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# TREATMENT OF THE ACUTE CRISIS IN MAPLE SYRUP URINE DISEASE

**Details**

Written by William L. Nyhan, M.D., Ph.D.

Published: 20 July 2009

The acute crisis of metabolic imbalance is the most dangerous situation for the patient with maple syrup urine disease (MSUD). It may occur in response to a lapse in good dietary discipline, or to a major trauma or surgery, but in infants and young children it is most often a consequence of infection. This makes it difficult to avoid. Sometimes the first sign of a new viral infection is the characteristic maple syrup odor, a bout of vomiting, or a positive test for ketones in the urine.

We teach parents of our patients with MSUD to test the urine for ketones. A positive test is a strong alert but not a very sensitive index of imbalance.* The most important criterion is the plasma concentration of leucine, which can be very high before ketonuria is evident, so we also teach parents to come in for plasma amino acids at the first inkling that something is wrong. With this disease you do not want to delay treatment. If we catch it early, it is often possible to institute a regimen that reverses the imbalance and keeps the patient out of the hospital.

Quite often the first episode occurs in an infant before diagnosis. The patient is admitted in serious metabolic imbalance. Most of these very young infants are admitted in coma. Similar episodes of imbalance can occur at any age, even in adult life after years of exemplary control. It is important to employ optimal methods of treatment to turn the situation around as rapidly as possible. Cerebral edema is the most dangerous complication of this crisis, but patients may die in coma even in the absence of edema of the brain. We need to do everything we can to prevent neurological damage and developmental delay.

The objective of therapy is to reduce the level of leucine as rapidly as possible. Early approaches to this via exchange transfusion or peritoneal dialysis were ineffective because very small amounts of branched-chain amino acids are removed in these ways. Hemodialysis is more effective, but the thought of undertaking hemodialysis every time an infant came down with an infection, such as, otitis media, is not an attractive prospect.

Our approach is to harness the forces of anabolism *[constructive phase of metabolism]* to get rid of the extra leucine in the blood by using it to make body protein. To do this we

provide energy in the form of intravenous glucose. At the same time, we provide a continuous supply of amino acids minus isoleucine, valine and leucine. In early approaches, we and others supplied these mixtures of amino acids as intravenous solutions. Results were very rewarding. There was a prompt, linear fall in levels of leucine, and clinical manifestations of the crisis receded. We devoted considerable thought to the design of optimal solutions for this purpose, as well as the development of maintenance solutions, which would be useful in a patient who is not in crisis but in need of parenteral therapy over a number of days - as we experienced in one patient with a tonsillectomy.

This use of intravenous solutions of amino acids remains an excellent approach to the treatment of metabolic imbalance in MSUD. It is particularly useful in a patient with vomiting. It is a mainstay of therapy by doctors Morton and Strauss at the Clinic for Special Children, where the solution is made in their pharmacy. Most institutions do not consider themselves equipped to generate these solutions. We obtained ours commercially, but it soon became evident that costs were prohibitive. The commercial supplier would generate the solution only in a large batch - much more than needed to revive an infant in crisis - and soon all of our hospitals and third parties refused to pay for these solutions. There were timing problems too. A patient admitted in crisis on Friday could seldom get solution before Tuesday. For these reasons we sought another treatment plan.

For ten years now we have successfully used enteral *[by way of the intestine]* solutions to serve the same purpose. This is accomplished by dripping the material very slowly, over 24 hours, through a nasogastric or gastrostomy tube. We have learned to employ the amino acid solutions in minimal volume, and that has been the secret of gastrointestinal tolerance even in patients that have been vomiting. It is possible to employ the same formulas that we use for every day feeding in MSUD, such as, Ketonex or other MSUD formulas. But with all the fat, carbohydrate and minerals that make these preparations so useful for every day use, they hardly meet the prescription of minimal volume. In one of our larger patients, we made a calorie per milliliter solution of a standard formula to provide a dose of 2 g/kg of amino acids, and it came to almost 2½ liters of fluid, hardly what you would like to give a vomiting patient. So we made up our own solutions that contained nothing but amino acids. We tried various mixtures in an attempt to find an optimal mixture. It worked, and we published our experience, with three episodes in 2 patients, in the *Archives of Pediatrics and Adolescent Medicine* (152:593-598, 1998). That published article prompted a request for this current article.

We have had experience with a number of patients, and it is clear that this anabolic therapy is the centerpiece of treatment. We no longer make our own mixtures because Applied Nutrition now supplies such mixes as Complex? Amino Acid Blend. We have learned a few things along the way. Among them is the fact that plasma valine and isoleucine concentrations always drop lower than leucine concentrations during therapy. If you put equal quantities of these branched-chain amino acids into protein, the isoleucine level drops too low, and the patient becomes catabolic *[destructive phase of metabolism]*, resulting in elevated leucine levels. Therefore, we supplement with isoleucine and valine.

It is also true that some infections make the patient too catabolic to overcome with this approach. In that situation we add insulin and more glucose to make the patient more anabolic and provide protein synthesis. More recently we have been using human growth hormone, a very powerful anabolic agent in this situation. At first we only turned to growth

hormone when amino acids plus insulin had not turned things around. More recently I have employed growth hormone earlier and have not needed to use insulin.
University of California San Diego Department of Pediatrics

** Editor's note: For many children and adults with MSUD, 2-4 DNPH is a more sensitive home monitoring test to determine leucine elevations. Urine is used for both DNPH and ketone tests. To read more about DNPH, check our web site, www.msud-support.org. In the index, under the topic* Medical Treatment, *is an article listed with the title* "Letter from Dr. Morton (Use of DNPH)." *It was printed in the April 1991 issue of the MSUD Newsletter.*

# MEETING AT THE NIH

**Details**

Written by Sandy Bulcher

Published: 20 July 2009

The MSUD Family Support Group took advantage of an exciting opportunity to meet with staff from the NIH (National Institutes of Health*). Adrienne and Irv Geffen, support group members from New Jersey, arranged the meeting to discuss MSUD research and the impact MSUD has on families and society. On Friday, December 12, 2003, eight members of the MSUD Family Support Group met with four members of the NIH in Bethesda, Maryland. Representing the support group were:

- Sandy Bulcher, mother of Jordan, age 14, classic MSUD
- Adrienne and Irv Geffen, parents of Elan, age 19, MSUD variant
- Susan Jasin, mother of Jake, age 4, classic MSUD
- Claude Mayberry, grandfather of Matthew, age 11, classic MSUD
- Denise Pinskey, mother of Zach, age 8, classic MSUD
- Tibbie Turner, mother of Nik, age 21, MSUD variant
- Michael Woorman, MSUD adult, age 29, MSUD variant

Discussing strategies: Left to right: Sandy Bulcher, Denise Pinskey, Irv Geffen, Adrienne Geffen, Tibbie Turner, Michael Woorman.

Prior to meeting with the NIH staff, the support group representatives met to discuss a strategy. Irv Geffen was appointed facilitator of the group because he had prior experience in this role. Our meeting started promptly at 11a.m. Staff present from the NIH included: Catherine McKeon, Ph.D., National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); Richard Farishian, Ph.D., NIDDK Policy office; Stephen Groft, Pharm. D., Office of Rare Disease; Mary Lou Oster Granite, Ph.D., National Institute of Child Health and Human Development.

We parents presented a brief description of our child's particular situation, including challenges and achievements. It was emotional to talk about our child's daily struggles. Michael Woorman, an adult with MSUD who is married to a woman with classic MSUD, shared his concerns about the financial impact of the cost of formula on his family. Other concerns included frustration with the lack of MSUD research, the slow progress in improving treatment, and the absence of standardized care. We also expressed concern about the long term outlook for those with MSUD and their quality of life. The NIH staff listened attentively to our family stories and concerns.

Dr. Catherine McKeon of the NIH explained how grants are funded. The process begins with investigators sending proposals to the NIH. A review board evaluates each application for merit, and grants are chosen for funding based on scientific merit and scientific priorities. Dr. McKeon then gave us an update on MSUD research funded by the NIH - there are currently three grants for ongoing studies. She also told us that the NIH denied funding for Dr. Harbhajan S. Paul's research with the MSUD mouse model because it is funding gene therapy research similar to his that could potentially benefit MSUD.

Next, we discussed the addition to the Appropriations Bill of language regarding NIH funding of MSUD research. We were surprised to learn the significance of this addition. The NIH will need to look more closely at MSUD research if the bill passes, which has the potential to benefit all of us. We also discussed several ways to increase the visibility of our organization, including more active participation in NORD (National Organization of Rare Diseases) and the Genetic Alliance.

The apparent lack of young researchers interested in MSUD was a concern of the NIH staff. To deal with this problem, there are several things that we can do as an organization. One is to contact the SIMD (Society of Inherited Metabolic Disorders) and share our concern over the lack of MSUD research. The NIH staff offered to contact local researchers in an attempt to increase interest in this research. They also offered to review current research and determine if any can directly benefit MSUD. It could also prove beneficial to invite prospective researchers to our Symposium.

As we are all aware, treatment for MSUD varies greatly from clinic to clinic. We were excited to learn that the NIH is willing to host a satellite meeting of physicians involved in treating MSUD to discuss standardized care and treatment. This meeting would be in conjunction with other meetings that physicians would be attending at the NIH.

Our meeting with the NIH staff ended at 1 p.m. Those present felt that it was very productive, and we look forward to progress in the areas that we discussed. This meeting was clearly the first step in forming a relationship between our MSUD Family Support Group and the NIH. It is of great importance to have a volunteer to act as a liaison between the two groups. We need to keep an active path of communication and follow up on suggestions offered to us. We will discuss this further at the Symposium in July.

*The NIH is the major funding agency for academic health research. It comprises 27 separate institutes and centers and is one of eight health agencies of the Public Health Service which, in turn, is part of the U.S. Department of Health and Human Services. It is a large agency with 17,000 employees, 10,000 of whom are scientists. The goal of NIH research is to acquire new knowledge to help prevent, detect, diagnose, and treat disease and disability, from the rarest genetic disorder to the common cold. NIH conducts research in its own laboratories; supports the research of non-federal scientists in universities, medical schools, hospitals, and research institutions throughout the country and abroad; helps in the training of research investigators; and fosters communication of medical and health sciences information.

NIH meets MSUD representatives, left to right: Front - MaryLou Oster Granite, Ph.D., Denise Pinskey, Tibbie Turner, Michael Woorman, Catherine

McKeon, Ph.D., Back - Adrienne Geffen, Irv Geffen, Sandy Bulcher, Richard Farishian, Ph.D., Stephen Groft, Pharm.D., Claude Mayberry, Susan Jasin.

# CURRENT STATUS OF THE MSUD MOUSE PROJECT

**Details**

Written by Harbhajan S. Paul, Ph.D.

Published: 20 July 2009

*Harbhajan S. Paul, Ph.D. of Biomed Research & Technologies, Inc. has provided a short review and an update on the research project that was reported in the last issue (Spring/Summer 2003) of the MSUD Newsletter. The MSUD Family Support Group has been supplying bridge funding for one year for this project that could lead to gene therapy for MSUD. Dr. Paul reports that his company was advised to submit a new grant to the NIH by April 1, 2004. Dr. Paul will give an update on this research at the MSUD Symposium 2004 in July.*

We had initially created a classic MSUD mouse which carries a knock-out gene of the E2 subunit of the branched-chain ketoacid dehydrogenase (BCKDH) complex. As expected, 25% of the offspring of such mice were completely deficient in BCKDH and died a few days after birth. This neonatal lethality severely limited the usefulness of this model system as it was impossible to perform studies with these mice, such as, developing gene therapy.

To overcome this problem and to increase the usefulness of the MSUD mouse model, we created a conditional transgenic rescue of the lethal phenotype. In this new model, the rescuing transgene is under the control of a tetracycline-responsive promoter, and the investigator controls the level of transgene expression by adding or removing tetracycline from the drinking water and/or food.

For the tetracycline-regulated system, it is essential to create and screen several transgenic lines of mice in order to find those that perform optimally and truly represent the disease model. This required extensive breeding and testing of a large number of mice - a very time-consuming process.

We have now produced several transgenic lines. One line looks most promising, because these mice survive to adulthood. These mice represent an intermediate MSUD mouse model. They have branched-chain amino acid levels in the blood that are intermediate between control values and those of the classic MSUD model. Four additional lines have been tested, and these mice did not survive into adulthood. Four other lines are currently being analyzed for their ability to survive to adulthood. Several other lines remain to be tested.

Our goal now is to complete the screening and characterization of as many lines as possible, and to select one to establish a stable mouse colony to provide a continuous and predictable source of animals to allow for long-term studies. Our characterization of the mouse model has four components: a) screen for long-term and high frequency of survival, b) confirm reproductive ability, c) characterize blood amino acid levels, and d) monitor efficiency and reproducibility of transgene regulation by tetracycline. At a later date, characterization may also include histo-pathological analysis of selected organs, such as the brain.

The progress of this project has been slow, but substantial. Because of the complex biochemistry involved in MSUD, the project has proved to be much more complicated than initially anticipated. Secondly, limited funds have precluded us from adding additional resources, such as, research staff and support. In spite of these difficulties, we have made significant progress and expect to establish a large and stable colony of MSUD mice.

Funds provided by the MSUD Support Group are being used for the following three categories:

1. Cost of animal care at the University of Pittsburgh. (Most of the funds are being used for housing the mice.)
2. Costs related to amino acid analysis of blood from the mice.
3. Some limited lab supplies.

In addition to funds provided by the MSUD Support Group, Biomed Research & Technologies, Inc. has continued to contribute funds and resources toward this project.

# CONGRESSIONAL ATTENTION DRAWN TO MSUD

**Details**

Written by Irv and Adrienne Geffen

Published: 20 July 2009

Requesting support from Senators and Representatives in the U.S. Congress is an excellent way to focus attention on MSUD research nationally. The National Institutes of Health (NIH) is funded every year by an annual appropriations bill. In the bill, Congress also directs the NIH on how to spend the funding it provides. While Congress doesn't detail exactly how much the NIH should spend on specific disorders - they leave that to the scientists - Congress almost always includes language in a report accompanying the bill that *encourages* the NIH to focus on a particular disorder. While report language like this doesn't have the force of law, it does represent a direction from Congress that most agencies (including the NIH) will follow.

We called our local Congressman, Representative Jim Saxton (R-NJ), and his staff agreed to meet with us. Through his staff, we asked our Congressman to contact the House Appropriations Committee in support of MSUD research. Rather than asking for a specific dollar amount to be allocated for MSUD research, Representative Saxton simply asked that the Committee include report language encouraging the NIH to support MSUD research efforts. The House Appropriations Committee agreed, and report language supporting MSUD research was included in the NIH's Fiscal Year 2004 budget. The result is that the NIH will most likely be funding some new research projects this year.

Members of the MSUD Family Support Group can have a similar effect by meeting with their own Senators and Representatives or writing to them. In your meetings or letters, talk about your own experiences with MSUD and ask them to contact the Appropriations Committee and request the Committee to include similar MSUD-related report language every year. If the NIH is aware of the continuing interest shown by Congress, the agency will be likely to expend more resources on research related to MSUD.
Editor's note:

*A copy of the letter that Representative Saxton wrote to the House Appropriations Subcommittee can be viewed by* ***clicking here****. At the end of the letter, Representative Saxton submitted language concerning the need for funding MSUD research. The language was changed in the final report and was as follows:* "Branched chain ketoaciduria is a rare inherited disorder that prevents the proper metabolism of the three branched-chain amino acids found in all protein, and can lead to mental retardation, physical disabilities and death. The conferees are aware of modeling research currently being performed on mice, with the goal of finding a permanent cure for the disease. The conferees encourage NIDDK to provide support for this type of research and other branched

chain ketoaciduria-related research.*Branched chain ketoaciduria is a descriptive name for MSUD, and was used instead of the common name, maple syrup urine disease, which was used in the original request.*


**U.S. House of Representatives**
**Washington, DC 20515**

October 29, 2003

The Honorable Ralph Regula
Chairman
House Appropriations Subcommittee on Labor, Health and Human Services, and Education
2358 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Regula:

As you continue conference negotiations with the Senate on the Fiscal Year 2004 Labor-HHS Appropriations Bill, I would appreciate your consideration of a health research issue that is very important to my constituents.

Maple Syrup Urine Disease (MSUD) is an inherited metabolic disorder, that, if untreated, causes mental retardation, physical disabilities and death. MSUD derives its name from the sweet, burnt sugar, or maple syrup smell of the urine. First described as a disease in 1954, it is a rare disorder, with a national incidence of 1 in 225,000 births.

The disorder affects the way the body metabolizes the three branched-chain amino acids in protein. These amino acids accumulate in the blood causing a toxic effect that interferes with brain functions. The first symptoms in an infant are poor appetite, irritability, and the characteristic odor of the urine. Within days they lose their sucking reflex and grow listless, have a high-pitched cry, and become limp with episodes of rigidity. Without diagnosis and treatment, symptoms progress rapidly to seizures, coma and death.

Aside from the direct health effects of MSUD, families and the insurance industry alike must incur substantial costs for management of the disorder. The high cost of special education, dietary supplements, medical care and physical therapy often place a heavy financial burden on families whose children live with MSUD every day.

As an extremely rare disorder, very little research funding is made available for MSUD. Indeed, although the National Institutes of Health (NIH) has provided funding in the past, current activities are being carried out on a shoestring budget. In that regard, I have been made aware of a funding proposal that has been submitted to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to continue modeling work being performed on a "family" of mice with MSUD.

Therefore, I respectfully request the inclusion of the following supportive language in the Conference Report accompanying the Fiscal Year 2004 Labor-HHS Appropriations Bill that further encourages NIDDK to consider providing research funding for MSUD:

"*Maple Syrup Urine Disease (MSUD).* - This rare inherited disorder prevents the proper metabolism of the three branched-chain amino acids found in all protein, and can lead to mental retardation, physical disabilities and death. In addition, families whose children live with MSUD must deal with the often staggering financial implications of special education and medical care associated with MSUD management. The Committee is aware of modeling research currently being performed on mice, with the goal of finding a permanent cure for the disease. NIDDK is encouraged to provide support for this and other worthy MSUD-related research."

Thank you for your consideration of this request. Should you have any questions or need any additional information, please do not hesitate to contact Erica Stocker, of my staff, at x54765.

Sincerely,

Jim Saxton
Member of Congress

# PERSONALLY FROM THE BRUBACHERS

**Details**

Written by Wayne, Joyce & Shayla Brubacher

Published: 20 July 2009

I am retiring from my responsibilities in the MSUD Family Support Group. (Wayne says I can't retire since I was never hired!) This is my last issue as editor of the MSUD Newsletter. The load has grown too heavy for me at my age (62 - retirement age!). I announced my intentions to the MSUD eGroup last October with the hope that someone with enthusiasm and new ideas would offer to take over the work I have been doing for the organization. The consensus was that it was best to divide the jobs between several persons. My goal is to turn all these responsibilities over to others by the end of Symposium 2004. Then I can unclutter our office and my brain - how exciting!

I grew into these jobs. I had no formal preparation and only a high school education. Wayne and I are grateful for the talented and capable people who have offered to assume some of these responsibilities:

1. Dave and Sandy Bulcher - headquarters for the organization
2. Dave Bulcher - maintain database
3. Adrienne Geffen - layout of MSUD Newsletter
4. Kay Larsen - contact person
5. Emily Talley - maintain web site

Two important jobs remain for the work of the organization to continue:

1. Editor to gather and edit material for the Newsletter.
2. Someone to keep the MSUD web site material updated.

We are grateful for the dedication Dave and Sandy have shown as treasurer and contact person and are confident that they will serve well with their additional responsibilities. I plan to transfer the database to Dave Bulcher as soon as I use it to make an updated family address list. These lists will be available at the Symposium in July and also available from Sandy on request.

Adrienne Geffen is a graphic artist who designed this attractive issue. Kay Larsen has begun helping with e-mail and phone inquiries as a contact person. There is always a constant flow of those to answer and Kay is doing a great job. Emily Talley is a web developer and will post material on our web site. But someone is needed to keep resource lists and other information on the site updated and prepared for Emily to post.

The job of editor is critical to the continuance of the MSUD Family Support Group because the Newsletter keeps the group informed. In our group of 640 families and professionals, there surely are a number of persons capable of editing the Newsletter. Perhaps a grandparent or other member of the family would be interested? It would be best if someone

volunteered to be in charge of the MSUD Newsletter before the Symposium in order to cover it in the next issue. Please contact me if you are interested.
It has been an honor and a privilege to serve the MSUD Family Support Group since its origin in 1982. I enjoyed the challenge of editing the Newsletter and having our home serve as headquarters for the Support Group. I have learned skills that will help me in the future projects I hope to pursue. As long as Wayne is on the board of directors, we will still be actively involved in the Support Group and want to keep in touch with families as members of the MSUD eGroup.

We have learned to know several hundred wonderful families and professionals during these years and have made many lasting friendships. What we have learned has helped us give our daughter Shayla better care. (She looks forward to having Mom more available to talk to.) Most amazing of all to me has been the wonderful way the Lord has answered my prayers in many instances that looked hopeless. We feel the Lord called us to this field of work when He gave us two children with MSUD. We thank him for this opportunity and want to give Him all the glory. It has been a great blessing to us and worth all the challenges and trying times. Now I want to pass this privilege on to others. May God continue to direct and bless this wonderful Support Group as it strives to meet the needs of those involved with MSUD.

# THOUSANDS OF MILES APART

**Details**

Written by Monica Falconer

Published: 20 July 2009

It was early morning in Anchorage, Alaska. I opened my MSUD e-mail account like I do every day. It's become a routine, and the MSUD eGroup is a wonderful source of knowledge for me. There were a few messages that day from members of the group, but one subject in particular caught my eye. It said something like "family from Spain needs information." Seeing the name of my country of origin in the subject made me click on this message and read it right away. The Bazan Martos family from Cadiz, in the southern part of Spain, was asking for information and help.

The Martos family had a three-year-old adopted daughter, Hindou, with MSUD. Without hesitation, I offered to share the little information I had about MSUD. I mentioned that I would like to exchange e-mails with them and was willing to translate information that was shared on the MSUD eGroup.

I received a reply the next day, and from then on we exchanged messages on a daily basis, often several times a day. It is a wonderful feeling of relief to finally establish communication with a family who share the same language, culture and

a similar situation. Jeronimo and Charo, the parents, told me about their three biological daughters, Laura, Sonia and Elena, and their youngest daughter, Hindou, who came to them when she was ten months old. They are a wonderful family who are always just a click away. We chat about our families and routines, laugh together, exchange low protein recipes, share concerns and help each other with our MSUD experiences. They even told me how to make a low protein version of one my favorite dishes from Spain, "tortilla de patata."

The Bazan Martos family provided us with information about MSUD-related issues in Spain. They told us where to buy low protein products in that country and how to order them ahead of time. This is going to be a big help when we pack for our trip this coming summer. Marlon, our son, and I will be spending two months in Spain, and my husband, Navid, will join us there for a month. We are excited about spending a full summer with my family, but it is always stressful to have to think about all the special supplies we'll need during our vacation.

Recently we decided to try chatting with our new friends online using webcams. We had a wonderful time. Our little children, Marlon and Hindou, both with MSUD, even played peek-a-boo thousands of miles apart. We were all thrilled to see our children's big smiles. The children have a lot in common, and for the first time, they had the opportunity to play with each other and enjoy themselves despite the distance. We are making plans to meet the Bazan Martos family in Spain this coming summer when we go to visit my family, and we are really looking forward to it.

We never would have met this family had it not been for the MSUD eGroup. Our friendship grew with the exchange of communication through the Spanish chat group, which we started a few months ago. This MSUD Spanish eGroup is available for all families and adults dealing with MSUD who speak Spanish. To access this group, e-mail me at: monicazf@yahoo.com.

# IMPORTANCE OF MEDICAL IDENTIFICATION

**Details**

Written by Denise Pinskey

Published: 20 July 2009

We have been convinced that we need medical identification for our 8-year-old son Zachary. Previously we thought that it was unnecessary because he was always with a family member or at school. We now realize how shortsighted we were. One of the worst experiences to happen to our family changed our minds.

During this past summer, we were enjoying a family vacation at a State Park in Michigan. Zachary walked on ahead of his father and was missing for two and a half hours. You can imagine the panic and horror we felt. This story, fortunately, had a happy ending. Zachary had been looking for us outside the park when a nice lady found him and called the police. We got him back safe and sound. It was a very long two and a half hours with park rangers, police and strangers all looking for Zachary.We came within five minutes of having our missing boy reported on national news. The police had already contacted Amber Alert, which helps find missing children. This process happened quickly because of Zachary's special medical circumstances and an attempted abduction the day before in this same county. I know I felt even worse when the police shared the abduction fact with me. After finding Zachary, the police and EMS staff both reminded us that it would be a good idea to have medical alert information on our son. This was not a proud parenting moment!

Currently Zachary is wearing a bracelet because we thought the necklace might get caught while he was playing on the playground. The bracelet for his wrist is quite small so we could only fit his name, maple syrup urine disease and my cell phone number on it. I suspect in time his needs will change.

Because of this experience, I have learned some interesting information by checking on the Internet and corresponding with the MSUD eGroup parents. There are many choices of medical ID's available, such as, bracelets, necklaces, sports bands, medallions and dog tag style necklaces. These can be engraved with basic information. I found several sites for medical ID's, two of which are:

**Childs ID**
Web site: www.childsid.com

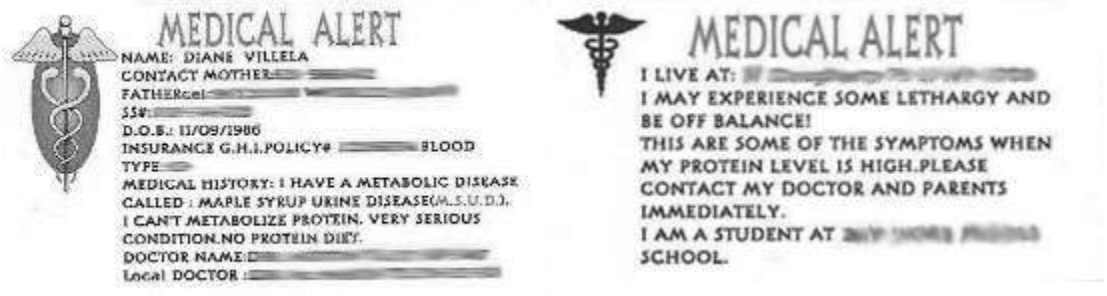
Toll free number: 866-654-4340
E-mail: childsid@netzero.com

**American Medical Identifications**
Web site: www.americanmedical-id.com
Toll free number: 800-363-5985

For someone who travels a lot or who lives independently, the MedicAlert Identification would be a good option. The MedicAlert Foundation is a nonprofit membership organization available worldwide which provides personal medical information 24 hours a day to authorized medical professionals. Their contact information is:

**MedicAlert Foundation**
Web site: www.medicalert.org
Toll free number in the U.S.: 888-633-4298
Phone number outside the U.S.: 209-668-3333
Fax: 209-669-2450
E-mail: customer_service@medicalert.org

I asked the MSUD eGroup what they were using for medical identification. From the responses, I learned that various kinds of medical alert jewelry are being used. Several of the teens and adults with MSUD carry information in their wallet or purse. Ruth Villela, who has two children with MSUD, made laminated medical alert cards for her children to carry in a purse or wallet on which this information was listed: name; address; several contact people and their phone numbers; social security number; date of birth; insurance card number; blood type; the name, symptoms and a short description and of the medical condition; doctor's name and phone number; and name of school. She got all this information on a small card using both sides.
We hope this gives you some information to think about.




*AllegroMedical.com markets a MedScope medical ID key chain/pendant. It is a medical information viewer which contains 25 lines of medical data and contact information and attaches easily to a belt loop, jewelry, key chain or luggage. Call 800-861-3211 for more information.*
*Carrying a card or letter with medical emergency information is fine, but other identification, such as, jewelry, is needed to alert medics to look in a wallet or purse for more detailed information. There are a number of companies offering medical ID's. Just type in "medical identification" in a search engine to find a list of web sites.*

# TRIAL OF FAMILY FROM INDIA

**Details**

Written by Nirmal Parmar

Published: 20 December 2004

I'm Nirmal Parmar, from India. I'm now in the United States with my wife and child, Mihir, for help with his medical treatment. In the following account, I tell how the life of our newborn child in India was saved with the help of Dr. Rekha Gohel and the support of doctors in the U.S. I recount our experience with the rare, life-threatening disease, maple syrup urine disease.

**Birth and First Days**

My son Mihir was born on July 4, 2003. Our family was filled with joy and happiness after the normal birth of our healthy baby boy. It was a great feeling to become a father and have my dreams fulfilled. My wife, Mital, was discharged the very next day, and we went home with our newborn to rejoice with family and friends. On the third day, my father, who is a doctor, found something unusual in Mihir's behavior.

That same day a local pediatrician was contacted and a neurologist examined Mihir. He was showing some body posturing movements, and my father and the other doctors suspected Mihir was hypertonic. The blood and CT scan reports were normal, except that some toxic levels in the blood were high. Mihir was then hospitalized. His condition was worsening, and we were all worried about him.

The pediatrician was not able to diagnose him, and two days later, at 7 days of age, Mihir was flown to the Hinduja Hospital in Mumbai. This was a terrible and confusing experience for us. Mital, Mihir's mother, was shocked and rushed to Mumbai along with many other family members. Dr. Rekha Gohel, Mital's sister, who lives in the U.S., was in continuous contact with us. She and her family were worried too.

**Early Hospitalization at Hinduja and Diagnosis**

Mihir was admitted to the ICU for newborns at Hinduja Hospital under Dr. Vrajesh Udani, a leading neuro-physician from India, and Dr. Soonu Udani, the pediatrician in charge of ICU. Mihir was in poor condition and connected to several monitoring machines/instruments. Routine blood tests were done several times a day, and his urine was sent to Japan for further tests. The toxic blood levels were affecting Mihir's brain, and he was going into a coma. The doctors suspected a metabolic disease because no drug or treatment was making a significant change in Mihir's blood levels. My wife and I and other family members felt so helpless. The days and sleepless nights passed with more worries and tension.

After a week of many MRI's and other tests, Dr. Vrajesh Udani diagnosed the problem as a rare metabolic disorder, maple syrup urine disease. My family and I were stunned to hear that there were no doctors in India who treat MSUD. We never imagined anything like this could happen to us. Mihir's aunt, Dr. Rekha Gohel was our only hope. I sent her daily reports by e-mail, and we kept in contact by phone.

**Post Diagnostic Treatment and Recovery from Coma**

As soon as we had a diagnosis, Dr. Gobel searched for information and learned of a metabolic center in Pennsylvania that is dedicated to treating MSUD and helping families to manage the disease. She met personally with Dr. Strauss from the Clinic for Special Children in Pennsylvania. He reviewed Mihir's records and gave Dr. Gobel the supplements and medications needed to bring Mihir's toxic blood levels down.

Back in India, the doctors, unable to do much, tried to convince my family there was no hope for Mihir. But we had hope in Dr. Strauss and Dr. Gobel. We insisted Dr. Udani contact these doctors and learn how to treat our child. Dr. Strauss sent a detailed care plan. The doctors at Hinduja ignored it and kept trying their own methods. Dr. Gohel called the doctors, but they still would not respond. Against Dr. Strauss's advice, they gave Mihir a blood transfusion. That produced no change in levels and a second transfusion was done. Again the same outcome. Later they tried peritoneal dialysis, which failed half way through, and they had to stop. I was keeping doctors Gohel and Strauss updated and Dr. Strauss was not in favor of the treatment they were giving Mihir.

Meanwhile, Dr. Gohel was trying hard to figure a way to send the supplements to India. Frustrated with the way treatment was going, she decided to go to India herself. She wanted so much to save my child that she left her two young children and family on short notice and flew to India. As soon as Dr. Gohel arrived, she contacted Dr. Soonu Udani in charge of the ICU at Hinduja Hospital. The doctor refused to treat Mihir according to Dr. Strauss's care plan. Dr. Strauss called her personally and tried to explain. Higher authorities were contacted at the hospital, and the top management was asked to make Dr. Udani follow the guidance of Dr. Strauss. Under pressure, Dr. Udani finally agreed.

It was taking too long to test the blood levels at the hospital. Dr. Gohel and I contacted the laboratory and asked them to contact Dr. Strauss about how the tests are done in the U.S. Dr. Gohel, my brother-in-law and I kept watch to make sure the right treatment was given. We visited many times at midnight to check Mihir's condition. Dr. Gohel managed to convince the hospital staff to give Mihir the desired treatment. She mailed daily reports to Dr. Strauss in the middle of the night because of the time difference between India and the U.S. Mihir responded to the new treatment, and his blood levels came down drastically. Even Dr. Strauss was amazed. In just four days, his levels dropped from 4000 µmol/l to 900, and he was out of his coma.

**Going to the U.S. for Medical Support**

With the support of Dr. Gohel, we made a quick decision to take Mihir to the U.S. for treatment. We had one goal in mind—to save Mihir. Ordinarily it takes 15 days to 3 months to get passports

and visas. After September 11, procedures to get to the U.S. had changed, and it was not easy to do. Everyone in the family helped, and we were able to get Mihir's passport from Mumbai in just one day. Dr. Gohel got an appointment at the U.S. embassy here in Mumbai by meeting with the top authorities from the U.S. embassy. Dr. Strauss faxed a letter showing the urgency of the situation. Dr. Gohel's husband, Manish, faxed a letter of support which was necessary for getting the visas. The embassy cooperated, and we had our visas in two days!

Then there was the problem of Mihir traveling in an airplane. Critically ill patients have to go through a medical checkup to ensure safe travel. The airlines have their own panel of doctors who make the final decision. Dr. Gohel called the British Airways doctors in London and managed to convince them to let Mihir fly to the U.S., and the tickets were granted.

Dr. Gohel is a doctor of Internal Medicine and had no experience handling newborn babies in critical condition. Mihir was coming out of ICU, and Dr. Gohel had to manage Mihir all the way to the U.S. without any help or monitoring support. She got a crash course from the doctors at the hospital. Mihir was being fed through an NG tube. Dr. Gohel packed all the dietary supplements for each two-hour feeding and individually packed the shots Mihir needed while traveling. Everything worked out like a fairy tale, and we were soon on the plane.

Being new parents, my wife and I had no experience handling a newborn. It was Dr. Gohel's courage and determination that gave us strength to take my child to the U.S. Mihir, with a feeding tube and IV, was 22 days old when we moved him directly from ICU unto the plane. Dr. Gohel managed Mihir those 24 hours on the plane. The British Airways crew was also helpful.

We landed at the Newark airport on Sunday and left for the Lancaster General Hospital in Pennsylvania. Dr. Morton, founder of the Clinic for Special Children, was waiting for Mihir at the hospital, and we were in continuous contact with him. Mihir's condition was worsening on the way. Manish, Dr. Gohel's husband, tried his best to drive at the maximum speed to get Mihir there quickly, but Sunday traffic was heavy. Dr. Gohel was trying hard to manage Mihir, but he needed oxygen and other monitoring. We called 911 after we crossed the Pennsylvania line so he would not be taken to an emergency room in New Jersey. Mihir was transferred to an ambulance on the highway and taken directly to the ICU in the Lancaster General Hospital. Dr. Morton responded quickly. Mihir was admitted and a blood test was done. Here it takes 15 minutes to get the blood levels done, and the treatment was started quickly. Mihir did well and was discharged on the fourth day.

**My family's Present Situation**

We are living with Dr. Gohel in New Jersey. Now my wife and I manage Mihir's treatment with Dr. Gohel's help. We send blood to the clinic twice a week, and the doctors there guide us in adjusting the dietary supplements. Previously, we visited the clinic every week, but now we go every two weeks. Overall Mihir is doing well, and his growth is normal. Twice we took him to the Clinic in an emergency. Since Mihir was in a coma for a while, the doctors suspect some brain damage. As of now, his growth looks normal for his age, and he is doing well. This would not have been possible without the unconditional support of the Clinic for Special Children and the staff there.

Every day since Mihir's birth has been a day with some new hurdles. It's been hard on us to go through all this, and it is very difficult to explain it all. Mihir's disease is lifelong and with no medical support available in India, my family needs to stay here in the U.S. Like every newly married couple, we had many dreams and plans for our life. We had to leave India on very short notice, leaving my business, our families, our friends and all our belongings behind. Right now we don't know what else to do, as there is no way out of this situation. Many times I think of my past in India with my family and friends, but now the MSUD support group is our new family and friends. We share the same experiences and encourage one another. This has made MSUD easier for us.

Dr. Gohel's family is supporting and caring for us now. She helped us get our visas extended six months. I'm a qualified automobile engineer and own a small business servicing cars. My wife is a microbiologist and certified as a medical lab technician. But here in the U.S. we cannot get employment without a work permit and an employer sponsoring us. I'm trying hard to find a sponsorship.

- Nirmal Parmar