CURRENT EXPERIENCE WITH LIVER TRANSPLANTATION FOR MSD

George V. Mazariegos, M.D.
Director Pediatric Transplantation
Children’s Hospital of Pittsburgh

Since the first successful liver transplantation was performed in a child almost 40 years ago, this option has increasingly become a life-saving therapy for children with liver diseases such as biliary atresia. Interestingly, the next most common indication for liver transplant in children has been metabolic diseases such as tyrosinemia or urea cycle defects. Despite the availability of medical therapy for these diseases, the unpredictable nature of the disease and the potential long-term complications of tumors or neurologic problems has led to the use of liver transplant in these children. Results for liver transplantation have increasingly improved with experienced centers demonstrating high rates of survival exceeding 90% at 1 to 2 years. Of note, this includes caring for children who present in very sick condition with acute liver failure or for children with other conditions such as liver tumors. At Children’s Hospital of Pittsburgh we have been very focused not only on successful survival outcome but also on assuring that children who undergo transplantation are achieving a highly improved quality of life. One of the ways that this has been achieved has been by developing new ways of handling immunosuppression, i.e., the medicines that are used to prevent rejection of the transplanted organ.

For example, by eliminating the routine steroids used in transplantation, we have seen a reduction with their associated side effects such as growth delay or infections. At the same time, by modifying immunosuppression our hope is to achieve a higher rate of children that are able to be on very minimal post-transplant immunosuppression or potentially be completely off immunosuppression altogether in the future. These developments led to collaboration with the Clinic for Special Children under the direction of Dr. Holmes Morten and Dr. Kevin Strauss who, in conjunction with our transplant team and Dr. Robert Squires, Clinical Director of Gastroenterology and Hepatology at Children’s Hospital of Pittsburgh, have developed a protocol for consideration of liver transplantation.

(Mazariegos, M.D. cont. on page 3)
**Kathryn Burkholder: First MSUD Liver Transplantee**

This letter is from Mabel Burkholder from PA, mother of 3 MSUD children. Kathryn is 16 years old and free of MSUD symptoms after a liver transplant 8 years ago. Her other children with MSUD are Ellamae, age 12, and Norman JR, age 7. They follow the traditional treatment of MSUD. Because of her situation, Mabel has a unique perspective on treatment of MSUD via liver transplantation and traditional treatment.

(See MSUD Newsletter Vol. 16, No. 1 Spring/Summer 1998 for more details of Kathryn's liver transplant)

Eight years ago at the age of 8, our daughter Kathryn was in liver failure from Vitamin A toxicity. She needed a liver transplant to survive. Dr. Morton said that it might affect the future of MSUD treatment if we allowed the transplant. We decided to go through with the transplant. We want others to benefit from what was learned by Kathryn’s transplant.

Kathryn was in the hospital for the first 3 months after the transplant. The next 6 months were difficult also. Since that time, Kathryn has been fairly healthy and without too many transplant related problems. Eventually, we were glad that we went through with the transplant. Dr Morton’s theory proved correct and Kathryn’s MSUD was cured by the liver transplant.

Recently, Kathryn was hospitalized in Pittsburgh for a rejection episode. This was scary for us. The doctors were concerned that she was not taking all of her Prograf (antirejection medication). Kathryn is mostly compliant with her medication and had only missed two doses before the hospitalization.

We’d been thinking about having our other MSUD children transplanted, but will move slowly with that decision, since Kathryn’s recent hospitalization. Ellamae is not interested in a liver transplant at this time. Norman JR would like to have a transplant, because he wants to eat meat and eggs. We’ll wait awhile to decide about transplanting the other children. In the meantime, I’ll pray for strength for those that decide to go through with the transplant.

Note: Following a liver transplant for MSUD, children and adults with MSUD no longer have to follow a diet or drink formula. The disease, however, can still be passed onto their children.

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It is with great sadness that we announce the death of Althea Roberts.
Althea was the 21 year old daughter of Aline Roberts of Jesup, GA. Althea passed away in August of 2004.
Our thoughts and prayers are with the family.
in children presenting with classic Maple Syrup disease (MSD). Our aim was to provide a comprehensive plan for assessing children and adults with MSD and offering transplantation to appropriate patients in the safest way possible. As many of you are aware, liver transplantation was reported in a patient with MSD who had developed acute liver failure due to another cause in 1997; when this child received a liver transplant to correct her acute liver failure, her previously diagnosed MSD was metabolically cured. Since the inception of the MSD transplant protocol here last May, we have transplanted an additional 7 children with classic MSD. These children ranged in age from 1.9 to 8.7 years and are now approximately an average of 7 months after transplant (range of 1.3 to 10.9 months). All the children have normal liver function and are currently enjoying an unrestricted diet. Amino acid profiles have normalized within a few hours after transplant and have remained so despite advancing to a regular diet of unrestricted protein. The initial patient transplanted is now stable over 5 years of follow-up; the more recently transplanted patients have also demonstrated normal liver function with normal plasma amino acid profiles.

Immunosuppression, as we noted earlier, remains one of the long-term concerns that post-transplant patients encounter. As opposed to earlier protocols that featured multiple drug regimens, our current immunosuppression relies on single drug therapy with steroid use only if there are episodes of rejection. Currently, approximately 40% of patients may encounter an easily treated rejection episode after liver transplant. Three out of 7 of our recently transplanted MSD patients experienced a mild episode of rejection that did require a brief course of steroids. All of the children are on a single drug (Tacrolimus) to control rejection, except for one child who is currently receiving steroids for rejection.

Infections have historically been an important risk factor for transplantation, but we are seeing an improved infection rate following transplantation. For example, virus infections such as those related to CMV and EBV (cytomegalovirus and Epstein Barr Viral, respectively) have steadily decreased to less than 4% in our experience. A more feared complication, post-transplant lymphoproliferative disorder (PTLD) has similarly decreased to less than 3%. In our MSD patients, no patient has developed CMV disease or PTLD.

Significant neurological recovery has been noted in the long-term patient who underwent transplant and subtle but clear improvements have been reported in several of the recently transplanted patients. These findings are now being objectively quantified by neuro-developmental testing done pre and post-transplant in subsequent transplant recipients.

Liver transplantation may also prove be a cost effective therapy for MSD that may reduce the long-term cost associated with medical care and treatment for acute metabolic decompensation. Most importantly, the uncertain risk of a devastating neurologic complication can be prevented with a successful liver transplantation. Although these children continue to have MSD genetically, the transplanted liver supplies sufficient enzyme activity to metabolize unrestricted protein diets and maintain branch chain amino acid homeostasis.

These early results are encouraging and support the role of transplant as a treatment options for children and even adults with MSD. We encourage review and discussion with families and their physicians regarding transplant as a therapeutic option. Our transplant team is available for any questions regarding transplantation for MSD at Children’s Hospital of Pittsburgh (412) 692-6110 or by e:mail at George.Mazariegos@chp.edu. You may also reach our transplant coordinator, Lynn Seward, by phone or e:mail: Lynn.Seward@chp.edu.

We hope that with the addition of liver transplantation as a therapeutic option, the quality of life and outcome for children with MSD will be greatly improved.

“For our family, the experience of going through the transplant was less stressful than going through a metabolic crisis because the outcome was much more predictable. Our life has been improved beyond measure in the last year, we don’t look back and we have no regrets.”
Jay and Oula Haddad, parents of Grace age almost 4, transplanted June 24, 2004
LIVER TRANSPLANT AS TREATMENT FOR MAPLE SYRUP DISEASE:  
OUR PERSPECTIVE AS PEDIATRICIANS  
D. Holmes Morton MD and Kevin A. Strauss MD  
Clinic for Special Children  

THE EFFECT OF LIVER TRANSPLANTS  
ON MAPLE SYRUP DISEASE:  
In May 2005 Dr. George Mazariiegos from the Children’s  
Hospital of Pittsburgh Starzl Transplant Institute presented  
an abstract at the annual Pediatric Surgery and Transplant  
Meetings entitled, Liver Transplantation for Maple Syrup  
Urine Disease (MSD): Protocol and Preliminary Results.  
(Mazaregos G et al 2005) The perioperative management  
protocol for MSD and the liver transplants were the  
result of a two year collaboration between the Clinic for  
Special Children and Starzl Institute. The results of 6 cases  
were discussed by Dr. Mazariiegos, including a MSD patient  
from the Clinic for Special Children who was transplanted 8  
years ago at Childrens of Philadelphia, but now receives  
post-transplant care in Pittsburgh. The 6 patients were 2-8  
years of age at the time of transplant with a whole cadaveric  
liver. In two cases, rejection was managed with Prograf and  
steroids, and, in four cases, with antithymocyte precondition- 
ing followed by Prograf monotherapy. All patients recovered  
from the surgery. Allograft function remains normal in all  
patients. Metabolic cure was apparent in all cases as an  
immediate and sustained increase in dietary leucine toler- 
ance from 15-20 mg/kg-day to an unrestricted protein diets.  
Leucine intakes greater than 150 mg/kg-day were tolerated by  
al all six patients, and plasma amino acid profiles were stable  
during periods of fasting, after steroid use, and during  
catabolic illnesses provoked by intercurrent infectious. The  
molar ratios of the branched-chain amino acids concentra- 
tions in blood remained stable, which indicates rate of  
oxidation amino acids in liver was regulated to maintain  
constant plasma amino acid profiles. (FIG 1 & 2 see page 14)  
In our first MSD transplant patient the metabolic effects of 
the liver transplant have been stable for more than 8 years.  
In addition to biochemical stabilization, all patients to have  
shown unanticipated neurological benefits of stabilized  
plasma amino acid concentrations. Decreased hyperactive  
behavior, better attention span, improvements in gross motor  
and fine motor skills have been observed. Marked improve- 
ments in the neurological exam was especially apparent in  
our first transplant patient over the first two years after her  
transplant. Formal studies are in progress to document and  
explain these effects of liver transplants upon the brain.  
Since submission of the Abstract in December 2004, two more  
elective transplants for MSD patients have been done at  
Children’s of Pittsburgh. Worldwide 15 liver transplants have  
been done as treatment for MSD. There was one periopera- 
tive death in a MSD patient referred for elective transplant.  
She had a living related donor transplant in Boston, and died  
soon after surgery because of acute graft rejection. The Clinic  
for Special Children and Childrens Hospital of Pittsburgh  
proposed our collaborative effort to develop a periopera- 
tive protocol and formally evaluate the benefits of  
elective cadaveric liver transplants for MSD, not only  
because of the remarkable success in our first our MSD  
transplant patient, but also in response to the death of the  
second patient.

THE CLINIC FOR SPECIAL CHILDREN PERSPECTIVE ON 
PROBLEMS RELATED TO LIFETIME MEDICAL  
TREATMENT OF MAPLE SYRUP DISEASE:  
Over 16 years, we have cared for 46 newborns with Maple  
Syrup Disease (MSD). When compared to patients with MSD  
from 20-30 years ago, when death, long hospital stays, and  
chronic disabilities were commonplace, our group of  
young patients has done well. (Morton 2000, Strauss &  
Morton 2003) Before 1988, 14 of 36 (44%) Mennonite  
infants died before age 10 years from brain herniation.  
Since 1988, we have not had a death from cerebral edema  
in our patients, but, one of our 5 year old patients did suffer  
a stroke as a result of acute brain edema.  
Our opinions about the problems and risks of long term  
medical treatment of MSD, versus risks and benefit of liver  
transplant, are influenced by the continued risk of brain  
injury and death from cerebral edema during the first 10  
years of life, and by emerging problems related to the care  
of teenagers and adults with MSD. For either group of  
patients, risks and costs of medical management versus  
transplant should be assessed over intervals of 10 years or  
longer. Although we have reported significant improve- 
ments in the care of infants and children with MSD patients  
within Pennsylvania, elsewhere neonatal diagnosis and  
treatment are delayed, appropriate long term monitoring  
of therapy is not available, and access to care during  
intercurrent illnesses is limited. (Morton 2002a) When  
access to treatment is poor, then the risks and costs for  
younger MSD patients remains high. The care of older MSD  
patients is problematic everywhere. Within our prospectiv- 
ely treated group of 46 patients, 11 are now teenagers.  
We are also responsible for 18 adults with MSD, who came  
to the Clinic after diagnosis and treatment at other medi- 
cal centers. In Pennsylvania, as elsewhere, medical services  
for patients with MSD who are over 18 years of age are  
emphatically non-existent. No Internal Medicine practices  
in Pennsylvania offer outpatient specialty medical care for  
adults with MSD. No hospital in Pennsylvania has an  
experience medical staff, MSD-TPN, and amino acid  
analysis to provide care for an adult with MSD and

(Morton, M.D./Strauss, M.D. cont. on page 5)
metabolic illness. A MSD counterpart to maternal PKU doesn’t exist. All support for treatment of MSD through the Pennsylvania Newborn Screening Follow-up Program ends when patients reach age 21. The lack of medical services for adults with MSD is the major risk factor when estimating the cumulative risks of disability or death from MSD over a 10 year span of adult life. In addition to the lack of medical services for the adults with MSD, it is increasingly apparent that adults with MSD have different problems than infants and young children. Adherence to strict dietary therapy is difficult for teenagers. As growth slows and muscle mass increases in the late teenage years, tolerance of dietary protein decreases and dietary control becomes more difficult, even with good compliance. Reversal of catabolic illnesses is no less difficult in adults than in younger patients. And, subtle, and not so subtle, neurological problems are being observed that arise from the cumulative effects of poor metabolic control, unbalanced uptake of amino acids into the brain, and, no doubt, trace nutrient deficiencies that arise from severely restricted diets and dependence upon formulas and other artificial foods.

**LIVER TRANSPLANTS AS TREATMENT FOR GENETIC DISORDERS AND THE LOW POTENTIAL OF HEPATIC GENE THERAPY:**

The collaborative liver transplant program for MSD at the Starzl Institute reflects a significant change in our thinking about therapeutic liver transplant. The majority of liver transplants, in Pittsburgh and elsewhere, are done because of liver failure. Our patient with MSD who first underwent transplant was referred because of vitamin A induced liver failure. Elective transplants are now being done for MSD, Crigler-Najjar disease, and urea cycle defects to protect the brain. In these, and many other genetic disorders, the liver is a central site of metabolic control for amino acids, bilirubin, ammonia, and other compounds that cause acute injury or chronic degeneration of the brain. As more is understood about the relationship between liver metabolism and brain growth, development, and function such indications for transplant will increase.

Our collaboration also reflects an opinion that the potential for cure of MSD by hepatic gene therapy within the next 10-20 years is extremely low. This is an issue we have thought about carefully.

Between 1990 and 2003, the Clinic avoided making referrals for liver transplants in patients with Crigler-Najjar disease (CN), which a severe form of hyperbilirubinemia for which liver transplant had been an accepted therapy. We developed treatments to prevent bilirubin injury of the brain in infants and children, then waited for an effective gene therapy to develop. In the early 1990s, many physicians and scientists felt that CN patients would be ideal candidates for “hepatic gene therapies.” And, in 1990, most of us believed that a form of gene therapy would be available to these patients in 5 years or less, that is, before 1995. The Clinic sponsored two scientific meetings to review possible methods of hepatic gene therapy for Crigler-Najjar disease in 1999, and 2003. Dr. Morton also gave talks about the treatment of CN disease at two international meetings at Rockefeller University in New York in 1996, and at Erasmus University in the Netherlands in 2000. After these four meetings to discuss experimental gene therapies, we concluded by June 2003 that liver transplant was the only form of “hepatic gene therapy” that would be available to our patients with CN disease within the next 10-20 years. This conclusion reflected a perceived lack of progress in human gene therapy, and improvements in the outcomes of patient undergoing liver transplants. We now think delaying the liver transplants for patients with Crigler-Najjar disease with the rational that the many problems with human gene therapies would soon be solved, is not a justifiable. In the past year, 4 of our 24 CN patients have undergone elective liver transplants at Pittsburgh Childrens. Three of the patients have recovered from the transplant, one continues to have problems with rejection and side effects from immune suppression. The most obvious reason to refer patients with CN and MSD for liver transplant, rather than wait for gene therapy, is that transplant is available as an established, curative therapy. No form of hepatic gene therapy is available. Liver transplants have been done for more than 20 years, Childrens of Pittsburgh has done more than 4000 liver transplants in children. Over this time many complex problems related to surgery and graft tolerance have been solved. Outcomes have steadily improved. In contrast, the translation of the most promising forms of experimental hepatic gene therapy into the earliest “Phase 1” human studies, using patients with CN or MSD, has not begun. The first experimental studies of a new technique would not be a therapeutic trial, but would be studies to evaluate the safety of the proposed method of gene therapy.

The highly publicized death of a young man in Philadelphia in 1999 made it very unlikely that Phase 1 Trials will ever be done again with patients who have unstable underlying metabolic disorders. He had a urea cycle disorder and died during the Phase 1 study of hepatic gene therapy using a virus to infect the liver and thereby, temporarily, introduce a new gene into a small number of liver cells. An immune response to the virus caused fever and catabolism, and, ultimately, the boy died of an inflammatory response to the virus that delivered the new gene, and the resulting biochemical intoxication from his metabolic disorder. Had these same studies been conducted with patient with Crigler-Najjar disease...
Jakob’s Journey

In May 2003, Jakob was evaluated for liver transplantation at Pittsburgh Children’s Hospital (PCH). After a long road of disappointment, we found our way to PCH’s doorstep. The evaluation process was relatively easy, but two very long days for a 3 year old little boy. Meeting the surgeons was an emotional, validating experience for me, and one that I will remember for the rest of my life. For the first time I felt as if a team of doctors really listened to my concerns about raising a child with Maple Syrup Urine Disease (MSUD), and the life-long difficulties we faced relying on dietary therapy to manage his disease. The treatment options, dietary therapy versus liver transplantation, are complex and personal decisions that should remain private family matters. However, suffice to say, after evaluating our own family situation, Jake’s future, and his potential for a viable life as a full functioning adult, we decided to go ahead and list him for transplant.

PCH is the most respected hospital for transplantation in the country, and had performed numerous transplants for metabolic diseases, but Jake would be their first for MSUD. As such, PCH took every precaution to ensure the safety of transplanting a child with a disease as volatile as MSUD. Early on, the transplant team partnered with the Clinic for Special Children (CSC) to learn more about MSUD risk factors and to develop a protocol, the first of its kind anywhere, to transplant children specifically with MSUD. The PCH protocol incorporated rapid turnaround in the lab for results of amino acid levels, educating nurses and support staff about the effects of MSUD, and having MSUD TPN available if needed. Developing a protocol of this nature was no small feat and it took the hospital, along with the assistance from CSC, eight months to establish. Meanwhile, Jake was listed on the United Network of Organ Sharing (UNOS) list in May.

At the time Jakob was listed, the UNOS ranking system spanned from negative 10, meaning non-critical and a likely extensive wait for an organ, to plus 40, which is a priority, to Status 1 meaning emergent. Jakob was initially listed at a negative 10 while PCH continued to develop the protocol. For us, his listing was a test of our patience since Jake would remain in a hold status until the protocol was in place. I made countless phone calls to our coordinator, Lynn Seward at PCH, to see how the protocol was progressing. It was frustrating to be listed knowing this wasn’t even the real wait for the transplant, but I knew it was best, not just for Jakob, but also for the safety of everyone transplanted in the future with MSUD. While Jake was not in liver failure, his need for a liver to stop brain deterioration was still regarded as a priority given the fact that once brain damage occurs it cannot be reversed. Prior to completion of the protocol, PCH met with the UNOS board and successfully petitioned to get Jake’s score elevated to a plus 40 status. This now meant our wait wouldn’t be very long. Jake’s score also established the precedent for other MSUD patients to receive an equally high score and to help our battle with insurance coverage, as it demonstrated just how perilous it is to live with MSUD.

In January of 2004 the protocol was complete and Jake came off the “hold” status...finally! Now the real waiting would begin. I can’t fully explain to anyone who hasn’t gone through this process just how tough the waiting is, and I feel for everyone that will go through it. Deciding to transplant is hard enough, but then to wait for it to happen is the most stressful ordeal I’ve ever faced. On Mother’s Day 2004 we received the call we’d been waiting for. PCH had a liver for Jake. At that moment I went into what I’d rehearsed in my head for so many months, but it didn’t really go the way I had planned. I remember feeling slightly disoriented like I couldn’t quite get my act together. I called the charter flight company we had chosen to fly us to Pittsburgh and told them to fuel up the plane.

(Journey cont. on page 7)
On our way out the door to drive to the airport, roughly an hour after the first call, we received a second call canceling our trip. PCH determined the liver was too small for Jakob so they passed it on to a better match. My husband and I sank on our front steps in shock, while all the adrenaline plummeted, but we agreed that things happen for a reason, and it was not Jakob’s time.

At Midnight On May 29th 2004 we again received the call from PCH and this one proved to be the one that would end our waiting! Jake and I were visiting relatives in Charleston, South Carolina while my husband was at home in Virginia. This time everything went smoothly and it only took us 20 minutes to get ready and out the door to the airport! My mom, Jake, and I boarded a charter plane at 1:30 a.m. bound for Pittsburgh. The flight was frantic due to some bad weather but we made it to Pittsburgh by about 5:30 in the morning while my husband arrived by car shortly afterwards. When we arrived at the hospital, our coordinator, Lynn Seward, who by now had become a family friend, was standing there to greet us. It would take some time, and sedation, to get an IV started but once it was in we waited for them to tell us it was “time”. I was thankful for the sedation because Jake was resting peacefully and he didn’t notice me pacing the floor with tears in my eyes. Around 2:30 p.m. it was finally “time”, so we walked, with Jake on his gurney, down the hall where we said our good-byes. Luckily he was really sedated so that part wasn’t bad, but watching him go behind closed doors was now the most difficult thing I’ve ever experienced. In fact, writing about it now still makes me emotional.

Since the surgery happened on a holiday weekend, we didn’t get updates like we normally do when the hospital is fully staffed, so every once in a while I would ask a nurse from the PICU for information. Everything was going well and by 9:00 p.m. Dr. Sindhi came in to the family surgical waiting area to tell us the surgery was a success! We would be able to see him. Jakob looked great right after his surgery. I was actually surprised at how good he looked. It was while looking at him in that PICU bed that I realized how really brave and strong he is, and all I could do was thank God for sharing him with me!

Jake’s recovery went relatively smooth. He stayed in the PICU for 2 days, and then onto the transplant floor for another 8 days before being discharged. Every day he gained a little more strength and began to resemble the Jake I knew before surgery. We had some obstacles with recovery, but as each one would come up the Pittsburgh team would address it and we’d move on. I could list the issues we encountered but I think it’s best not to get into the particulars. Let it suffice to say that everyone handles the surgery differently and the transplant team is the best source of information on how to best address any complications that may arise post-transplant.

A year after transplant our lives are totally different, and Jakob is doing better than we expected. We’ve noticed a great deal of improvement in his ability to focus, his speech, and lately, his gross motor skills. The medications have tapered off and I’m thankful he’s already been weaned to such a low dose. I don’t want to gloss over the trials of a transplant but I want to be honest about the changes that have occurred in our lives. Since transplant we’ve seen the progress in Jake intellectually. I watch him eat anything he wants with other children and he’s now able to keep up with them physically. I can now rest assured knowing his future is brighter in regards to his physical, mental, and emotional well-being. Speaking for myself, and I know many of you can relate to this, …now I can breathe!

Thank you for letting me share my story and if anyone is interested in discussing liver transplantation as an option, you can e-mail me at curemsud@earthlink.net

Susan JasIn
Mom to Jakob, successfully transplanted
May 30, 2004
Liver Transplant Evaluation

We decided that we would like to look into the option of Liver Transplant for our son Zachary. We wanted to make sure we had all the facts regarding this option. We called Children’s Hospital of Pittsburgh and spoke with Lynn Seward, a nurse coordinator, who explained what would take place. I then had to do lots of work with our insurance company to get the approval for the evaluation. This process took me 5 months before I got an approval. I have an HMO and they deny, deny and deny with the hope that you will give up. One of the positive things that MSUD has taught me well is NEVER GIVE UP! Here is a day-by-day account of the process we went through.

Day One
8 a.m. - Register and get blood drawn – 12 tubes - By far the most traumatic part of the evaluation for Zac.

9 a.m. - Neurological Psychological evaluation. Children’s Hospital of Pittsburgh is asking 10 people with MSUD to have this evaluation at the time of their liver transplant evaluation and then repeat the testing one-year after transplant. They want to have scientific data showing what the outcome has been.

The psychologist asked Ron and I background questions, then asked to meet with Zac alone. Zac stayed with her for about an hour. The information that was reported is what we expected.

11:30 a.m. - Meet with Lynette Rosser, the transplant social worker. Basically she wants to make sure you have a support system. She can find supports to help if there are concerns.

We then left the hospital and enjoyed the afternoon. I went back to the hospital in the evening to see Yasmeen Maisari, who had her transplant 10 days prior to this date.

Day Two
9:20 a.m. - Ultrasound and chest x-ray – Zac could not eat for 6 hours before these tests. He did very well through both of these tests.

11:00 a.m. - Transplant clinic – We then met with Dr. Soltys (transplant surgeon), Lynn Seward (one of the nurse coordinators), and several other support personnel. They explained the transplant pros and cons. They answered our questions and invited us to send additional questions to their email if we thought of any later. Dr. Sindhi (transplant surgeon) then came in by himself and we went thru another question and answer. The staff was very informal and we felt comfortable asking questions. Dr. Squires also came and talked with us about our concerns with transplant. The entire staff was very open to questions. They gave us the sense that they could fix the problems that come after transplant.

1:00 p.m. - Cardiology – Zac had an EKG-Echo cardiogram and consultation. He watched a video thru this procedure and he did not mind it at all. Once again very nice people performed the procedure.

3:30 p.m. - We were able to leave the hospital and get something to eat. We then ran into Katy Martin, mother of Amy Martin (child with Crigler Najjar) who had a transplant 10 months ago. Her journey has been bumpy. She has had quite a few rejections requiring numerous hospitalizations.

Day Three
9:00-11:00 a.m. - Meeting with Beverly Kosmach – Clinical Nurse Specialist. She explained all the potential issues we could have after transplant. She explained medicines, cautions and shared pictures of children at camp who have had transplants.

As we were waiting for the above meeting, Dr. Mazariegos (transplant surgeon) came and talked with us to see if we had any questions regarding transplant.

12:00 p.m. - Blood draw – 2 or 3 tubes

1:00 p.m. - Met with a person who explained anesthesia for the procedure.

1:30 p.m. - Met with Renee Jones-Hoots who explained the financial concerns regarding transplant. She also gave information about accommodations during transplant. We then went to see Yasmeen and Amy Martin once again to say our good-byes and to wish them a speedy recovery. Because of the great MSUD support groups we felt pretty well informed. We have decided to place Zac on the Liver Transplant list. At this point, we have gotten the call for Zac to be transplanted, but he had a cold so we will continue to wait and pray. I hope everyone supports us on our decision for what we feel is best for our family. We will continue to pray for all MSUD people and their families.

Submitted by – Denise Pinskey

Please Note:
Zac was transplanted on Monday, June 27th.
Three-In-One Bread

830 grams wheatstarch
1/2 cup Equate brand Metamucil
4 teaspoons yeast
2 teaspoons salt
2 tablespoons Methylcellulose
1/4 cup brown sugar
1/2 cup oil
700 grams water

Weigh wheatstarch into mixing bowl. Add other ingredients; adding water last. Mix on slow speed for 4 - 5 minutes. Divide dough into 3 parts. Note: There is no need to proof the yeast. Add it with the dry ingredients. The dough divides easily if you use a well greased spatula.

PART 1: Shape 1 part into a loaf for white bread. Place in a well greased bread pan. Let rise until 1 inch over edge of pan. 14 slices bread.

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PART 2: Monkey Bread-
1/2 cup brown sugar, 1 teaspoon cinnamon
Mix sugar and cinnamon together. Drop and roll bread dough by rounded teaspoonful in sugar mixture. Place all in well greased bread pan. Let rise until 1 inch over the edge of pan. 14 slices bread.

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PART 3: Garlic Bread Sticks-
1/2 cup melted butter, garlic powder
Roll dough into a 12”x15” rectangle. Cut into 1”x12” strips. Dip into melted butter and sprinkle with garlic powder. Place on a greased cookie sheet. Let rise 45 minutes. 15 bread sticks.

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BAKING: Preheat oven to 350. Bake breadsticks 25 - 30 minutes. Bake both loaves for 35 minutes.

3 breads; one recipe!

Grilled Mushrooms

1/2 pound medium mushrooms
1/4 cup melted butter
1/2 teaspoon dill weed
1/2 teaspoon garlic powder

Thread mushroom on skewers. Combine butter and seasoning; brush on mushrooms. Grill over hot coals for 10 - 20 minutes, basting and turning every 5 minutes. Makes 4 servings.

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Campfire Potatoes

5 medium potatoes, peeled (925 grams)
1 medium onion, sliced (180 grams)
6 tablespoons butter
2 tablespoons minced fresh parsley
1 tablespoon Worcestershire sauce
salt and pepper
1/3 cup water
1 packet Washington’s Golden Seasoning

Place thinly sliced potatoes and onions on a large heavy-duty aluminum foil; dot with butter. Combine parsley, Worcestershire sauce, salt and pepper, and sprinkle over potatoes. Fold foil up around potatoes and add water and the seasoning packet contents. Seal the edges of the foil well. Grill, covered over medium coals for 30 - 40 minutes. Makes 8 servings.

Note: I use a double layer of foil. Can also be baked in oven at 350 for 30 - 40 minutes.

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<td>Per serving:</td>
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Bubble Gum Ice Cream

1/2 cup small gumballs
1 8oz. Cool Whip

In a dry blender jar, blend gum balls till they are in small pieces. It works best to turn blender on and off several times. Fold into thawed cool whip. Refreeze.

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<tr>
<th></th>
<th>Protein</th>
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</thead>
<tbody>
<tr>
<td>Per tablespoon:</td>
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<td>5 mg</td>
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Tips to Making Bread:

Mix dough well with an electric mixer, about 5 minutes. Dough will be somewhat thin at first the will set up stiffer, but be sticky. Rub hands with oil before forming bread loaves and sticks. Spray tops of loaves with PAM spray before baking for a nice brown color. If you have trouble with loaves caving in after baking, bake 5-8 minutes longer. Let bread cool 15-20 minutes; then put into bags. This will help soften crust if it’s a little too hard for your child.
Cambrooke Foods

Look for a new Scoop and Bake Cookie Dough; a plain cheese fresh-filled Ravioli as well as other new low protein products – all coming soon. Now available are Aproten Cream Filled Wafers - a favorite with the little kids. Bring Camburgers to your next picnic, for a quick and easy meal from the grill. Old favorites include fresh-filled pastas, specialty breads, pastries, cream cheeses, dry pastas, baking mixes and seasoning blends. All available for making delicious summer meals.

Coming soon - DietWell™! Monitor and understand how your diet and protein supplements are affecting your wellness with Cambrooke’s new Dietary Wellness Network™. This is a free, use-at-home, web-based collaboration environment for metabolic patients and their clinics that will allow you to record and monitor your daily protein intake in a secure environment. You will be able to see the relationship between your diet, your wellness level and receive personalized reports that track all – perfect to bring to your clinic visits. Best of all, you will receive DietWell™ points for using the program that you can use as credit toward Cambrooke food purchases.

Contact Cambrooke if you would like to take control of your wellness with DietWell™.

We would like to welcome Erica Lesperance, RD., LD, to the Cambrooke Foods team. She brings her expertise and experience from the Emory Clinic to the Cambrooke family.

Summer goes by quick. Get a jump on the next school year with Cambrooke’s School Lunch Program. Our School Lunch Program packet includes all the forms and instructions that you and your school lunch staff will need to have your child join the school lunch line. Contact us to receive your copy.

Do you like to receive weekly recipes and special promotions? Make sure Cambrooke has your correct e-mail address and we will send these out to you. See our posted recipes on our website under the “Recipes and Tips” tab.

We are 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 your orders to us at (978) 443-1318.

MSUD Maxamum:
The trusted MSUD medical food now meeting new vitamin and mineral recommendations.

SHS North America has updated our Maxamum product line, including MSUD Maxamum, in accordance with the new Dietary Reference Intakes (DRIs) recommendations and in our tradition of providing the best in clinical nutrition products. This product line now meets or exceeds the DRI recommendations at adequate protein intake from medical food. To help with the transition to the new formulations, SHS will offer both old and new formulations for a limited time. We are also providing patients with a two-can sample pack in an attractive cooler lunch bag together with a useful transition brochure. Patients should contact their clinic for free samples. For additional information on new MSUD Maxamum, give our nutrition experts a call at 1-800-365-7354. Canadian customers, please call 1-877-636-2283.

The Dietary Reference Intakes (DRIs) are issued by The Food and Nutrition Board of the Institute of Medicine. These recommendations encompass the dietary intake of protein, carbohydrate, fat, vitamins and minerals. The DRIs are used in planning and assessing diets for individuals or groups as well as helping to monitor inadequate or excessive nutrient intakes.

It is important for metabolic patients to be aware of these recommendations as those for several crucial vitamins and minerals have changed (for example vitamin B12, folate, calcium and iron). These micronutrients are important to monitor as they are mostly found in meat and dairy products, foods that are excluded from protein-restricted diets such as the MSUD diet. If your medical food does not contain vitamin and minerals, be sure to get enough from other sources such as vitamin and mineral rich foods or supplements. If you have any questions or concerns regarding vitamin and mineral intake, talk to your dietitian or physician.

by Amy Merwarth, RD, Nutrition Specialist
SHS North America

PKU Perspectives is a new line of Low Protein food.
The website is www.pkuperspectives.com and the phone number is 1-866-758-3663.
They have scrambled egg mix, hotdog mix and ice cream mix.
Glenda, our Food News Editor, has tried these 3 products and has highly recommended them!
A Look at Transplant as an MSD Option

Robert Squires, M.D., Professor of Pediatrics, University of Pittsburgh
Clinical Director, Gastroenterology/Hepatology, Children's Hospital of Pittsburgh

Having maple syrup disease (MSD) requires a daily dietary vigilance to maintain proper metabolic control of this genetic condition. Strict adherence to the carefully planned diet will maximize a child's potential with this condition. However, such restrictions can be a challenge for the growing child and adolescent who becomes naturally curious to try new foods and new tastes. There are no food holidays or special occasions. The diet must be followed without exceptions. While it can be a tough diet to adhere to, it is doable.

Despite best efforts to strictly follow the diet requirements, a viral infection or vomiting spell can quickly result in poor metabolic control and precipitate a metabolic crisis. Early recognition and intervention during these “sick days” can prevent the more serious and devastating spells that result in brain swelling, coma and even death. Unfortunately, MSD does not always play fair. A patient can carefully and dutifully follow “the rules” of the diet and still develop a crisis. It is precisely this unpredictability that has prompted many patients, families, and health professionals to seek a more permanent solution.

As this is a genetic condition, it naturally follows that gene therapy could potentially cure the disease. This hope cannot be abandoned. However, gene therapy has not moved forward as quickly as many had hoped. Finding and developing the critical genetic material, safely incorporating it into the genetic material of the patient, and ensuring the material will produce a functional enzyme that will replace the defective one are just a few of the mountains on the horizon.

The defective enzyme in MSD is not located exclusively in the liver. In fact, other organs such as the brain, intestine, muscle and heart have high levels of the enzyme. Therefore, the idea that a liver transplant could provide a cure for an enzyme deficiency that is present in many body tissues seemed far-fetched. However, in the early 1990’s a young French girl, diagnosed with MSD in infancy and with a history of metabolic crises, contracted the hepatitis A virus. This young lady was one of the unfortunate few who developed rapid liver failure from the hepatitis A viral infection and received an emergent liver transplant for that reason. Surprisingly, after the liver transplant, the child was able to eat a regular, unrestricted diet without developing a metabolic crisis. She underwent more sophisticated testing a few years after the transplant and her doctors found that while her isoleucine levels were very mildly elevated, her body could process large amounts of branch chain amino acids as quickly and efficiently as patients without MSD. It is following this experience, as well as and that gained from a MSD patient who received a liver transplant as a result of vitamin A toxicity, that has prompted a closer look into the possibility that liver transplant could serve as a potential metabolic cure for the disease.

Over the last 20 years of experience with liver transplant in children, patient survival and the complications associated with medications to prevent rejection have improved drastically. As the outcomes following liver transplant have improved, and the outcomes for dietary management of MSD are not without consequences, some families are beginning to consider liver transplant as a treatment option for their child.

The decision by the patient, family and health care provider to choose continued dietary management or liver transplantation is not easy. On the one hand, MSD is controlled by diet, the metabolic defect is not isolated to the liver and there are risks associated with liver transplant. On the other hand, dietary management is not all that easy, specific gene therapy is not on the horizon, there is genuine anxiety about the sudden development of a metabolic crisis, the cost for medical management is between $7,000-9,000 per year for well children and $100,000-500,000 for severe metabolic crises, and many issues surrounding liver transplant have been improved. (See Drs. Morton/Strauss’ article for an estimate of medical treatment costs.)

At the University of Pittsburgh and the Children’s Hospital of Pittsburgh, we gathered a number of critical personnel to develop a program to provide liver transplantation as an option for children with MSD. Those personnel included transplant surgeons, pediatric specialists in areas of metabolic disease, liver disease, and intensive care, pharmacist, dietitian, nurse practitioners, nursing staff with expertise in patient care and coordination, and the hospital administration. Our goal was to identify the best candidates for transplant, identify the best liver graft for the patient, and minimize the metabolic stress that would be associated with preparation for surgery. In addition, we needed to
potential problems and have a strategy, which included TPN if necessary, to intervene should an altered metabolic state develop.

A strict decision “tree” was put into place once a MSD child was placed on the transplant list. First, only a healthy, whole, blood-type and size matched donor liver would be considered. Once a proper graft was identified and matched to a MSD patient, the family is notified. If the child has been clinically well and has not required a special or “sick day” formula within the last 3 weeks, the initial preparations for liver transplant were initiated. Once the child arrives in the hospital, their metabolic stability is assessed and a glucose infusion is started to minimize the metabolic stress. There is always the possibility that even if a patient is “called in”, circumstances could arise that would result in the cancellation of the transplant. It is critical that all the proper pieces of the transplant puzzle be in place, and if they are not, then it is safer to cancel the operation and wait for the next time.

In the end, the decision to proceed with a liver transplant for a child with MSD comes down to an imperfect, but an increasingly better understood, effort to balance the various probabilities associated with proceeding with a transplant or not. The decision to continue with medical management is, on the one hand, comfortable, familiar, and avoids trading one disease (MSD) for another (suppressed immune system following liver transplant). On the other hand, dietary therapy is restrictive, expensive, associated with a number of quality of life issues, and does not guarantee freedom from the broad range of neurologic and metabolic crises. The decision to proceed to liver transplant is, on the one hand, free of dietary restrictions, and is associated with newer immunosuppression regimens that do not include steroids that allow some patients to eventually reduce medications significantly or come off of them entirely. On the other hand, it is also expensive, associated with real, albeit rare, risks of the operation, and requires daily medication which, for most, will be life long.

There is no “right” or “wrong” decision. The family, along with consultation from health care providers, will make the right choice for their child and family. At the same time, there will be some angst associated with the decision process, but this will allow one to become more familiar with themselves, their child’s condition, and what the future might hold for their child; and this is a good thing.

Robert Squires, M.D.
Professor of Pediatrics
University of Pittsburgh
Clinical Director, Gastroenterology/Hepatology
Children’s Hospital of Pittsburgh

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Galen Carrington Jr. Competes in Indiana State Swimming Championships!

Jody and Galen Carrington of Lawrenceburg, Indiana are very proud to announce their son, Galen Jr. age 15 (intermittent MSUD), went to Indiana’s State Swimming Championships in March. Galen Jr. qualified to swim in 2 relays: the 200yd Freestyle Relay and the 200yd Medley Relay where Galen swam the butterfly stroke. His team placed 7th and 14th out of 24 teams across Indiana. Galen started his swimming career 3 and 1/2 yrs ago with East Central Swim Team, knowing only the freestyle stroke. Who could ever imagine that in just 3 short years Galen, who has MSUD, would swim at the state level! Galen has far exceeded any expectations, especially when his endurance is such an issue. Galen takes several supplements including Carnitine, flax seed oil, extra Thiamine and B complex vitamins which he feels helps with energy levels. (Please consult your physician before taking any supplements. The role of these supplements in increasing energy levels has not been scientifically proven.). When Galen was born, he was labeled as “classic MSUD” and was hospitalized 5 times before the age of 3. On one occasion, he even stopped breathing. As he got older, Galen was able to tolerate higher levels of Leucine and was allowed 15 grams of protein per day. Now Galen is relatively healthy, although he has trouble eating enough calories to maintain his weight while swimming 3 miles a day! Galen is currently having a hard time switching formulas since MSUD Diet Powder will no longer be available.

Congratulations to Galen and continued success with his swimming career!!!
conducted with patient with Crigler-Najjar disease or MSD, the result would have been the same – metabolic intoxication, brain injury, and death, arising from the catabolic response to viral gene vector. For the foreseeable future, gene therapy trials that involve patients with unstable metabolic disorders will be considered unethical.

When, or if, a new method of hepatic gene therapy does complete the earliest non-therapeutic studies about safety, complex questions will remain to be answered about how well the new gene-enzyme complex controls blood and brain biochemistry after a high protein meal and during catabolic illnesses. Successful treatment of MSD by gene replacement, in particular, will require that a very high percentage of liver cells, probably more than 80%, acquire stable, highly regulated BCKAD enzymatic function. Current methods of hepatic gene therapy in animals introduce very low levels of gene/enzyme activity, typically into less than 1% of liver cells. For this reason, even if one of the current hepatic gene therapies could be safely done in humans, such low levels of enzyme expression would not be therapeutic for MSD.

The lethal response to the viral vector in the urea cycle trial in Philadelphia suggests too that problems can be expected related to long term immune tolerance of the liver cells transformed by gene therapies. Controlling immune responses to viral gene vectors is likely to be no less problematic than the immune suppression now needed to allow tolerance of a transplanted liver. For these, and many other reasons, our opinion is that therapeutic trials in humans to prove that any form of hepatic gene therapy for MSD is as safe, as effective, and as enduring as whole liver transplants are extremely unlikely within the next 10-20 years. The choice facing parents and patients with MSD is between long term medical treatment and liver transplant.

WHY HAVE SOME PATIENTS WITH MAPLE SYRUP DISEASE UNDERGONE ELECTIVE LIVER TRANSPLANT S?

First, when MSD is poorly controlled by diet, and access to specialized care during metabolic crisis is not available, then the risk of progressive neurological disabilities, or death from cerebral edema, over a 10 year period is very high, and, in our opinion, exceeds the risks associated with liver transplant. This is true for children and adults. Second, liver transplant for MSD controls the biochemistry of MSD sufficiently to allow an unrestricted diet, and afford protection of the brain during intercurrent illnesses. (Morton et al. 2002b; Bodner-Leidecker et al. 2000; Wendel et al. 1999; Netter et al. 1994)

It is also of great interest to us, that cure of MSD through liver transplant has been associated with unexpected improvements in brain function. We attribute this to the stabilization of the plasma amino acid profile. (FIG 1&2) Many effects of MSD upon the brain can be understood in terms of the abnormal use of 8 essential amino acids that compete with leucine for entry into the brain. In infancy, the slow uptake of one or more essential amino acids by the brain results in poor growth and development of the brain. Clinical signs of the amino acid dysmetabolism in infancy include chronic irritability and anorexia, but, years later are manifest as mental retardation and cerebral palsy-like physical disabilities. Poor metabolic control in school age children is associated with hyperactivity, attention deficit disorder, impulsivity, and mood disorders. The same chronic biochemical disorders in teenagers and adults cause adult variants of attention deficit disorder, generalized anxiety disorder, panic attacks, mood and appetite disorders. Maternal MSD will become an increasingly important issue. Fetal exposure to poorly-controlled maternal MSD will, as in PKU, place these infants at high risk for severe neurodevelopmental problems that begin in utero. Our experience suggests that middle age adults with poorly controlled MSD may have declining cognitive function, early onset parkinsonism, and mood disorders. We do not doubt that many of these problems can be prevented by better metabolic control, through improvements in formulas and metabolic foods combined with better medical treatment of MSD during intercurrent illnesses. However, under the best of circumstances, current medical treatment of MSD in the adult does not appear to benefit brain nutrition and function as much as liver transplant does. As the neurological effects of liver transplant are better understood and documented, this may emerge as an important indication for transplant, particularly in teenagers and adults.

COSTS OF LONG TERM MEDICAL TREATMENT OF MAPLE SYRUP DISEASE AND LIVER TRANSPLANT:
The costs of liver transplant are high - $200,000 is a figure often quoted, but the actual costs depend upon the method of payment and complications after transplant. As with MSD, the ultimate costs of liver transplant in an individual patient over a 10 year period are difficult to predict. At the Clinic for Special Children, the average cost of medical care for a patient with MSD is relatively low because we are a non-profit medical Clinic, and are heavily subsidized by the Mennonite and Amish Communities. We estimate $7,000-9,000 per patient per year, or about $80,000 per 10 years of follow-up. However, we have little control over in-hospital treatment of illnesses. Over a 16 year period, we have managed patients through more than 200 hospitalizations for acute illnesses. Approximately
1/10 of these admissions were prolonged and generated hospital bills in excess of $100,000. The cost of even routine hospital care for our patient has increased dramatically. The daily room rate at our hospital has increased from $350/day in 1989 to over $1700 per day. One of our patients was recently billed over $11,000 for a single day in hospital because of a respiratory tract infection. More than $9000 this bill was a hospital pharmacy charge for purchase and preparation of a medication called Synagis. At the Clinic the purchase and administration of the same medicine costs $900. Costs associated with management of a newborn with MSD who needed bowel surgery and heart surgery exceeded $500,000. Two life threatening cases of cerebral edema exceeded $500,000 each. The lifetime medical costs associated with neurological disabilities are extremely high. One 5 year old MSD child suffered injury from brain herniation that cause partial paralysis, speech impairment, and blindness, generated medical costs approaching $1 million dollars. Finally, it is especially difficult to estimate the long term costs of adults with MSD who, because of brain injury or chronic metabolic intoxication, cannot work or live independently.

Much of the debate regarding transplant for MSD centers on the "treatability" of this complex disorder over the lifetime of the patient. Based upon our experience at the Clinic for Special Children, physicians, parents, public health officials, and medical insurers have underestimate the long term risks of neurological problems that accrue even with the best medical and nutritional management. We now expect all of our patients with MSD to survive to adulthood. The cumulative costs for medical treatment of an individual with MSD over 10, 20 and 40 years will, in the majority of cases, exceed the cost of liver transplantation.

CONCLUSION:
Liver transplant provides adequate control of Maple Syrup Disease to allow a normal diet, and prevents systemic metabolic intoxication and cerebral edema during catabolic illnesses. The stabilization of blood amino acid concentrations following transplant is associated with significant improvements in brain function. We do not recommend liver transplant for all patients with MSD. Risks and costs must be assessed on a case-by-case basis. For some patients, liver transplant is reasonable, cost effective treatment.

A FINAL COMMENT: The use of organ transplants to treat genetic diseases is one way to translate the remarkable recent advances in the molecular biology and genetics into genetic medicine. As our understanding of genetic diseases increases, organ transplantation should become an increasingly important way to help patients who suffer from these difficult disorders. Being able to provide this help depends most obviously upon the innovative, difficult work of those in transplant centers, and upon organ donor programs. Yet, ultimately, the ability to provide such extraordinary help to an individual requires the sustained belief within our society that such care is a necessary and important part of health care.
An Introduction to Your New Newsletter Editor

My husband and I have been receiving the MSUD newsletters for about 10 years now. They have been enormously helpful to us as we learned more about how to care for our daughter and what to expect as she grew. I look forward to giving back to this organization which has given so much to me. Here is my story: I married at the relatively ripe old age of 35. Knowing that time was of the essence, I carefully underwent genetic testing for known Jewish genetic diseases while I was planning my wedding. Everything was negative.

When our daughter Hannah was born after an uneventful pregnancy, we were told we had a wonderful, healthy baby girl. We left the hospital on a beautiful May Friday, full of promise and expectations of how perfect our lives were and would continue to be. Over the weekend, Hannah seemed to lose her appetite. I thought it was because I was inexperienced at nursing. I also noticed that her diapers felt dry. On Monday morning I called the pediatrician, who told me that she probably wasn’t very hungry. I went to a nursing specialist at the hospital for help with my technique. By Tuesday night she was experiencing episodes of hypertonicity and had developed a strange, high-pitched cry. Clearly something was wrong. I brought her to the doctor the next morning, still thinking that the problem was an inability to nurse adequately. He weighed her, saw she had lost almost 2 pounds, and immediately admitted her. That afternoon she lapsed into a coma. Unfortunately, it wasn’t until 2 days later, when she was 10 days old and still in a coma, that the results of the newborn screening came in. Hannah had Maple Syrup Urine Disease. She was transferred to New York University Hospital and placed under the care of Dr. Claude Sansaricq. Under his treatment she immediately began to recover. We were lucky. Although she had spent 2 ½ days in a coma and wasn’t diagnosed until her 10th day of life, Hannah has very mild physical delays and no apparent mental deficits. She has received excellent care throughout her 11 years. While she had several severe decompensations in her early years, she has been stable for the last several years. She is a special child, as are all of yours.

Unlike most of you, I suspect, the name given to her disease wasn’t completely foreign to me. I received a Master’s degree in Food and Nutrition and became a Registered Dietitian in the early 1980’s and have been practicing in the field ever since. This was one of those diseases that I had heard of way back when in one of my graduate courses. Whenever I tell people about my daughter, they ask if I became a dietitian in response to her disease. No, I say, it was simply a twist of fate. My education has probably made it easier for me to deal with her disease and dietary management. I have not experienced anxiety over my abilities to adhere to her restrictions, as perhaps some of you have.

I decided to go back to school after Hannah was born and earn a doctoral degree. I thought about specializing in metabolic diseases, but for me it was easier to keep my work and my child’s life separate. I specialize in sports nutrition and obesity management. While much of the work I do is with athletes, I also maintain a clinical practice where I see people with diabetes, heart disease, kidney disease…just about everything but metabolic diseases.

Hannah receives her care through the Mt. Sinai School of Medicine, which has an extensive Department of Human Genetics. In 1997 we founded the Genetic Disease Foundation, represented by friends and families affected by genetic diseases including metabolic diseases, Tay Sachs, Neimann-Picks, Cystic Fibrosis, Canavan Disease and others. I serve on the board of this organization, whose mission is to support education and research for the prevention and cure of genetic diseases.

I look forward to working with you all. If you have suggestions for the content of future newsletters, please contact me at krdhed@aol.com or 914-723-5458.

Thank you.

Karen R. Dolins, EdD, RD, CDN

Dr. Eric and Sondra Tompkins, parents of Nathan, transplanted 2004