceptible to disease one is, the less likely one is to be able to realize those dreams.

Many people who deal with MSUD and individuals with MSUD on a regular basis, and know the reality of the disorder may find it a bit odd that someone living with the condition feels as comfortable with travel as I do. In order to understand why that is, they must consider my diet, nutrition knowledge, mental conditioning, and understanding of my own body chemistry. I not only try to eat within the diet as much as possible, I also pay a lot of attention to vitamin intake, ingredients in food that may

(MyLife *cont. on page 18***)**

(MouseModel *cont. from page 15***)**

expected. We continue to work to determine why that is in order to make corrections that will optimize treatment. Despite this recent data, we uphold that MSUD is a promising candidate for gene therapy.

Cell-based Therapies.

I now plan to dedicate more time towards cell based therapies, such as differentiated ESCs and hepatoctye transfer, to cure MSUD. Preliminary studies in our lab have determined that cultured ESCs can be induced to become hepatocyte-like cells simply by culturing them in the presence of specific growth factors. Importantly, these differentiated cells express the BCKDH subunit E2 at the level of healthy liver. This technique has already been successful in curing hemophilia in a mouse model (PNAS. 2005, 102:8). Thus, ESCs may be able to provide an unlimited source of therapeutically useful cells that could be used to treat MSUD (and other diseases). Hepatocyte transfer has had promising early results for the treatment of a variety of liver diseases in mouse models and has been used clinically to treat Crigler-Najjar syndrome, an inherited liver disease characterized by a missing enzyme –much like MSUD. Though still in the experimental stages, these exciting early results suggest that cellular therapies could be less expensive, less invasive, have fewer complications, and require less immunosuppression compared to whole liver transplantation.

Conclusions.

In conclusion, I currently have an excellent animal model of MSUD. I am using this model to test and optimize therapies to treat and cure the disease. If successful, my lab plans to translate what I learn to human-dedicated therapies.

This work was supported by the Laverty Foundation, the Scott C. Foster Metabolic Disease Fund, and the MSUD Family Support Group. ■

(**MyLife** *cont. from page 17*)

cause my metabolism to be even slower (such as corn syrup), and things that speed my metabolism such as coffee. I always try and eat as diversely as I can, and that includes broccoli, which has recently been shown to help brain function. Additionally, I am aware that stress negatively impacts leucine levels in various negative ways. I regulate my work stress, stress from exercise, and from inter-personal relationships, by building my comfort level and confidence gradually in order to prevent overload. I have learned to do these things in order to self regulate and perform at the level I know I am capable of.

In my opinion, it is never okay to just assume that someone who has not strictly followed a low protein diet cannot improve cognizance and make-up for lost time, so to speak, if they remedy the circumstance. I ate off the diet consistently in high school, and knew that after a good first college semester, I was failing myself in the second, by eating too much protein from foods such as pasta and vegetable setan (a vegetarian meat substitute). I had to drop calculus, and managed a 3.1 for the semester, but I was fuming. I knew some things weren't right: my levels 13! I was lucky to be functioning. I detoxed, as I put it, over the summer.

When I traveled to Israel in my sophomore year, I learned what not to do when traveling: live off of French fries, try a taste of falafel (chickpeas, who knew), not bring water to climb Masada, forget to have my breakfast and lunch drink, leaving them at the hotel for the day. I knew my levels were not great, and it made the trip less than enjoyable; fortunately I didn't get sick, and was aware that there are great medical facilities in Israel that are familiar with MSUD. Additionally the whole country is only 9 miles across, and about 3 hours to drive from north to south.

I have found that if my levels are 2, I can usually afford to travel, treck through the woods, canoe, bike, explore as long as I have enough packets (pre-made/measured), water, and a plastic bottle. It is tough to go for awhile without food, a day or so for example: levels can rise because of the stress of withdrawal and lack of strength/fuel to the body and brain. At a 2 level, I can generally take the spike; also I can regulate the stress by not focusing on food. If I get sick, it is the same thing; I am great at fending off and fighting colds, because I always have vitamin C, and I bring some with me when I travel. I also make sure my levels are low enough so that I don't risk the decompensation factor. If I am hurt or suffering on a real adventure and have the good fortune at that point to be meda-vacted to the nearest hospital in Ghana, well I have already made the choice to endanger myself to that degree, and whether I have MSUD or not under these circumstances is kind of a mute point, except I would probably make sure my guide/translator could say "don't pump protein through the IV." That's why you plan trips, and you know what hospitals are available in advance; most major cities that have hospitals, have someone there who speaks English.

This being said, I am somewhat concerned about a new trend in MSUD treatment: the liver transplant.

A liver transplant poses some very serious potential risks to the body's overall health. When I ask my boyfriend whether or not I should get a liver transplant so I can eat normally his response is unequivocal, "Well the real question is would I rather be able to split the buffalo wings with you for a few years, or have a girlfriend and a future?" For me, he's right; why take an unnecessary risk when the reality of the disease has always been treated, by me and my family as a minor inconvenience to an otherwise healthy and intelligent human being? I trust my boyfriend's judgment; everyone in his family has advanced degrees in science including all four grandparents. My mom is one of the most nutritionally conscious people I know, besides my aunt and myself, so I really value her thoughts as well. My mom always says: "Yeah the diet's hard, and it's a pain at restaurants when you have to order a salad and a baked potato, sending the salad back when they forget to make it without cheese, but you have your health, why jeopardize that for a slice of pizza" (which isn't really great for you anyway with all that grease). She jokes, "Rachael, you will live to 100, because you have the healthiest diet out of all of us". I retort, "Yeah, well that's cause I stay away from a lot of the really starchy low -pro foods, I'll stick to brussel sprouts and low-pro-cheese, thanks". Mom says, "Oh yeah, how about the bread?" I'll reply, "Well yeah, but that doesn't count because I have it with tomato sauce and peppers and onions; it's like a greaseless pizza, the veggies cancel out the starch!" We joke like this a lot, but you have to. She tends to think that any surgery, particularly voluntary, is not worth the potential risk. Life is the way it is, and I would rather have the possibility of living to see much of the world, having a family, writing, and living until 100, than be on immuno-suppressant drugs for the rest of my life, which can happen if the body does not accept the new liver. My concern is that because of its effects on the immune system, transplant might result in far less travel and exploration (countries along the equator- out).

I feel that I can be healthy with MSUD. A cure would be nice if it didn't come at such a potentially high price. I'm personally waiting for them to be able to alter my liver cells with genetic engineering. ■

MSUD Support Group Board of Directors

By Mrs. Wayne (Joyce) Brubacher

The MSUD Family Support Group began with the first MSUD Symposium in 1982. A small group of founders did all the work and made all the final decisions for the first number of years. The first board members were elected by a majority vote of the attendees at the fifth MSUD Symposium which took place in Montreal, Canada in 1990. Board members who have served during the ensuing years have been chosen from the United States and Canada.

The Board of Directors represents the families and individuals who constitute the members of our support group. They make the final decisions concerning the functioning of the organization. It is nearly impossible to have regularly scheduled board meetings except at our biennial Symposiums due to the distance they would need to travel to be together. Board members are expected to attend the Symposiums. Between the Symposiums, contact is made with phone calls and e-mail messages. Several times three or four members have met to review projects. All travel expenses are paid by the members themselves.

The president and chairman of the board, currently Wayne Brubacher, conducts the board meetings, is consulted on matters relating to the support group, contacts other board members for consultations and is required to send consent forms in lieu of a board meeting. These forms are signed by the individual board members and then returned to a law firm in Virginia where the Support Group is registered as an organization.

The president is also is responsible for the travel assistance program. This program is supported by the United Services Foundation which provides money for those who need financial help to attend the Symposiums. Wayne contacts families referred by clinics and responds to other families who ask for assistance to attend. He helps those from other countries get proper documents and works with a travel agent to make travel and hotel arrangements.

The treasurer, currently Dave Bulcher, keeps very detailed records of finances, updates the data base, sends and receives fee slips, pays bills, and is responsible to pay fees to the state of Virginia and the law firm to keep our status as a non-profit organization. Dave also helps Wayne with the travel assistance program. He spends a great amount of time helping plan the Symposiums and paying bills during the Symposium years. These duties and others too numerous to list, keep Dave well occupied as treasurer.

Some of our Board Members and members of their families on a recent visit to Dr. Hutson: (L-R) Ivan & Mary Kathryn Martin; Joyce, Wayne & Shayla Brubacher; Jordan, Sandy & Dave Bulcher

The current secretary of the board is Anne Fredericks. She is responsible for recording the minutes of the board meetings. Other current board members are Ivan Martin, Tony Kohl and Denise Pinskey.

According to the bylaws of our organization, one board member is to be replaced every two years. This rule is generally followed, although some persons ask to be released from their position early and others are willing to commit for a longer length of time. Names of potential members are submitted to the board and chosen by a majority vote of the board members.

A strong and dedicated board is essential to our organization. Board members must be available to communicate regularly and be aware of issues facing our membership. All work is done on a voluntary basis and the board members themselves pay expenses related to board work, with no reimbursement except the satisfaction of a job well done for a worthy cause.

If you are asked to serve on the board, please consider giving of your time and talents to continue the work of our MSUD Family Support Group. You will be providing an invaluable service for those with MSUD and their families. ■

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SAVE THE DATE:
MSUD Symposium 2008 will be held on
June 26-28,2008
at the Columbus Embassy Suites in Columbus, Ohio.
Plan ahead to join us!

NUTRICIA North America
formerly SHS North America

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