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FEATURED FAMILIES - A MIRACLE CHILD

Details

Written by Angie Perdue

Published: 21 July 2009

This article was adapted from an article Angie Perdue wrote about her daughter Tangi in an effort to alert the public to the need for newborn screening for MSUD. She is involved in a personal campaign to get Texas, her home state, to screen for MSUD. This is the sad story of Tangi's delayed diagnosis.

I was seventeen when I became pregnant with my first child. There were no complications with my pregnancy. I gave birth to a baby girl on August 7, 1996 at the age of eighteen. Her father and I decided to name her Tangi after a girl on Buck Rodgers. Neither of us knew it then, but our world was about to change.

The minute Tangi was born she began crying nonstop. That did not alarm me, but then she kept crying and arching her little back. I knew the sound of a baby's cry, but this was different. It was more like a scream than a cry. Being a new mom, I was scared - scared to hold her. Deep down inside I could sense that something was wrong. She looked normal; she just did not act normal.

When my husband and I brought Tangi home from the hospital, we stayed with my mom so that she could help me care for Tangi and teach me a little about how to be a mom. After all, she raised seven children. She was an expert in my eyes. That first night at Mom's was a nightmare. Tangi cried nonstop. She would not suck her bottle, would not sleep, did not urinate, and she was still arching her back.

I was raised in an Assembly of God Church, and God was no stranger to me. I knew that God was telling me something was wrong with this baby. We took Tangi to the emergency room two or three different times those first couple days as well as to the pediatrician. Our baby was getting worse. We took her to the emergency room again when she was three days old. This time they did some tests and a nurse saw Tangi having a seizure. From the

test results, the doctor thought she was having some brain problems. They decided to send Tangi to a hospital in Galveston for more tests.

I was very scared. I remember sitting in the hospital room at my daughter's bedside looking out the window up into the heavens and asking God *why*? *What have I done to deserve this? It was not supposed to turn out like this. Why my daughter?* My mom came and sat beside me crying. I just looked at her and said, "Why? What did I do?" She said, "Angie, God is in control of this situation. Who knows why God does things or allows things to happen. God has a purpose for everything, even though you don't understand or may never understand. Remember God is in control." When the nurses brought Tangi back to the room, I held her and said, *God this is your child, not mine.* I knew my job was to raise this child for God.

In Galveston, Tangi was put in the neonatal intensive care unit. We waited for hours not knowing what to expect. When we saw her again, it was a scary sight. She was hooked up to so many wires. Test results showed Tangi's brain was swelling. Why? The doctors did not know.

Tangi eventually went into a coma. My aunt called and told me that God had given her a message for me. God said that this child is not of death. I cannot put into words the joy that I felt. It was like someone was right there in the room with me. In my spirit I could feel Jesus giving me this huge hug. I needed that; it kept me going. Deep down I felt God was telling me that everything was going to be okay.

The circumstances did not look good. The doctors said that if our daughter came out of the coma, more than likely, she would not be able to see, hear, speak or even walk. But I remembered what God had said, "This child is not of death." I held onto God's word and thanked Him every day for that.

Then at one month of age a test result showed Tangi had a rare metabolic disease known as maple syrup urine disease. I had never heard of it before. The doctors put her on a special formula. After a week, she came out of the coma. Thank you Jesus! Now was the time for her father and I to learn about this disease and how to care for her. It took us a month to learn how to make her formula and learn what foods she could eat.

It was very scary to bring our little girl home when she was three months old. We lived two hours away from my mom and any of our family. I knew God was looking over our little girl and was right there helping us, because He did not take her home to be with him when she was so sick.

At first I prayed every day for my daughter's sight, speech, hearing and ability to talk, but then I started thanking him for those abilities. We had noticed Tangi staring at the light and her eyes would flutter when I shut a cabinet door. God gave me dreams of Tangi as a normal little girl. I held on to my dreams.

Tangi's care was transferred to Baylor University Medical Center in Houston. She was doing okay until she became sick when she was six months old. She was admitted to the hospital, but I soon sensed she was getting worse. She had a rash under her neck and on her

bottom. It was no normal baby rash. It looked awful and so painful. No one knew what caused the rash.

My mother-in-law called and told us of a doctor in Lancaster, Pennsylvania who specialized in treating MSUD. After speaking with Dr. Holmes Morton on the phone, and praying about the situation, I knew I had to get Tangi to this doctor. The question now was how? We had no money. I had never flown or even been out of the state of Texas before. I prayed and put the situation in God's hands. Two days later our friend's father gave us the money to fly to Pennsylvania to see Dr. Morton. Now I had to convince the doctors, as well as my husband, to let me go. They did not approve. My husband thought she was okay where she was and did not feel comfortable with me and a sick baby traveling alone. I could understand that. However, I also knew that God wanted me to go; so that's what I did.

Tangi and I flew into Pittsburgh, Pennsylvania. My mother-in-law and sister-in-law picked us up and drove us to Lancaster to meet with Dr. Morton. Dr. Morton admitted Tangi into the Lancaster General Hospital. We stayed there for a month. He checked all of her amino acid levels and straightened them out. Tangi was like a new baby - no rashes or anything. She looked great. Dr. Morton and his staff took excellent care of Tangi and I both. I had never been to a doctor who loves his patients and cares for them as much as Dr. Morton. He truly loves and cares for these children with rare diseases. He stayed at the hospital with Tangi all day and through the night. That is dedication, and I thank God every day for putting Dr. Morton in our lives.

Tangi is almost seven years old. She can see, hear, speak and walk. Thank you Jesus! She plays outside on the swing set with her younger sister and enjoys life. Tangi does have learning disabilities. She is hyperactive and cannot stay focused for a long period of time. She recently learned how to count to ten. She is behind in some areas, but does some things better than we expected. We are very proud of the progress she is making.

We see Dr. Morton at the Clinic for Special Children twice a year for check-ups. Tangi has a Mickey Tube *[another name for a G-tube or gastrostomy tube]* in her belly for the formula. She refused to drink her formula anymore, so Dr. Morton thought it would be best to use a Mickey Tube because Tangi is his patient, and we live so far away in Texas. Since she is under Dr. Morton's care, we have not had any serious problems.

God told me He was going to heal Tangi of MSUD. I don't know how or when, but I know that He has a plan, and He will heal her. I ask that when you pray, you help me thank God for what He has done in my daughter's life, and what He is going to do in the future. Tangi's bad experience could have been prevented if she had been diagnosed at birth. Some states screen for MSUD, however, Texas is not one of those states. It needs to be. More doctors need to learn about MSUD. It is surprising how many doctors have never heard of this disease. It is rare, but people need to be aware of it.

GENE THERAPY FOR MSUD TAKES A BIG STEP

Details

Written by Harbhajan S. Paul, Ph.D.

Published: 20 July 2009

At the end of May, 2003, Harbhajan S. Paul, Ph.D. contacted our MSUD Family Support Group explaining his research and the possibility of its termination. The National Institute of Health (NIH) had supported his studies for the past four years. The grant application he submitted last year, in which he proposed to use his newly created MSUD mouse model to treat MSUD with gene therapy, was not funded. The MSUD Family Support Group made a decision to supply bridge funding (bridging the gap) for one year with the hope that his revised grant application to the NIH will receive the funding he needs for continuing his research. Bridge funding will not only keep his MSUD animal models alive, but keep alive the hope of gene therapy as a cure for MSUD. In this article, Dr. Paul answers questions concerning his studies.

Dr. Paul, tell us about your early research in the metabolism of the branched-chain amino acids.

I became interested in MSUD from my interest in the metabolism of the branched-chain amino acids (BCAAs), leucine, isoleucine and valine. Since 1974, I have been involved with research on BCAA metabolism, first at the University of Pittsburgh School of Medicine and more recently at Biomed Research & Technologies, Inc., a biotech company that I founded in 1996.

In our earlier studies, we investigated the effect of nutritional and hormonal changes, such as starvation and diabetes, on the metabolism of the BCAAs. These studies were carried out largely in the liver and skeletal muscle of laboratory animals. We also studied the effect of carnitine and ketone bodies on BCAA metabolism.

As more information about the branched-chain keto acid dehydrogenase (BCKDH) - the enzyme responsible for the catabolism of the BCAAs - became available, our studies focused on the regulation of this critical enzyme. For example, we, along with others, were able to show the regulation of the BCKDH by phosphorylation and dephosphorylation cycle. We also studied factors and physiological states that play a role in the interconversion of the enzyme from an active to inactive form in various tissues.

Subsequently, we studied the gene expression of the BCKDH in cultured liver cells, as well as in animal tissues. We found that expression of the BCKDH subunit genes is affected by hormones and drugs. We also studied the expression of the BCKDH kinase gene by hormones and drugs. All the above studies provided very useful information about the BCKDH, particularly its regulation and gene expression.[1]

How did these studies on the metabolism of the BCAAs and the BCKDH influence your interest in MSUD?
With most of the basic research on the BCKDH completed, we then focused our attention towards clinical application. Obviously, the most important clinical problem in this area was MSUD. As you know, there are several clinical variants of the disease, the classic form being the most severe form of MSUD. We were aware of the difficulties in managing this disease. In spite of dietary intervention, the disease produces several complications, the most notable being mental retardation. Moreover, even if successful, dietary intervention does not cure the disease.

How did this lead to gene therapy as a cure for MSUD?
Because of the limitation of the dietary approach in managing MSUD, we began to think of other possible treatment options. By this time, genes encoding the BCKDH subunits were cloned and vectors to deliver genes were becoming available. Because of these advances, we began to think of the possible use of gene therapy to cure this disease. As a first step, and to establish feasibility of such an approach, we tested gene therapy in cultured cells derived from an MSUD patient. We obtained skin fibroblasts carrying a mutation in the E2 subunit of the BCKDH. These cells expressed less than 2% of the BCKDH activity as compared to normal cells. Using a retroviral vector, we were able to deliver the normal E2 gene into mutant cells. Following E2 gene delivery, the level of the BCKDH was restored to 93% of the level observed in normal fibroblasts. We also showed that the newly synthesized E2 protein was localized to mitochondria, the site of BCKDH.

The above results established the correction of the BCKDH deficiency at the cellular level by the transfer of the normal gene to cells derived from an MSUD patient. Our results with cultured cells were very encouraging and confirmed that further studies can now be undertaken to cure MSUD by gene therapy.

After you were successful in correcting the enzyme deficiency which causes MSUD at the cellular level, what was the next step?
To advance the research from the cellular level to the level of the whole animal, we now needed an animal model of this disease. Unfortunately, no animal model of MSUD was available.

At this time, I sought the help and advice of Gregg E. Homanics, Ph.D., a professor at the University of Pittsburgh School of Medicine. Dr. Homanics is very experienced in creating animal (mouse) models of human diseases by gene targeting in embryonic stem cells (ES cells). Dr. Homanics not only agreed to help me create an animal model, but also showed a strong interest and enthusiasm for the MSUD project. I was, indeed, fortunate to have him team up with me.

With Dr. Honanics help, we embarked on creating a mouse model of MSUD. This animal model was not only essential to show feasibility of gene therapy but also to establish the long-term safety of an unproven treatment. Because our previous gene therapy experience was with cells carrying a mutation in the E2 subunit, we decided to make an MSUD mouse model with a mutation in the same E2 subunit. Also, on a world-wide basis, the highest incidence of MSUD was reported to be due to a mutation in the E2 subunit. However, it is the E1 mutation that is found in the Mennonite population, as well as in other Caucasians, and in Italians, Japanese, Hispanics and several other ethnic groups.

Have you been successful in developing an MSUD mouse to use for researching gene therapy for this disease?
Yes, after nearly six years of research, we finally were successful in creating a mouse model for MSUD. As I mentioned before, this model was created by targeted inactivation of the E2 subunit of the BCKDH. The BCKDH is made up of several subunits and all subunits are essential for enzyme activity. Therefore, mutation or inactivation of any subunits, including the E2, results in MSUD.

As to be expected of our MSUD mouse model, all homozygous pups were normal at birth, but as they suckled their mother's milk, within hours they became sick and eventually died. Nearly 80% of the MSUD mouse pups died within a day after birth and the remaining 20% died during the next 6 to 7 days. Such a rapid and high rate of mortality in this model was due to the fact that there is a 100% loss of enzyme activity because the E2 gene knockout is complete. The heterozygous litter mates (which have half of the enzyme activity as compared to normal controls) remained normal and healthy. Because of this neonatal lethality of the homozygous pups, we were unable to test any new treatments.

The fact that these first MSUD mice could not be kept alive long enough to permit gene therapy must have been discouraging. How did you address this issue?

While we were disappointed with this neonatal lethality, we were also reassured that we have indeed created a model which mimicked the classic form of MSUD.

To overcome this problem, we undertook to create a conditional transgenic rescue of the neonatal phenotype of the MSUD mouse. In this new transgenic line, the E2 gene is under the control of a tetracycline responsive promoter, and the investigator can control the level of transgene expression by simply adding (or removing) tetracycline from the drinking water. Since the level of gene expression can be controlled, not only can an MSUD null phenotype be created, but intermediate phenotypes with low levels of residual enzyme activity, mimicking what is observed in many MSUD humans, can also be created by partially suppressing the expression of the gene.

We have completed all the work and have now produced the transgenic rescue model. In this improved MSUD model, most of the homozygous pups do not die. As a result, we are now able to keep these animals alive for several months. Our longest surviving MSUD mouse is nearly a year old.

What is the advantage of keeping these mice alive for a longer period of time?

There are three major advantages to keeping these animals alive on a long-term basis. First, we can now use these animals to test gene therapy for MSUD. Most gene therapy protocols require the use of viral vectors as a gene delivery system. Most currently available vectors do not show the effect of the delivered gene immediately, but require 7 to 10 days to show the effect. We could not test gene therapy in our first MSUD model because the animals died within a week. The fact that we can now keep the improved MSUD mice alive for several months provides the opportunity to test gene therapy for MSUD.

Second, by keeping the animals alive, we allow the animal to develop and grow normally to adulthood before testing gene therapy.

Third, in the longer surviving animals, we can control the transgene expression by tetracycline. By titrating the dose of this drug, we can partially or fully suppress the expression of the gene. The use of an appropriate dose of tetracycline allows us to produce mice not only of the classic form of MSUD, but also of the intermediate and intermittent form of the disease, which will make it possible to test gene therapy on all variants of MSUD.

Do heterozygous mice (carriers - each having one copy of the gene) reproduce with the same incidence of MSUD in their offspring as do humans?
Yes, pups derived from heterozygous by heterozygous mating were born at the expected frequency. Genotype analysis of the pups revealed that wild types [normal], heterozygotes, and homozygotes were present at nearly the expected 1:2:1 [25%, 50%, 25%] frequency. Thus, our heterozygous mice accurately model the genetics and reproduction of the human MSUD.

Evidently there is a great deal of time and cost involved in producing and maintaining these lines?
In making the improved and non-lethal MSUD model, we first created several tetracycline regulated E2 transgenic mouse lines. We then crossed some of these lines to the original MSUD knockout mouse in order to produce the non-lethal improved MSUD model. All this work requires maintaining a large colony of both types of mice. As an example, the cost of maintaining 200 mouse cages exceeds $70,000 per year. Also, considerable time and breeding are required to produce improved MSUD mice. For example, only 14% of the offspring are expected to be homozygous for both genes. This requires a great deal of time and cost to carry out such a project. Finally, genotyping all the newborn pups and their further characterization, such as testing their response to tetracycline by blood amino acid analysis, requires additional cost and time.

You mentioned the mutation in the E2 subunit. What about the other mutations in persons with MSUD? Will it be necessary to create a mouse model for each mutation of MSUD in order to test gene therapy for that mutation?
Our current model represents only one variant of MSUD, namely a mutation in the E2 subunit. Additional mouse models with a mutation in the E1 subunit will have to be created to cover all the MSUD phenotypes.

Which tissues are you planning to target for gene therapy?
Our initial thinking was to deliver the gene to the liver. Recent studies with human tissues, however, have shown that a significant amount of BCKDH is present also in skeletal muscle. Therefore we are now planning to target both the liver and the skeletal muscle. We believe delivering the gene at these two sites would be more effective in curing MSUD than delivering it to a single tissue such as the liver. Moreover, skeletal muscle is a much bigger tissue than liver, and restoration of the enzyme activity in this tissue is expected to be very effective in the disposal of the BCAAs in MSUD mice and in human patients.

A project of this magnitude must require a significant amount of funds. How is a small company such as yours able to do this research?
We have been fortunate to obtain funding in the past from the NIH to support this project. In addition, the founders of the company have continued to use their own family resources for the project. We are very appreciative of the financial help provided by the MSUD Family Support Group. We are hopeful for the continued support of the project by the NIH in the

future. As we continue to make progress, we anticipate drawing the interest of one or more mid to large size companies for this project that could lead to research or a business alliance with one of these companies.

What is your long-term goal in creating these MSUD mice.
Our long-term goal is to develop novel therapies through research using these mice. We believe our MSUD mouse will serve as a very practical resource to test gene therapy, and possibly other therapies, to cure MSUD. These studies will establish the long-term safety and efficacy of gene therapy for this disease. The experience gained from animal studies will pave the way for subsequent gene therapy for MSUD in humans.

A successful gene therapy model for MSUD could be applicable and transferable to other similar disorders. Furthermore, the defects of MSUD cross boundaries into other diseases. For example, neurologic and myelin disorders, GABA-related disorders, and neural cell apoptosis are also prevalent in other diseases. Thus, the MSUD mouse could provide a model for an expanded clinical disease base far beyond MSUD.

Is there a possibility of clinical trials on humans with MSUD in the near future?
Clinical trials on humans will depend on the outcome of gene therapy studies with animals. Successful demonstration of gene therapy in animals, including its long-term safety, would establish the "proof-of-principle" and would reduce the risk for similar studies in humans. Other issues that must be considered before embarking with clinical trials are related to adverse reactions, such as an immune response to vectors used to deliver normal genes. Therefore, a lot more needs to be done in a pre-clinical settings before gene therapy could be attempted in humans.

Besides gene therapy, other approaches to correct genetic diseases are being developed. For example, experiments are being attempted that target genetic repair of the defective gene. Whether this new approach at gene repair would be better than gene therapy remains to be seen. Even for these new approaches, our animal model will remain a very valuable resource.

1. Dr. Paul and colleagues have published 25 papers related to BCAA metabolism between 1976 and 1999.

A rich man once asked a friend, "Why am I criticized for being so miserly? Everyone knows I will leave everything to charity when I die." "Well," said the friend, "let me tell you about the pig and the cow. The pig was lamenting to the cow one day about how unpopular he was, "People are always talking about your gentleness and your kind eyes," said the pig. "Sure you give milk and cream, but I give more. I give bacon, ham and bristles. They even pickle my feet. Still nobody likes me. Why is this?" The cow thought a minute, then replied, "Well, maybe it's because I give while I'm still living."

MSUD SYMPOSIUMS IN BRAZIL

Details

Written by Selma M. B. Jeronimo, MD

Published: 20 July 2009

Dr. Selma Jeronimo from Brazil (photo taken at Symposium 2002 in Ann Arbor, MI)

A group of physicians and families of patients with inborn errors of metabolism in Brazil organized a symposium in December 2002. The objective of the symposium was to assess these illnesses in northeast Brazil and to organize a protocol to treat and follow those patients. Five families from Rio Grande do Norte and one family from Cear- who have children with MSUD attended the meeting. In addition, physicians from Paraíba, Pernambuco and Cear- (northeastern states of Brazil), medical students and residents participated in the symposium. A total of 75 attended the 3-day meeting.

Guest speakers and their topics:

- Dr. Ricardo Pires, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, spoke on Inborn Errors of Metabolism.
- Dr. Renata Benardes de Oliveira Nutritional, Universidade Federal de Sáo Paulo, spoke on the Nutritional Aspect of MSUD and Phenylketonuria.
- Dr. Paulo Matos, Universidade Federal do Rio Grande do Norte, spoke on the Profile of Inborn Errors of Metabolism in Rio Grande do Norte.
- Dr. Selma M.B. Jeronimo, Universidade Federal do Rio Grande do Norte, spoke on The Laboratory Support For the Diagnosis of Inborn Errors of Metabolism.
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Eimard Fernandes and Giovanni Medeiros (who attended Symposium 2000 in the United States) spoke on The Difficulties and the Stress of Caring for Children With MSUD.

We had originally planned to have Dr. Kevin Strauss from the Clinic for Special Children join us at the December symposium. However, his visit was postponed until March 2003 when he spent three days at a Natal symposium speaking to physicians, nutritionists and five families of patients with MSUD. Dr. Strauss also held a clinic and reviewed some cases of MSUD. There was a discussion on the protocol for treating MSUD and on plans for setting up a laboratory for monitoring children with the disease.

Dr. Strauss with Laura (MSUD), the daughter of Giovanni & Aninha Medeiros from Brazil (photo provided by Giovanni)

As a result of these two meetings, a group of physicians and nutritionists interested in inborn errors of metabolism met to discuss plans for establishing a laboratory. We are hoping that within a year a better hospital and laboratory support will be established here in Natal as a result of these discussions. A project for funding the laboratory was submitted to the Brazilian Minister of Health.

Funds for the organization of both symposiums were provided by the Brazilian families with MSUD and the Federal University of Rio Grande do Norte. The families were the major force behind the organization of the professional meeting and the symposiums. I think that those families with MSUD patients, both here and in the United States, are unique in terms of their efforts to cope in a very positive way with the disease and to influence changes in the way we physicians conduct research and treat patients. I was quite impressed by the attitudes of the families both here in Natal and the ones we had the privilege to interact with when I attended Symposium 2002 in Ann Arbor, Michigan last July.

NOTE: *The United Services Foundation has been giving generous donations to support the MSUD Family Support Group Symposiums which are held every other year in the United States. This support provides an opportunity for the organization to assist families who would like to attend a Symposium for the first time. With this support, the Eimard Fernandes and Giovanni Medeiros families from Brazil attended the MSUD Symposium held near Boston, Massachusetts in the summer of 2000. They returned to Brazil determined to earn enough money to attend the next Symposium in 2002. Instead, they made a decision to use the money, which they and other families raised, to send Dr. Selma Jeronimo from Brazil to the U.S. Symposium in Michigan in 2002. The above article tells the results of that wise decision. Through the determination and sacrifice of these families, MSUD treatment is improving in Brazil. We commend these families and the professionals who are working to improve the treatment and lives of those with MSUD in Brazil.*

MSUD IV SOLUTION AVAILABLE FROM GERMANY

Details

Written by Joyce Brubacher

Published: 20 July 2009

After Symposium 2000, Giovanni Medeiros from Brazil was convinced of the need to have MSUD total parenteral nutrition (TPN) available for the children with MSUD in Brazil. Obtaining this IV solution when an MSUD child is hospitalized is often difficult in the United

States and has been nearly impossible in many other countries. Giovanni was determined to find a ready source of the MSUD IV solution to use in TPN for MSUD. MSUD TPN is used to quickly lower the branched chain amino acids (BCAAs) in sick children who cannot take their formula by mouth.

Giovanni located a source in Germany from which doctors can order the solution. The Pharmacy of the Municipal Hospital Munich-Bogenhausen, Englschalkinger Str. 77, 81925 Munchen, stocks an MSUD 7.6 % solution free of the BCAAs. The solution is produced as an infusion with a shelf life of 3 years when stored at 8°C. Further compounds can be added to make the MSUD TPN.

The pharmacy may be contacted by e-mail: KMB.Apotheke@extern.lrz-muenchen.de, fax: 49/89/92702316, or phone: 49/89/9270-2320. Two additional companies have expressed interest in making an internationally available amino acid solution. One company is in the United States.

FEATURED FAMILIES - DALMA S NEW HOME

Details

Written by Edna Newswanger

Published: 20 July 2009

See ***From the* Heart of the "Other Mother"** *for background information on Dalma.*
On December 11, 2002 we became foster parents to a four year old girl with MSUD named Dalma. She came to our home all the way from Texas. We also have three married daughters and a son Neil, 21, with MSUD. *[More on Neil in editor's note at end of article.]*

It was only through God's leading hand that we found out about Dalma. When we signed up for foster care in October 2001, we applied for special needs children. We realized that all children who come into the agency have special needs, but we were willing to take the ones with extra special needs - the ones most people don't take as foster children. We were approved in February 2002, and five days after approval we were given two girls ages three and four. They were a challenge. The one is still with us, and the other left after staying six months.

In July my husband Amos, our son Neil, and I attended the MSUD Symposium 2002 in Michigan. We heard Becky Sanford, a foster mother from Texas, tell about Dalma and ask if someone who is familiar with MSUD would give Dalma a home. Amos and I looked at each other and knew right away we would give Becky our name. What really touched me and caused me to choke up was the poem Becky had on the screen:


Dalma in her new home with the Newswangers

What Matters
One hundred years from now it will not matter what kind of car I drove or what kind of clothes I wore.

All that will matter is that I made a difference in the life of a child.
- Author unknown

When we talked to Becky, we were amazed at how much Dalma seemed to be like our son Neil. Her delays were so similar. Our hearts went out to Dalma with her needs, but we didn't want to get our hopes too high. We knew others might ask for her also.

We didn't hear from Texas for a couple months. One day Amos called Becky. She said our name was given to the adoption agency. We waited again. Then Becky called and said she would like to bring Dalma here for a visit.

Becky, with her seven year old daughter and Dalma, arrived for a visit in October. She drove all the way from Texas with the two girls. Dalma was 4 years old and made herself right at home. She had no problem adjusting to Neil or to the other foster children (a girl four and a boy six and one half months old). It was an interesting and busy week. Some of the other mothers with MSUD children in the area came to meet Becky and Dalma. Foster parents from this area also stopped in one day. We even managed to visit the Clinic For Special Children in Strasburg so that Dr. Morton could meet Dalma. *[He is Neil's doctor.]* After Dalma's visit we wondered how long it would take for all the paper work to be done. The agency in Texas was trying to place her here for Christmas. We waited patiently but were eager to get her settled in before winter.

I remember telling my husband one day, "I really wonder if it will happen. Maybe we should call again." He said he had decided if it was the Lord's will for her to come, she would come. That same day we got a call from Texas saying everything was going through as planned. Then on December 3, we got a call from a caseworker named Bill. He planned to fly with Dalma on December 11, leaving in the morning and arriving around 6:30 in the evening. He would stay in Pennsylvania for several days visiting family after leaving Dalma with us.

When the big day finally arrived, everything was covered with ice, and our local airport was closed. Bill called as they were getting started on their journey. He was surprised to hear we

were having a winter ice storm. We hoped the weather would be better later in the day, but it didn't change much. Bill called again and asked if we had a jacket for Dalma because she only had a light-weight one for Texas weather. He said he would stay in Pittsburgh for the night if necessary. We kept calling our local airport, but there were no flights leaving or arriving. Then another call came just when it was time for us to leave for the airport. Amazingly, the only plane arriving that day was the one with Bill and Dalma! Although a little late, they arrived safely. God's protecting hand was over them and our prayers for a miracle were answered.

Amos met Bill and Dalma up at the airport. I stayed home with the children because of the icy weather. Dalma went right to Amos for a hug and was all smiles. When she walked into our kitchen, she made herself right at home and checked everything out. She had no problem settling into bed that night.

Edna Newswanger - photo taken at Symposium 2002

The next day Bill stopped in for a visit before leaving. When he prepared to leave, Dalma backed away as though she was afraid he might take her away again.

Dalma adjusted very well to our family, and Neil was excited too. We could tell he thought it was great that she drank a special formula like he did. He wasn't impressed, however, when she wanted all of his attention after he came home each day from the adult training facility he attends. Dalma would go around in circles in front of Neil and laugh or hang on to the pockets on his pants. Sometimes she would sit on the floor right in front of him and make noises. He wouldn't pay much attention to her until it got to be too much; then he would say, "Dalma!" quite loudly to let us know she was pestering him. After a month of this, Dalma decided she wasn't getting the attention she wanted and quit.

Dalma greatly improved as days went by. We had to find the level of leucine she tolerated. We started at 300 to 400 mg and continued increasing it up to 800 mg per day. Then gradually we had to back down to 650 mg of leucine. At first we were sending blood samples to the Clinic every week but later changed to every other week.

Dalma had an ear infection and ran a high fever soon after she came to us, but she took her formula and kept eating. We had no serious problems through those illnesses. Our other four year old had scarlet fever, but thankfully, Dalma didn't get it.

A month after she arrived, Dalma started going in the mornings to a preschool for children with developmental delays. She turned five on June 19, 2003. We think she has shown

improvement in a number of ways. Her speech is limited, but she has a few words others can understand. She called me mamma right away, and Amos is da-da. She didn't act as if the great amount of cold and snow we had this winter was anything new. She plays nicely with toys for short periods of time. Our other four-year-old leads her around everywhere, and Dalma goes right with her - most of the time. She is usually a smiling, happy girl.
We are thankful to Becky for attending the Symposium and pleading for someone to give Dalma a home. Becky was brave and trusted someone was there for Dalma. We feel very fortunate to have this very precious, special girl to care for. We can only do this with the help of our heavenly Father. We never dreamed we would get a child with MSUD when we signed up for foster care. Although foster care was all we were going to do, we plan to adopt Dalma in the near future. The Lord moves in mysterious ways. We need to take only one day at a time.

Amos and Edna Newswanger, a Mennonite family who live in Martinsburg, Pennsylvania, have a wealth of love for special needs children. Their only son, Neil Ray, was born July 28, 1980. His case was unusual in that he survived a very late diagnosis even though he has the Mennonite classic mutation of MSUD with zero enzyme activity. Neil had the early classic symptoms of MSUD and was hospitalized off and on until diagnosed at 6½ months of age when he was in critical condition. Undiagnosed children with this mutation usually die within the first weeks of life.

Neil was hospitalized a number of times during his childhood and suffered extensive brain damage. Since then he has grown to be a strong and physically healthy young man. He communicates mostly with grunts and words understood only by those close to him. His highest level of development is in his gross motor area. He can walk and enjoys being outdoors and swinging on an outdoor swing. He is particularly fond of pens and toothbrushes. He has a collection of over 500 toothbrushes. He remains on seizure medications and works in an adult training facility. He now has a sister with whom to share MSUD experiences.

THE CHALLENGE OF PREPARING THE INDIVIDUAL EDUCATION PROGRAM

Details

Written by Marcia Hubbard

Published: 20 July 2009

Marcia Hubbard lives in Missouri and has two grandchildren who require individualized educational programs. One grandchild, Jonathan Devantier, has MSUD. In the following article she shares what she has learned through her experience and extensive research in pursuing the best education for her grandchildren with special needs.

Special education departments are mandated to provide specific services for special education students. However, laws may be interpreted differently and cooperation of school district personnel may vary. Contact your State Department of Education for information on your State's requirements.

Just when we think we have learned to provide the best care possible for our children with MSUD, they enter the school setting. Whether the child is mildly or severely affected by MSUD, there is new terminology and legalities to learn in order to get a Free Appropriate Public Education (FAPE). Since public schools are governed by federal and state laws, the scenario can get complicated and downright daunting at times. This article deals with understanding what is involved in getting the best education for your child in elementary, secondary and post secondary public schools. (Check the law regarding private schools.)

Educated parents are the key for an optimum outcome. However, the schools that will be educating your child will not necessarily educate you for this process. Parents need to take the initiative to do research and educate themselves. I'm thankful for the many educational tools currently available and for the laws that prohibit discrimination. You will need to do your homework to determine which is the right classification for your child and to what degree you will use these regulations and services for their benefit.

Some of the following information comes from the document, "Procedural Safeguards for Children and Parents" that is mandated to be given to parents during the IEP process. I also used web sites providing information to the public recommended to me by the child advocacy group MPAC-Missouri Parents Act. (*See list of web sites at the end of this article.*) Your own local child advocacy groups can provide help when needed. I am not intending to give legal advice, but to help educate parents for this task.

Individual Education Program (IEP)

The Individual Education Program, or IEP, is a written, legal and binding document made between members of the school staff and the parents of a child. It is written during a meeting with all those who will be directly responsible to carry out the terms of the IEP. As the name implies, you have the right to request the services for your child based on the *individual* needs of the child.

The IEP outlines the steps, plans, procedures, etc. needed to address these needs. This can be as simple as stating a time to allow your child to drink their formula or as complex as dealing with issues related to learning disorders and physical, emotional and behavioral challenges. A parent has the right to review these terms or change them, and must notify the school in writing when a new IEP is desired. The best way to identify your child's needs is to imagine you are describing your child to a stranger who will be taking your child for a day trip. Then for each special need ask, "What will the district do about this?" and "How can we judge if these actions serve to meet my child's needs?"

Prior to the passage of the Individuals with Disabilities Education Act (IDEA) in 1975, the law legally allowed schools to offer only the programs or services they had available. The primary

purpose of the IDEA was to change that and entitle students to services individually designed to meet their unique needs without regard to the availability of the needed services.
The IEP process must determine:

- Which needs or characteristics require special education or individualization of services.
- Exactly what special education-related services or modifications the district will provide.
- How and when the results of those services will be evaluated.

The Participants
The law specifies that in addition to the parent and student (if the parent wishes the student to be present), a teacher of the student, and a district representative must be present. The IDEA regulations allow the district substantial discretion in determining which teacher will be at the IEP meeting. In addition, at least one team member must be qualified (by state standards) in the area of the student's disability. If this is not the teacher, it must be the district representative. The district representative must provide or be qualified to supervise special education, have the authority to allocate district resources, and be able to guarantee no administrative veto of the IEP team's decisions.

In addition to the parent, the teacher, the district representative and possibly the student, the first IEP meeting for a given student must be attended by a member of the evaluation team or someone familiar with the evaluation. In addition, either the district or the parent may invite anyone else. The district must inform the parent ahead of time of all persons invited by the district who will be at the IEP meeting. There is no similar requirement for parents to inform the district of anyone they may invite.

Finding the Proper Category
An IEP is written for those individuals that qualify for services under the Americans with Disabilities Act (ADA) or IDEA. Your child must be eligible in at least one category. Often the schools evaluation/screening process helps determine whether or not the student qualifies for such services.

The following chart gives a reasonable, brief description of each category. Some individuals will exhibit characteristics that will place them in one category without question; others may not be as well defined. I think it is safe to say that all children with MSUD will fall under Section 504 due to their special dietary needs, which is addressed by Federal Government laws governing school lunch programs.

See the chart on the next two pages for more information on Section 504. The descriptions in the chart are brief and should not be used as the sole source for determining the status of a child.

Americans With Disabilities Act of 1990 (ADA)	**Individuals with Disabilities Education Act (IDEA), amended in 1997**	**Section 504 of The Rehabilitation Act of 1973**
Type/Purpose		
A civil rights law to prohibit discrimination solely on the basis of disability in employment, public services, and accommodations.	An education act to provide federal financial assistance to state and local education agencies to guarantee special education and related services to eligible children with disabilities.	A civil rights law to prohibit discrimination on the basis of disability in programs and activities, public and private, that receive federal financial assistance.
Who Is Eligible?		
Any individual with a disability who (1) has a physical or mental impairment that substantially limits one or more life activities; or (2) has a record of such an impairment; or (3) is regarded as having such an impairment. Further, the person must be qualified for the program, service or job.	Children and youth aged 3-21 who are determined through an individualized evaluation and by a multidisciplinary team (including the parent) to be eligible in one or more of 13 categories and who need special education and related services. The categories are autism, deaf-blindness, deafness, emotional disturbance, hearing impairment, mental retardation, multiple disabilities, orthopedic impairment, other health impairment, specific learning disability, speech or language impairment, traumatic brain injury, and visual impairment including blindness. Children aged 3 through 9 experiencing developmental delays may also be eligible. Infants and toddlers from birth through age 2 may be eligible for early intervention services,	Any person who (1) has a physical or mental impairment that substantially limits one or more major life activities, (2) has a record of such an impairment, or (3) is regarded as having such an impairment. Major life activities include caring for oneself, performing manual tasks, walking, seeing, hearing, speaking, breathing, learning, and working. The person must be qualified for the services or job; in the case of school services, the person must be of an age when nondisabled peers are typically served or be eligible under IDEA.

	delivered in accordance with an individualized family service plan.	
Responsibility To Provide a Free, Appropriate Public Education (FAPE)?		
Not directly. However, ADA provides additional protection in combination with actions brought under Section 504 and IDEA. ADA protections apply to nonsectarian private schools, but not to organizations or entities controlled by religious organizations. Reasonable accommodations are required for eligible students with a disability to perform essential functions of the job. This applies to any part of the special education program that may be community-based and involve job training/ placement. Although not required, an IEP under IDEA will fulfill requirements of Title II of the ADA for an appropriate education for a student with disabilities.	Yes. A FAPE is defined to mean special education and related services that are provided at no charge to parents, meet other state educational standards, and are consistent with an individualized educational program (IEP). Special education means "specially designed instruction, at no cost to the parents, to meet the unique needs of the child with a disability." Related services are those required to assist a child to benefit from special education, including speech-language pathology, physical and occupational therapy, and others. A team of professionals and parents develop and review at least annually, an IEP for each child with a disability. IDEA requires certain content in the IEP.	Yes. An "appropriate" education means an education comparable to that provided to students without disabilities. This may be regular or special education. Students can receive related services under Section 504 even if they are not provided any special education. These are to be provided at no additional cost to the child and his or her parents. Section 504 requires provision of educational and related aids and services that are designed to meet the individual educational needs of the child. The individualized educational program of IDEA may be used to meet the Section 504 requirement.
Funding To Implement Requirements?		
No, but limited tax credits may be available for removing architectural or transportation barriers. Also, many federal agencies provide grants to public and private institutions to support training and technical assistance.	Yes. IDEA provides federal funds under Parts B and C to assist state and local educational agencies in meeting IDEA requirements to serve infants, toddlers, children, and youth with disabilities.	No. State and local jurisdictions have responsibility. IDEA funds may not be used to serve children found eligible only under Section 504.

Procedural Safeguards/Due Process		
The ADA does not specify procedural safeguards related to special education; it does detail the administrative requirements, complaint procedures, and con-sequences for noncompliance related to both services and employment. The ADA also does not delineate specific due process procedures. People with disabilities have the same remedies that are available under Title VII of the Civil Rights Act of 1964, as amended by the Civil Rights Act of 1991. Thus, individuals who are discriminated against may file a complaint with the relevant federal agency or sue in federal court. Enforcement agencies encourage informal mediation and voluntary compliance.	IDEA provides for procedural safeguards and due process rights to parents in the identification, evaluation and educational placement of their child. Prior written notice of procedural safeguards and of proposals or refusals to initiate or change identification, evaluation, or placement must be provided to parents. IDEA delineates the required components of these notices. Disputes may be resolved through mediation, impartial due process hearings, appeal of hearing decisions, and/or civil action.	Section 504 requires notice to parents regarding identification, evaluation, placement, and before a "significant change" in placement. Written notice is recommended. Following IDEA procedural safeguards is one way to meet Section 504 mandates. Local education agencies are required to provide impartial hearings for parents who disagree with the identification, evaluation, or placement of a student. Parents must have an opportunity to participate in the hearing process and to be represented by counsel. Beyond this, due process is left to the discretion of local districts. It is recommended that they develop policy guidance and procedures.
Evaluation/Placement Procedures		
The ADA does not specify evaluation and placement procedures; it does specify provision of reasonable accommodations for eligible students across educational activities and settings. Reasonable accommodations may include, but are not limited to, redesigning equipment, assigning aides, providing written communication in	With parental consent, an individualized evaluation must be conducted using a variety of technically sound, unbiased assessment tools. Based on the results, a team of professionals (including the parent of the child) determines eligibility for special education. Reevaluations are conducted at least every 3 years. Results are used to	Section 504 provides for a placement evaluation that must involve multiple assessment tools tailored to assess specific areas of educational need. Placement decisions must be made by a team of persons familiar with the student who understand the evaluation information and placement options. Students with disabilities may be placed in a separate class

alternative formats, modifying tests, reassigning services to accessible locations, altering existing facilities, and building new facilities.	develop an IEP that specifies the special education, related services, and supplemental aids and services to be provided to address the child's goals. Placement in the least restrictive environment (LRE) is selected from a continuum of alternative placements, based on the child's IEP, and reviewed at least annually. IEPs must be reviewed at least annually to see whether annual goals are being met. IDEA contains specific provisions about IEP team composition, parent participation, IEP content, and consideration of special factors.	or facility only if they cannot be educated satisfactorily in the regular education setting with the use of supplementary aids and services. Significant changes to placement must be preceded by an evaluation.Section 504 provides for periodic reevaluation. Parental consent is not required for evaluation or placement.

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List of Resources For Preparing an IEP
The web addresses and toll free numbers listed below can be used to obtain further information if needed, including full copies of the laws given in the chart on the previous pages.

Wrights Law: Copies of the law and instructions how to apply it: www.wrightslaw.com

National Information Center for Children and Youth with Disabilities: Excellent for obtaining lists of state resources.
NICHCY
www.nichcy.org
P.O. Box 1492
Washington, DC 20013
v/tty: 800-695-0285 fax: 202-884-8441

Office of Special Education Programs: Numerous items that can be received by mail.
Office of Special Education Programs
Office of Special Education and Rehabilitative Services

U.S. Department of Education
400 Maryland Ave. SW
Washington, DC 20202
Phone: 202-205-5507
www.ed.gov/offices/OSERS/Policy

The Americans with Disabilities Act (ADA)
1-800-514-0301 or 1-800-541-0383 (TDD)
http://www.usdoj.gov/crt/ada/adahom.1.htm

Section 504 of the Rehabilitation Act
http://www.ed.gov/offices/OCR/disability.htm

Individuals with Disabilities Education Act
http://www.ideapractices.org/lawandregs.htm

U.S. Office of Civil Rights
1-800-421-3481

Marcia Hubbard also contributed a poem written by her father,
Red James, to his great grandson, Johnathan Devantier, who was
born on April 15, 1998. The poem was written during Johnathan's initial metabolic crisis when he was in the Intensive Care Unit. Red had little formal education, but has done well in his business as a farm equipment dealer. He is well known locally for his poetic talent. As Marcia wrote, "Being diagnosed with MSUD, touches generations of the family." The poem was named after Johnathan's namesake fruit, Jonathan apples.

Little Apple
Oh little Boy I have not yet saw,
I think of you, your Great-Grandpa.
A week old now, and so very bad,
You being so sick, makes me sad.
Get well I pray ever so much,
So sometime soon I can feel your touch.
You are so small; be strong young lad,
I wish you to come home with your mom and dad.
My life has been blessed with all my kin,
I'm sure to us, God must had to send,
so that we could pass out all of our love
just as he does from Heaven above.
Little Apple, I call your name
my prayers and best wishes are the same.
Fight hard; we will help in any way
so I will get to see and hold you some day.
- Your Great Grandpa (Red James)

FEATURED FAMILIES - FROM THE HEART OF THE "OTHER MOTHER"

Details

Written by Becky Sanford

Published: 20 July 2009

Greetings from Texas! I am Becky Sanford, former foster mother to Dalma. Those of you who attended the July 2002 MSUD Symposium in Michigan might remember that I put a picture of a little girl named Dalma on the overhead and said that I was looking for loving, Christian parents to adopt this beautiful little girl with MSUD. I explained that Dalma could really benefit from doctors who are innovative and up-to-date on MSUD. This is the beginning of the story of our life with precious Dalma until she became the daughter of Amos and Edna Newswanger from Pennsylvania. *[See next article for Amos and Edna's story.]*

My cell phone rang in May 1999, almost exactly four years ago from the day that I am writing this. Child Protective Services of Texas (CPS) asked if we would take a little girl as a foster child. CPS explained that the baby was a few weeks from being one year old but wasn't able to sit up yet. They thought she was a "failure to thrive" child. Her name was Dalma.

The timing wasn't good. My mother was dying of cancer, and I was spending almost 20 hours with her each day. I talked to my husband and oldest daughter because they would have to care for her since I was so involved with Mom. We agreed that it was "do-able," so I went to the CPS office to pick her up.

I expected to see a frail, thin, sickly little girl, but Dalma was average size for her age (almost a year old). She had a very bad skin rash and couldn't roll over, sit up, or hold her head up. She couldn't lift her arms or legs, didn't make eye contact at all, and made only moaning sounds. She just broke my heart.

The caseworker said that Dalma's grandmother told them to tell me to feed her only baby food vegetables and fruits and watered down milk, or she would "be sick." (Now I realize how attentive her birth family was to her because they created a personal diet to help her. Amazing!)

I took her home and proceeded to give her formula which made her "be sick" - just like the grandma had said. The next day I called my pediatrician because, after caring for several "failure to thrive" children, I knew that we were dealing with something more than "failure to thrive" here! He informed me that he was going out of town, so I asked him to make an

emergency appointment for her at Cook Children's Hospital in Fort Worth (two hours away) with a neurologist. He did!

On day three, we met with Dr. Ryals, and he agreed that something was definitely wrong with Dalma. He called me on day five and said he had learned from her blood work that she had maple syrup urine disease. He had never seen a case but found a metabolic doctor in Dallas who had treated a case.

The metabolic doctor called and informed me to eliminate all protein from her diet until we could see him first thing the next day. On that visit the doctor gave me Ketonex I and a Ross manual on MSUD. I was told to come back in one month for more blood work. I had never heard of MSUD and felt completely overwhelmed! (Each of you knows that feeling!)

The following day while I was with my mother, she regained consciousness and asked about the children, so I told her about Dalma. She was so pleased that we had taken her because she knew that we had refused three other children that month so that I could spend time with her. She went to be with the Lord exactly one week after Dalma arrived.

The timing for Dalma's arrival had to have been from God. She flourished on her new formula. Slowly her skin began to clear up, and within a month she could hold her head up. She still had a floppy baby body, but she was starting to smile and make happy sounds. She even started physical therapy and speech therapy (much to her dismay).

Dalma's physical age was still "in the womb" due to the fact that she had no muscle control whatsoever. She did not like doing therapy at all, but we were soon seeing progress. At a year old, Dalma learned to tolerate being on her stomach and to wiggle her arms and legs. Slowly she learned to grasp our fingers. We cheered at every new level of achievement. Soon she learned to make baby sounds. Dalma now smiled when she was happy and learned to roll from her stomach to her back.

By eighteen months, she had progressed to the "army crawl" with her arms dragging her legs. At two years old, she could finally sit alone. We heard her first words of Nana (for me), Nat-a-le (for Natalie) and nite-nite. To be honest, they all sounded alike, but Natalie, our four year old, knew what she meant and interpreted for the rest of us. At two years, Dalma could crawl, wave bye-bye, give sloppy kisses and was the light of our lives.

Dalma turned three in June of 2001, and in August she started Early Childhood Intervention at our local elementary school. She went to school in the mornings from eight to twelve. By this time Dalma had a walker to help her cruise the halls and had charmed all of her teachers with her vivacious personality and happy smile. Her nickname was Nosey Rosy. While her physical condition had improved dramatically, her mental capacity hadn't made as much progress. For the first time in her life, she learned new tricks - like how to throw a fit, bite, and destroy the teachers' desktops at school! Up until now, she had been in toddler mode, but now she was able to walk and reach anything and everything.

As most of you know, attending school creates a whole new problem of lunches and snacks! For a few months I just tried to pick her vegetables and fruits from the school lunch menu but soon realized it was much easier (for better control) to pack her lunch every day.

Dalma had a huge problem with chewing. She refused to do it, so we just mashed all of her food so she could swallow it.

I attended the MSUD Symposium in Michigan in July of 2002. At this conference, I realized that maybe if Dalma's diet was changed and her levels were monitored more closely, she might improve even more. Dalma was not on any supplements to help with her levels. When I told the people at my table and a couple of the Symposium speakers what her levels were, they were concerned. I learned that there was a lot of new information that my doctor in Texas would not use. His line was that she was so much better than when we first got her. But *my* question was, "How much better could she be with more aggressive medical care?"

At the Symposium, when I made a plea for an adoptive family for Dalma, three families expressed their interest and asked for additional information. This is where Amos and Edna Newswanger entered the picture. They were very interested in adopting Dalma! We were so excited. We visited by phone several times after the Symposium.

Then in October of 2002, Dalma, Natalie (my six year old daughter) and I packed up our Suburban and headed toward Amos and Edna's to stay a few days with them. We also wanted to meet Dr. Morton and visit the Clinic. It was a long, beautiful drive, and the girls did great! It was about 1500 miles and took us about 23 hours. We never got lost until we were within a few blocks of Amos' house!

Amos and Edna welcomed us with open arms. We visited Amos' woodworking shop and Edna's fabric store, and we rode in their horse-drawn buggy. We stayed in their home and enjoyed fellowship with their church members and other foster parents and visited with their son Neil and their daughters. We enjoyed meeting Dr. Morton and visiting again with Dr. Kevin Strauss. It was such a wonderful trip.

We brought Dalma back home with us, and by that time all the paperwork for an interstate adoption had begun. In December 2002, our caseworker, Mr. Bill, flew Dalma to Pennsylvania. (I wish I could have been a fly on the wall!) Dalma remembered Amos and Edna, and the rest is history in the making. I am so grateful for Amos, Edna, and their loving family. God is good!!