VOLUME 19-1

Spring/Summer, 2001

NATIONAL CONFERENCE IN OHIO - OVERVIEW OF CONFERENCE

Details

Written by Kay Larsen

Published: 20 July 2009

Dublin, Ohio was the site of the National Coalition for PKU and Allied Disorders Metabolic Conference on the weekend of May 3, 4, and 5. Attendees gathered at the beautiful Embassy Suite Hotel for a jam-packed conference, starting with reception on Thursday evening, and finishing off with a question and answer session with a professional panel on Saturday afternoon.

Friday morning and afternoon were devoted to breakout sessions for the following diseases: phenylketonuria (PKU), MSUD, organic acidemias (OAs), fatty oxidation disorders FODs, homocystinuria (HCU), and tyrosinemia (TYR). On Friday evening from 7 p.m. until 10:30 p.m., there were talks on different aspects of newborn screening with a question and answer time at the conclusion. On Saturday, the entire group came together in the large ballroom for back to back lectures on the following topics:

1. Self Esteem Issues of A Child with an Inborn Error of Metabolism
2. The Prevalence of ADHD in Metabolic Disorders
3. Federal Legislation for Metabolic Formulas
4. Universal Newborn Screening, It's Time Has Arrived!
5. Obtaining Metabolic Formula Reimbursement
6. Gene Therapy Update

There was a great deal of sharing and interacting among the families. For many of the families it was their first opportunity to attend a conference like this. There were approximately 320 people (families and professionals) present from thirty-one states and seven foreign countries. Twenty-one metabolic disorders were represented. Eight MSUD families attended.

Between sessions, the participants were able to enjoy the pool and other amenities of the hotel. Terrific low protein food was provided for those on low protein diets. Vendors from

several companies displayed the latest in low protein foods and medical foods for low protein diets.

The organizers of this event included: Trish Mullaley, Massachusetts, who is the President of the National Coalition for PKU and Allied Disorders; our own Sandy Bulcher, Ohio, who is Vice-President of the Coalition; Kathy Stagni, Minnesota, from the Organic Acidemia Organization; Cay Welch, Pennsylvania, representing the International Organization of Glutaric Aciduria; Teresa Cornette, Kentucky, Fatty Oxidation Disorders; Karen Lewis, Massachusetts, homocystinuria; and Jennifer Hebberer, Maine, Tyrosinemia.

We realized that despite our differences, there is much that we share in common. We can, and should, work together to achieve our common goals. The next conference will be held in Minnesota. Check the msud-support.org web site for updates.

DESCRIPTION & TREATMENT OF MAPLE SYRUP URINE DISEASE

Details

Written by Rebecca S. Wappner, M.D.

Published: 20 July 2009

The following was adapted from an outline of the presentation given by Rebecca S. Wappner, M.D., Riley Hospital for Children, Indianapolis, Indiana at the National Coalition for PKU and Allied Disorders Metabolic Conference in Ohio in May 2001.

Symptoms of MSUD result from elevated body fluid levels of:

- Branched-chain amino acids (BCAA): leucine, isoleucine & valine.
- Keto acid (2-Oxoacid) derivatives: a-ketoisocaproate (KIC), a-ketomethylvalerate (KMV) a-ketoisovalerate (KIV).
- Alloisoleucine - diagnostic compound from isoleucine metabolites.

Branched-chain amino acids (BCAA)

- Essential amino acids - building blocks for the body.
- Used to make:
    - Body tissue (especially skeletal muscle 35%).
    - Glucose (gluconeogenic).
    - Ketone bodies (ketogenic).
        - Fatty acids and cholesterol (needed to make hormones).

- Energy.

MSUD results from

1. Decreased activity of the enzyme Branched-Chain a-Keto acid Dehydrogenase (BCKD).
2. BCKD - large complex molecule with 6 components, coded for by 6 different genes.
    1. Carboxylase (thiamine co-factor).
        1. Subunit a (E1a), 22 mutations.
            1. Classic: Mennonites & others in U.S.
            2. Intermediate: Hispanic.
        2. Subunit b (E1b), 7 mutations.
            1. Intermediate & Intermittent.
            2. French Canadian, Afro-American & Whites.
    2. Transacylase (E2), 28 mutations: Japanese.
    3. Dehydrogenase (E3), 5 mutations.
        1. Japanese (Ashkenazi).
        2. Eastern European Jews.
    4. Kinase (activator).
    5. Phosphorylase (inactivator).

History

1. 1954 Beginning of amino acid analysis.
2. 1954 Menkes, Hurst, Craig: first to describe MSUD; identified urine odor.
3. 1960 Dancis: demonstrated deficiency in decarboxylation of BCAA.
4. 1964 Snyderman: developed diet restricting BCAA; determined amount of BCAAs needed by the body.
5. 1971 Scriver: described a thiamine-responsive form of MSUD.
6. 1976 Means of identifying organic acids became available.
7. 1978 Reed: purification of the BCKD.
8. 1980s Beginning of molecular genetics and the identification of the subunits of the enzyme, BCKD.
9. 1990s Morton: improved treatment.

Types of MSUD

1. **Classic** - less than 2% of normal activity of BCKD.
    1. Most severe, most common.
    2. Leucine more elevated than other BCAAs.
    3. Symptoms - usually begin appearing at 4-7 days of age.
        1. Lethargy.
        2. Poor suck.
        3. Decreased intake.
        4. Weight loss.
        5. Neurologic signs.
            1. Alternating increased & decreased motor tone.
            2. Abnormal movements (dystonia).
        6. Ketosis - positive DNPH (dinitrophenylhydrazine).

7. Abnormal maple syrup odor (recognizable in ear wax before urine).
8. Seizures, coma, cerebral edema, death.

4. Even with newborn screening, some infants will be symptomatic before or at the time the testing results are known.
5. Various degrees of disabilities in many depending on when treatment was started and how well controlled.

2. **Intermediate** - 3-30% of normal activity of BCKD.
    1. Less severe than classic; less common.
    2. Symptoms appear later; may not be diagnosed until 5 months to 7 years of age when evaluated for delayed development.
    3. All BCAAs elevated, leucine less high than in classics.
    4. Catastrophic brain symptoms (encephalopathy) usually not present during newborn period.
    5. Delayed development, maple syrup odor, seizures.
3. **Intermittent -** 5-20% of normal activity of BCKD.
    1. Less severe than classic; less common.
    2. Usually no symptoms during newborn period.
    3. Episodes of acute loss of metabolic control usually begin between 5 months and 2 years.
        1. Present with ketosis & hypoglycemia.
        2. During episodes:
            1. Difficulty walking and keeping balance.
            2. Lethargy.
            3. Behavior/personality changes.
            4. Maple syrup odor in urine.
        3. Abnormal BCAAs only present with episodes.
    4. Growth and development usually normal.
4. **Thiamine-responsive** - 30-40% of normal activity of BCKD.
    1. Similar to intermediate/intermittent although less common.
    2. Usually no symptoms during newborn period.
    3. Episodes of acute loss of metabolic control may begin in infancy or early childhood.
    4. Abnormal BCAAs only present with episodes.
    5. Delayed development possible.
    6. Responsive to thiamine in daily doses of 100-150 mg.
5. **E3-combined dehydrogenase deficiencies (BCKD, pyruvate, 2-oxoglutarate).**
    1. Similar to intermediate form; very rare (4 or 5 reported cases).
    2. Symptoms may appear during the newborn period, but more often, later.
    3. Symptoms include a severe lactic acidosis.
    4. Elevated lactic acid and 2-oxoglutarate.

Treatment (Classic type)

1. **Acute newborn crisis or acute metabolic crisis:**

1. *Goal: to achieve control of leucine levels by providing enough calories and special medical food to stop catabolism (breaking down of own body stores)*.
2. *Hyper-caloric approach: is preferred treatment used today - superior to dialysis used in the past.*
3. Monitor BCAA levels every 12 hours to guide therapy.
4. Stop all sources of protein including those from formulas and breast milk.
5. Start special medical food (devoid of BCAAs). Give by nasogastric tube (NG) if cannot be taken by mouth due to poor suck.
6. Add leucine to diet in the form of regular formula or table foods only when leucine levels are normalized.
7. If special medical food cannot be tolerated, use special IV hyperalimentation [TPN] (complete feeding) low in the BCAAs.
8. Supplement with other amino acids.
    1. Isoleucine and valine. (Inversely related to the leucine levels; can protect the brain from high leucine levels - important to keep these levels from becoming deficient.)
    2. Tyrosine (also decreases leucine brain levels.)
    3. Glutamine and alanine (Brain levels of these neurotransmitters are low if leucine is high.)
9. May need:
    1. IV intralipids 20% to increase calories.
    2. IV Insulin (promotes glucose intake in cells).
    3. IV Propanolol (catecholamine antagonist).
10. Cerebral edema (brain swelling) must be prevented - the usual cause of death.
    1. Behavior changes are an important predictor.
    2. Use hypertonic saline solutions (high normal sodium, diuretics, Mannitol).

2. **Treatment of asymptomatic MSUD newborns [diagnosed before clinical symptoms appear]:**

1. Start special medical food to prevent catabolism.
2. Initial leucine intake: zero.
3. Add glutamine, alanine, and salt.
4. Add isoleucine and valine in approximately two days.
5. Give thiamine, 10mg/Kg daily on a trial basis, if not Mennonite classic.
6. Monitor blood levels at least daily.
7. Add leucine when leucine levels normalize.

1. **Long Term Treatment**
    1. Requires the use of special medical food to provide protein intake of 2-2.5 gm/kg daily.
    2. Diet low in leucine - only amount needed for growth.
        1. Varies with age - most needed *per kg of weight* during newborn period.
        2. By age 2-3 years, 300-600 mg and maintained daily for rest of life.
        3. Select and use one food list consistently.

        1. Leucine values vary from list to list
        2. Leucine can be figured in milligrams or exchanges.
    3. Supply isoleucine and valine.
        1. To meet growth needs and avoid deficiencies.
        2. To protect against high leucine levels.
    4. Add glutamine and alanine to prevent low levels of these two amino acids.
    5. Add table salt (sodium chloride) to offset high salt loss through kidneys, especially when leucine is high.
    6. Avoid prolonged low levels of the BCAA - leads to poor growth, decreased appetite, rashes and skin infections.
1. **Provide adequate caloric intake** - *the mainstay in the treatment of MSUD*
    1. To promote growth and avoid catabolism.
    2. Initially supplied by formula, later from table foods.
    3. Based on age and activity.
2. **Thiamine**
    1. Give approximately 10 mg/Kg daily (50-300 mg per day) for at least 3 weeks as a trial.
    2. Mennonite classic is not a thiamine-responsive type.
3. **Blood monitoring**
    1. Quantitative measurement of BCAAs using blood or blood filter paper card.
    2. Quick turn-around time very important.
    3. Done weekly until age 6-12 months; thereafter depending on leucine tolerance.
    4. When ill or suspect elevated levels.
    5. After changing diet.
4. **DNPH (2,4 dinitrophenylhydrazine) monitoring**
    1. Usually positive with leucine level over 450 µmol/l (6 mg/dl).
    2. Best done on morning urine specimen.
    3. Daily when starting initial treatment.
    4. When ill or suspect elevated levels.
    5. After changing diet.
5. **Traveling**
    1. Plan daily intake ahead of time.
    2. Take enough supplies, including for illness.
    3. Check itinerary for available resources along the route - children's hospitals, medical centers, etc.?
    4. Contact and alert the specialist in your travel area.
    5. Carry a "Help Letter" from your doctor - include enough information to prompt the local ER physician into action.
6. "**Sick Day" management**
    1. Have a "sick day" diet plan. (Update every time recommended intake changes.)
    2. Usual plan: give special medical food - no regular formula - and extra isoleucine and valine. (Give extra formula, not extra clear fluids.)
    3. Leucine intake from table food is minimal/zero.

4. *Give extra calories! calories! calories!*
5. Routine treatment for other medical illnesses (i.e., antibiotics for ear infection, etc.).
6. Zofran may help for nausea and vomiting (not a sedative but stops vomiting at the brain stem).
7. Monitor BCAAs levels as often as daily.
8. If no improvement within 12 hours, or symptoms are worse, seek professional help.

Outcome

1. Best outcomes occur in siblings of older affected children (diagnosed at birth) and in those on diet by 10 days of age.
2. Those diagnosed and treated later than 14 days of age rarely have a normal outcome.
3. Approximately 1/3 have IQs over 90 (normal); 1/3 have IQs between 70 and 90 (borderline); and 1/3 have IQs less than 70 (handicapped).
4. May have problems with attention span and learning disabilities.
5. May have problems with motor control (some severe, similar to what is seen with cerebral palsy).
6. Special education and rehabilitation services may be needed.
7. Strict dietary control is needed for life.
1. Older individuals not on strict diet can have problems with "dysmyelination" which affects ability to function.
2. Improvement may be seen after return to strict dietary control from a lenient diet.

The chart illustrates the rapid rate of growth in the first year of life, especially during the first 6 to 8 months. This is why the protein per kilogram of weight is much greater in infancy than at any other time in life. At some time between 8 and 12 months, the growth significantly slows and blood monitoring and diet adjustments are critical to prevent loss of control. An increase in the rate of growth occurs during teen years, but it

does not compare with the early
growth rate.

Family

1. Genetic counseling: The family has a 1 in 4 (25%) chance of having another affected baby with each subsequent pregnancy.
    1. Prenatal diagnosis is available.
    2. Early detection and treatment during the newborn period improves the outcome.
2. Carrier testing can be done by means of the newer molecular genetic tests that are available.
    1. If the gene mutations are known in the family.
    2. If the family is of Mennonite [Swiss/German] background.

MSUD IN SAUDI ARABIA

Details

Written by Kay Larsen

Published: 20 July 2009

From the presentation given at the National Coalition for PKU and Allied Disorders Metabolic Conference in Ohio in May 2001.

During the breakout session on Friday, the MSUD families heard Dr. Pinar Ozand of Saudi Arabia. A graduate of Ankara University School of Medicine, Ankara, Turkey, Dr. Ozand has studied and worked extensively in the United States. Since 1985, when he was recruited by the Saudi government, he has operated a very sophisticated clinical center for the diagnosis and treatment of inborn errors of metabolism at King Faisal Specialist Hospital in Riyadh. He gave us a new perspective on the care of these difficult metabolic diseases, especially MSUD, in a culture so different from our own.

One of the difficult problems in places such as Saudi Arabia, and other middle eastern countries, is that families tend to "hide" those suffering from diseases such as this. If parents do bring a child to be treated, they may not tell the rest of the family. It makes it very difficult to test other family members to see if they are carriers, and it can make it harder to nsure good follow-up care.

This is part of the MSUD Parent Group at the National
Coalition Conference

Dr. Ozand told us of his many early "bitter" failures in his attempts to treat MSUD. He sees three distinct time periods in his nearly 17-year-long career treating metabolic diseases: a period in which all his patients died; a period where he had limited success in treating the diseases; and a third period up to the present where he has been very successful in keeping the patients alive and has secured good outcomes.

Currently, Dr. Ozand has over 2,500 patients with over 140 different metabolic disorders under current follow-up in his own clinic. Metabolic cases are referred to him from all over the Arabian Peninsula.

An enthusiastic proponent of Tandem Mass Spectrometry, he opened the first mass scale application of it in Saudi Arabia in 1991. The clinic receives 400 to 500 new patients with inborn errors of metabolism each year; and thousands of blood samples are received each year for tandem MS and urine testing.

Dr. Ozand told us there are more MSUD in Saudi Arabia than PKU. He averages one new MSUD patient per month. He is a very busy doctor in a very needy area.

GENE THERAPY

Details

Written by Kay Larsen

Published: 20 July 2009

From the presentation given at the National Coalition for PKU and Allied Disorders Metabolic Conference in Ohio in May 2001.

Dr. Dean Danner, Vice Chair in the Dept. of Genetics, Emory University, presented an interesting talk on Gene Therapy. He did an excellent job explaining an extremely complex subject in a way we could understand. He addressed four questions about gene therapy:

1. What is the reason for hope in gene therapy?
2. Why is it so popular with inborn errors of metabolism?
3. What are the problems?
4. Where are we now in reaching the goal of gene therapy?

Currently, the hope of gene therapy involves a threefold approach:

1. Add a good gene and allow the body to make the necessary product - one not being made by the mutant gene [such as is the case with MSUD].
2. Add a gene to stimulate the immune system.
3. Add a gene to kill cancer cells.

The ultimate goal is to eventually replace a bad gene or to repair it completely.

The fact that inborn errors of metabolism involve only single gene defects means that replacement would offer a permanent cure and NO MORE DIET! Correction has been demonstrated in cultured cells for many single gene traits. There has been some success in rodents and some recent positive results in experiments with lower primates. But that is a long way from making it work in humans.

Certainly, it would be a mistake to minimize the problems that we face in making gene therapy feasible for humans. The problems include the health of the recipient and the questions of timing (i.e. do you treat in utero, in the new-born period, or later?). Each period for treatment presents its own set of problems. Only somatic (mostly non-dividing) cells can be treated, not embryonic stem cells. Can specific tissues be targeted? MSUD genes are expressed throughout the body; how can expression be regulated? How do we insure that the gene, once introduced, will continue to work; and what is the immune response of the body going to be to a new protein introduced into it? The mutant gene will still be present - how will that affect the functioning of the new gene? What will be the method of delivering the new gene into the system? The ever present bottom line is, of course, who is going to pay for the research needed and for the implementation of treatment when, and if, it becomes feasible?

The ideal vector for gene delivery into the body:

1. Should be easy to produce.
2. Should produce no immune response in the patient.
3. Should ensure that the product is continually produced after delivery.
4. Must ensure that it is expressed in the desired tissue (meaning you only want it to work where you want it to work).
5. Cannot restrict the size of the delivered gene.
6. Must be able to enter dividing and non-dividing cells.
7. Must be controlled expression of the gene.

How do you go about putting genes into cells? So far, researchers have used physical means such as electroporation, microinjection and liposomes to introduce the gene. They are now experimenting with viruses.

The non-viral system for gene therapy, naked DNA and liposomes, has the advantage of being inexpensive (relative to other systems), easy to produce, not toxic or immunogenic (having the ability to stimulate the formation of antibodies). However, on the downside, this system is inefficient because the effects don't last, and the procedure has to be repeated again and again.

Using viruses as a delivery system has the advantage of being easy to deliver into the cells and can produce the gene in many cells. Again, the flip side: gene size is limited; some viruses will only infect dividing cells; sometimes hard to produce in large amounts; and they do produce, to varying degrees, an immune system response in the patient.

Several different viruses are being studied for possible use in this way - including the virus which causes the common cold. Each virus has advantages and disadvantages which must be overcome. Some only work on non-dividing cells, some are highly toxic, some have a very short life. The ones that seem to have the greatest advantages, also seem to have the most disadvantages. For instance, the Herpes Simplex virus works in dividing or non-

dividing cells and neurons, but is highly toxic. The cold virus also works on dividing and non-dividing cells but has a very short life and is antigenic (capable of causing the production of an antibody).

The history of gene therapy (from 1980 to 2000) is one of limited successes and spectacular failures. Currently, there are more than 400 approved clinical trials ongoing worldwide. However, less than 15% of these are for single gene traits, the majority being in the area of cancer treatment and cardiovascular disease.

THE PREVALENCE OF ADHD IN METABOLIC DISORDERS

Details

Written by Kay Larsen

Published: 20 July 2009

From the presentation given at the National Coalition for PKU and Allied Disorders Metabolic Conference in Ohio in May 2001.

On Saturday, Kevin M. Antshel, Ph.D., a fellow in Pediatric Neuropsychology, Children's Hospital in Boston, and holder of an appointment from Harvard Medical School through the Department of Psychiatry, spoke to the entire group about the prevalence of ADHD in metabolic disorders. He presented an overview of ADHD, discussed ADHD and metabolic disorders, explained courses of action that can be taken if a child has ADHD, and told about the resources available for parents whose children have been diagnosed with the disorder.

The terminology of the disorder has changed over the years. In the late forties, it was known as Strauss Syndrome, later Minimal Brain Damage, and still later, Hyperkinesis. By the eighties, it had become Attention Deficit Disorder with or without hyperactivity and residual type. In 1987, it was shortened to Attention Deficit Hyperactivity Disorder (ADHD). By 1994, three subtypes of the disorder were recognized - ADHD-Hyperactivity/ impulsive type (ADHD-H), ADHD-Inattentive type (ADHD-I) and ADHD-Combine type (ADHD-C).

There are certain criteria for a diagnosis of ADHD:

1. There must be a persistent pattern of inattention and/or hyperactivity.
2. The symptoms must be present before the age of 7 and have lasted at least six months.
3. The symptoms must have been observed in at least two settings, such as home and school.

4. The symptoms must be severe enough to clearly interfere with developmentally appropriate functioning.
5. The disturbance does not occur exclusively during the course of:
    1. Developmental disorders (such as mental retardation).
    2. Schizophrenia or other psychotic disorders.
    3. It cannot be better accounted for by another psychological disorder such as mood or anxiety disorders.

The symptoms that differentiate the subtypes are:

1. Hyperactivity/impulsivity produces a peculiar behavior pattern where the child
    1. Fidgets and squirms in his/her seat, or just leaves his/her seat in the classroom.
    2. Runs about or climbs excessively in situations where inappropriate.
    3. Cannot play quietly, is always "on the go," or acts as if being driven by something.
    4. Talks excessively and blurts out answers.
    5. Has trouble waiting his turn, interrupts, intrudes on others.
2. Symptoms of inattention displayed by the child:
    1. Seems to make careless mistakes, or doesn't seem to pay attention to details.
    2. Has trouble sustaining attention, and does not seem to listen when spoken to directly.
    3. Fails to finish tasks, and has trouble organizing tasks and activities.
    4. Avoids tasks requiring sustained mental effort, and often loses things necessary for a task or activity (never remembers to bring a pencil to class or leaves his homework at school every day).
    5. Easily distracted by extraneous stimuli, and forgetful in daily activities.

To be diagnosed as ADHD-H, the child must display six or more symptoms of hyperactivity/impulsivity but less than six symptoms of inattention. Again, these must be observed in at least two settings and have lasted for more than six months. More males than females are diagnosed with this condition.

To be diagnosed with ADHD-I, there must be evidence of six or more symptoms of inattention, but less than six symptoms of hyperactivity/impulsivity that have been clearly observed in the two settings and have been present for six months or more. More females than males are diagnosed with this subtype. This diagnosis can be more easily missed because the child usually doesn't cause trouble for anyone (except, perhaps, the mother, who wonders why on earth the child can't remember to put her socks on in the morning). ADHD-I is more likely to be overlooked or diagnosed much later than the other types.

In the combined subtype, ADHD-C, there must be six or more symptoms of inattention and six or more symptoms of hyperactivity/impulsivity present with the symptoms observed in at least two settings and having the requisite duration of six months or more. This is the most common subtype, and the behavior of the child is more likely to cause peer rejection. It is the most common and most frustrating form, because it is the most resistant to treatment. Most children with ADHD-C engage in acts that are considered socially objectionable. Their excesses in behavior result from a combination of high social interest, explosive

temperaments, and an impulsive style. They are often out of sync with the events around them.

ADHD can be inherited and the chances range from 25 to 31% if one parent has ADHD. The chances increase if both parents are affected. Even if a parent has never been diagnosed with ADHD, the child has a greater chance of having the disorder if an aunt or uncle have ADHD.

About 3 to 5% of school-age children in this country have been diagnosed with ADHD, and there are no striking cultural or ethnic differences. It is usually first diagnosed in the elementary school years and is difficult, if not impossible, to diagnose in children under 4 or 5. In fact, Dr. Antshel stated his belief that to diagnose a child any earlier would be very wrong. Almost any two year old, for instance, has behaviors that would be consistent with ADHD. These behaviors are normal for that age, and the child will outgrow them in the normal course of events.

There are certain disorders that are associated with ADHD. These include learning disabilities, Oppositional-Defiant Disorder, and mood and anxiety disorders.

Currently there are only two metabolic disorders considered to be definitely associated with ADHD - PKU and the Urea Cycle Disorders. In PKU there is an area of the brain called the hypodopaminergic prefrontal cortex that appears to be compromised. There is also delayed myelination and structural brain damage caused by high blood Phe levels early in life and a "toxic" effect caused by concurrent Phe levels. Myelin is a fat-like substance, the principal component of a sheath that surrounds the nerve fibers in the brain and spinal cord. It protects the nerve fibers and allows for the conduction of nerve impulses. In the Urea Cycle Disorders, the high ammonia levels can give a presentation of ADHD particularly in the partial defects.

MSUD and Homocystinuria are two metabolic orders that are presently considered likely to be associated with ADHD. In MSUD there is also the phenomenon of delayed myelination, and there appears to be nerve cell loss in an area of the brain called the substantia nigra. Homocystinuria presents with decreased myelination, and isolated cell death occurs in a part of the brain called the globus pallidus. Other metabolic disorders are not, at this time, recognized as being associated with ADHD.

If you suspect that your child has ADHD, check with the school and arrange to have a multi-disciplinary evaluation. Treatment may involve therapy (behavioral and/or family), making academic modifications, medication and continued monitoring.

The bottom line is that *some* metabolic disorders are associated with an increased risk for ADHD and research is ongoing to determine whether there may be more. ADHD is treatable and treatment should be multifaceted. Research continues in new pharmacological and ecological treatments.

Resources are available for understanding and dealing with ADHD. Children and Adults with Attention-deficit/Hyperactivity Disorder (CHADD) is an organization devoted to informing people about the disorder. It can be accessed by mail at 8181 Professional Place, Suite 201, Landover, MD 20785 or on the web at www.chadd.org. *An ADHD Consensus*

Statement is accessible at http://odp.od.nih.gov/consensus/cons/10/110_statement.htm, and *The ADHD Report* is available from Guilford Publications on their web site: www.guilford.com or call 800-365-7006 or 212-431-9800.

MEETING NEEDS

Details

Written by Lou Ann Justus

Published: 20 July 2009

There is a heart-warming story regarding the desire of one family to attend the National Coalition Conference, and the wonderful way the funds were provided. It all began in Florida earlier this year. Lou Ann Justus works for the Scholastic Book Fairs. Twice a year the employees have a book and gift fair. The proceeds from the "extravaganza" are donated to a worthy charity. Lou Ann submitted a proposal asking that the funds from the current fair be given to MSUD. Following is the letter Lou Ann wrote to the employees where she works explaining her family's involvement with MSUD.

Lou Ann's Letter

A cure - how wonderful that would be - is probably a pretty lofty hope at this time. In our day-to-day life we hope to make sound decisions regarding the feeding and care of our daughter. We hope that we will recognize signs of distress. We hope that we can continue to learn more to help us as she grows. We cannot lose sight of the sobering reality that without proper education and excellent management our daughter Katie could lose her battle to maple syrup urine disease at any time . . . with very little notice.

Many of you know Katie, as you have been very supportive in her first two years. She is just one of this small group of spercial children afflicted with this disease. Most stories of the first months of these children's lives are very much like Katie's. They were born perfectly healthy babies and went home with very happy parents. Within a few days, they stopped eating, became lethargic, and in most cases began to have extreme difficulty breathing. Their brain is affected and progressively attacks each of their functions. Most are in intensive care within the first week, dependent on machines to help them stay alive. The long term effects in each case vary dependening on the number of days required for diagnosis. If the children were treated immediately, they would begin to recover and thrive on their own within a short period of time. If diagnosis took longer they would continually worsen as each of their bodily functions were attacked. Extreme brain swelling would usually result in permanent brain damage. Most times if diagnosis took longer than 12 to 15 days, the babies would die.

We were one of the fortunate families. A miracle occurred. It is possible that Katie has a variant form of this disease.

Although Katie was finally diagnosed at 28 days, was completely dependent on machines to keep her alive, and suffered extreme brain swelling, she appears to have suffered no permanent damage. We are also extremely fortunate because most of the children afflicted with classic MSUD are regularly hospitalized for episodes where their diet (protein levels) are out of control. Every normal childhood illness (even a cold) can throw the protein levels into a potentially deadly fluctuation. With each episode, there is an extreme risk of additional brain damage. Again, we have been blessed; Katie has not been in the hospital since she was released at 2, months old.

Maintenance is not easy. Continual education is vital. When Katie was diagnosed, we were devastated to hear that there were no adults with this disease. That evening we learned through the MSUD Family Support Group on the Internet that, YES indeed, there were in fact adults with this disease. A 22 year old was recently married and just announced that she was pregnant. We began to have hope. We are continually in touch with the Support Group as they provide a variety of helpful resources, family stories, helpful diets and tested ways to help children like Katie as they move through each developmental stage. The MSUD Support Group is a nonprofit organization serving many families like ours throughout the world.

Many of the families find difficulty contacting qualified labs and physicians to help in the care of these children. The Clinic for Special Children has been a great source for many families around the world. The Clinic is dedicated to the care of children afflicted with metabolic disorders and serves as a state of the art research facility in finding a cure for these children.
Please help us support these two organizations, so that they can continue to help families like ours around the world.
Thank you from Katie's family,
Lou Ann and Rick Justus,
Christopher and Michael

We applaud the efforts of one of our "family" members, Lou Ann Justus, and the generosity of the employees in the corporate office of Scholastic Book Fairs who raised $5,415 and divided the proceeds between the Clinic for Special Children and the MSUD Family Support Group. We thank you on behalf of all the families in our Support Group.

When Lou Ann called about the donation to our organization, she asked if there was anything in particular it would be used for. Yes; the Ali Akhlaghi family wanted to attend the National Coalition for PKU and Allied Disorders Conference in Ohio. They had asked if the MSUD Family Support Group would have some funds to help them pay travel and conference costs. The Support Group had no funds designated to help families attend this conference as it does for our MSUD Symposiums. The Lord was answering prayers to somehow provide the means for this family to attend possibly the only informative conference they would have the opportunity to attend while in the States.

Lou Ann thought that using some of the money for this purpose would be fine. Ali was notified. What a blessing that money was to one family and the remainder will help others.

The Family From Iran

The above photo pictures Simin Nejabati, holding son Ashkan (MSUD) and Jaime Hamilton, (MSUD) with daughter Hailey (non-MSUD), at the conference. Jaime is 23 and Ashkan is 10 months old.

Let me tell you a little about this interesting family from Iran. Mohammad Ali Aklaghi (a computer programer) and his wife Dr. Simin Nejabati (an anesthesiologist) were living quite comfortably in Iran. Their son, Ashkan was born on July 20, 2000 and soon became very sick. On Sept. 1, I received a fax from them asking about the Total Parenteral Nutrition IV solution which Ali read about on our web site. He also contacted Dr. Holmes Morton at the same time. Ashkan had been diagnosed at about 4 weeks of age. He had been hospitalized for 14 days and repeatedly dialyzed. They knew their child was being mismanaged as he was not improving and had severe diarrhea. Since MSUD is not well known in Iran, all the children who do survive are severely damaged.

Ali and Simin were desperate to get good care for their son. So desperate in fact, when their doctor would not follow Dr. Morton's instructions, they sold their possessions and left their careers in Iran to come to the U.S. with their son. They persevered through a great deal of legal technicalities to get visas. In the meantime, Dr. Morton was able to get amino acids to them via individuals willing to help. They made their own formula for Ashkan and followed instructions from Dr. Morton via fax and e-mail. In November 2000, they arrived in Maryland and soon moved to Lancaster, Pennsylvania to be near Dr. Morton's Clinic.

According to Dr. Morton, Ashkan has done remarkably well. He expects Ashkan will meet the normal milestones in development and his speech and intellectual function will be good. Ali and Simin are eager to meet other families and to learn all they can about MSUD. Following is the thank you note Ali wrote to Lou Ann.

> Dear Lou Ann Justus:
> I would like to express my deep appreciation for the donation you and the employees made to MSUD Family Support Group. Your donation made it possible for me and my family along with our only son with MSUD, to attend the Metabolic Conference held in Dublin, Ohio May 4-5, 2001.

We learned a lot about MSUD and met families with the same concern. I would particularly mention a lady with classic MSUD who had gone through pregnancy and has a perfectly healthy baby girl. I was impressed and encouraged as well to see how well these patients can do provided the disease can be well controlled and managed.

We gained knowledge of (1) MSUD: the disease, its management, relevant current studies (2) the diet including the available products (3) prevalence of ADHD in metabolic disorders (4) federal legislation for metabolic formulas and (5) the Scott C. Foster Metabolic Research Fund.

We came from Iran on Dec. 10, 2000 to save our 9-month-old son with MSUD. With the great help of Dr. Morton from the Clinic for Special Children and the MSUD Support Family Group, we have our son in normal condition and development. Otherwise he would have become profoundly mentally retarded and physically disabled.

If the donations were not made, organizations such as the MSUD Family Support Group and the Clinic for Special Children could not exist. I would like to thank you again and wish you and your families the best. I would also like to thank the MSUD Family Support Group for the help and support they have provided for us. And special thanks to Dr. Morton for his great help since we left Iran, without which Ashkan would certainly not have survived. May the grace of God be with you all.

Sincerely yours,

Ali Akhlaghi

BRITNEY'S JOURNEY TO PARADISE

Details

Written by Laurie Page (Britney's mother)

Published: 20 July 2009

Our trip to paradise was more than a vacation. It was an experience of a lifetime that has given us memories to cherish forever. The trip was a gift to Britney from her Grandpa and Grandma Turner. They have watched her fight for her life for the last eight years and want to make sure she also experiences the joys of life. What better place than Hawaii?!

Britney has MSUD and has been hospitalized several times since she was born. Last year she was in a coma three times. It has been a tough battle for her, but she has a strong will and refuses to give up. That is why her grandparents chose Hawaii, the most beautiful place on earth.

Originally Grandpa and Grandma were going to take her, but circumstances did not allow Grandpa to go, so I went in his place. It was a trip for us girls - Grandma, Mom, Britney and 2 year old Amanda. We had a blast!

Preparing for the trip was quite a bit of work, but it was well worth the effort. Grandma made all of the phone calls to plan the trip which included making arrangements with the airlines for a vegetarian meal for Britney. The airlines idea of a vegetarian meal was pathetic. We were prepared, as most of us are, with plenty of just in case food.

I pre-measured Britney's formula and packed it in zipper bags. We split the bags between our two carry-on bags - boy were they heavy! We were concerned that security would give us a problem at the airport when they X-rayed our bags and discovered all those bags of white powder, but they didn't. The guard insisted on running a special paper over the bags, then sent us on our way.

We needed to know where the hospitals were and what doctors to contact if Britney were to become ill. The Pediatric Neurology Clinic staff at Ann Arbor, Michigan gladly provided us with all of the information we needed. Dr. Allen provided a letter with detailed instructions for the doctors in case of an emergency. I don't know what I would do without the Clinic staff. They are fantastic people who go beyond the call of duty and then some.
When we stepped off the plane on Oahu, we were greeted with beautiful, fragrant leis. This was a wonderful beginning to a twelve-day adventure that would take us to four of the Hawaiian Islands.

Our first three days were spent on Oahu. The hotel we stayed in was on Waikiki Beach. Our first outing was to the Polynesian Cultural Center which is on the North Shore, as they call it. The drive there was incredible. The road twisted and turned along the shoreline which

has the most beautiful white sand beaches and the most brilliant turquoise water in the world. The Cultural Center was divided into areas depicting the different areas of Polynesia with demonstrations of activity indigenous to that culture. In the afternoon they have a parade of boats carrying singers and dancers representing different Polynesian tribes.

Britney was completely mesmerized by all of it. In the evening they have a Luau with several ceremonies and more singing and dancing throughout dinner. We informed our waitress that this was a special trip for Britney. She, in turn, told the entertainers who dedicated a song and hula about children to Britney. We cried through the whole thing. The next day we went to Pearl Harbor. That was definitely an experience. To stand over the spot where 1,000 men lost their lives for our country was heart wrenching. It's a place no one should miss if they go to Oahu.

The next island we visited was Kauai, the flower island. How beautiful. We visited Fern Grotto and Waimea Canyon (the Grand Canyon of Hawaii). The views were breathtaking. An interesting phenomenon on Kauai is that several years ago they experienced a hurricane that displaced all of the island's domestic chickens. The island now has wild chickens everywhere which just fascinated both girls.

Every evening our hotel had a traditional Hawaiian sunset ceremony with singers and hula dancers. Grandma had bought the girls grass skirts, and they decided to wear them to the ceremony one evening. One of the hotel employees saw the girls and brought them each a gorgeous fresh lei. When the singing and dancing began, Britney and Amanda got up and did the hula (pictured) along with the dancers. They received a great round of applause from the audience.

We next moved on to Maui. Our first stop was the Maui Ocean Center which has many different types of marine life as well as a huge glass area that is built out into the ocean where the girls loved watching the fish swim around us. The following morning Grandma and Britney went on a submarine trip. The submarine is launched from a platform a mile from shore, so they had to take a boat to the area. The captain sought Britney out and had her sit in his seat and drive the boat on the open ocean. She thought this was just great.

The next day, we went on a snorkel trip with the Pacific Whale Foundation. Several spinner dolphins swam around the boat jumping out of the water and spinning around. The marine biologists on board made Britney an Honorary Marine Biologist and had her help them set up things for the snorkel, which she and I did together. What a great experience. I had no idea how colorful the fish and coral are.

We left Maui and flew to our final island, Hawaii, the Big Island. This was to be the climax of our trip. The main reason we were in Hawaii was so that Britney could swim with the dolphins. The Hilton Waikoloa houses Dolphin Quest which is a research habitat to save the dolphins. Grandma had made prior arrangements, and we took an excited Britney down to the area for her dolphin swim. A marine biologist supervises the swim and gives instructions about what to expect and what to do. He handed out pieces of fish and had the children feed them to the dolphin. Britney went out into the water and splashed the dolphin who splashed her back. Then she kissed the dolphin (pictured) and rubbed his belly. The biologist gave Britney another piece of fish and a big red ball. He told her to throw the ball to the dolphin and that the dolphin would throw it back to her. Then she was to feed the piece

of fish to the dolphin, but if she did not catch the ball, she was going to have to eat the fish piece herself. She threw the ball, the dolphin threw it back, and she dropped it. The biologist told Britney she had to eat the fish. She looked at him, then at us, and replied, I'm not allowed to eat fish.

We had been laughing and crying through the whole experience, but now we didn't know whether to laugh or cry. The biologist told her that was okay, he was only kidding. She continued to play with the dolphin, swimming, splashing and having a great time. The whole experience was being professionally photographed and videotaped so we will have it forever.

The next day, we boarded a helicopter to fly over an active volcano and see the destruction it has caused. Most of what is visible is the black, dried lava top crust. The flowing lava is not usually visible, but we were lucky enough to witness a sky light that had opened, and to see the red/yellow lava as it flowed to the ocean enlarging the island by inches every day. As the helicopter pilot told us, You are witnessing the newest land on earth. The helicopter ride was our last great adventure in Hawaii.

As we boarded our plane for home, we bid a fond Aloha to Hawaii. What a wonderful experience for all of us, but especially so for Britney. We had no need for doctors, but a great need for tissues to dry our tears as we watched her laugh and sing and dance. We encountered some pretty wonderful people who went well out of their way to make sure Britney had an enchanting trip to paradise.

CROCHETED BABY BOOTIES & NEWBORN SCREENING

Details

Written by Joyce Brubacher

Published: 20 July 2009

Richard & Deborah Hamburg's son Christian was born August 7, 1967 in Arkansas and died October 17, 1982 in California. Born a seemingly healthy 9 pounder, he was taken back to the hospital 48 hours after leaving it. Christian was about one month old when he was sent to the University of Arkansas Medical Center where he was diagnosed with MSUD. Christian had slipped into a coma and suffered irreversible brain damage before he was diagnosed at about one month of age. The cause of his death at the age of 15 was a brain aneurysm.

Now his mother Deborah is spreading the message of newborn screening with a pair of baby booties - yes, a crocheted pair of baby booties. Deborah wears them pinned next to her heart. She knows a great deal about crocheting as Product Development Coordinator for Annie's Attic, a nationally known publishing company where she is responsible to acquire crochet designs for both Annie's Attic and The Needlecraft Shop. Deborah also knows about newborn screening. She has become involved with the Tyler For Life Foundation and its advocacy for screening newborns. Annie's Attic has published a crochet pattern book called Pretty Baby Booties which contains Christian's story and information about Tyler For Life.

When someone comments on the baby booties, Deborah uses the opportunity to tell them about the simple blood test that can save babies from the devastation of MSUD and other inborn errors of metabolism, and how her son might have grown up to become what he wanted to be - a disc jockey - had he had the newborn screening test at birth. So Deborah passes out the tiny pairs of booties along with information sheets about newborn screening. She is making an effort to keep others from going through the intense pain and sorrow she experienced with her child.

You can help prevent this pain and sorrow in the lives of other parents. Visit the web site of the Tyler For Life Foundation at www.TylerForLife.com. You will find information on your state's current testing program and information about being an advocate for newborn screening. Deborah Hamburg found a unique way to spread the word. We can all do our part by telling those around us of the availability of screening for all infants for 30 diseases for a small fee of $20. Check our MSUD web site for information on supplemental screening or call NeoGen Screening, 412-341-8658, or Baylor University Medical Center, 214-820-4533.

For more information on the crocheted booties, e-mail Mrs. Hamburg at deborah_hamburg@needlecraftshop.com

SANSE'S GALLBLADDER SURGERY

Details

Written by Patty Swenson

Published: 20 July 2009

This is a summary of what happened when our daughter, Sanse L. Swenson developed gallstones and had her gallbladder removed just recently. Sanse, who is 30 years old, resides in Denver, Colorado and has classic MSUD.

The day after Thanksgiving 2000, Sanse woke up early in the morning with severe abdominal pain. She could not lie down or find any comfortable position for about three or four hours. This was about the third time she had a episode similar to this in the past several months. On one of these occasions, we rushed her to the emergency room, and although many tests were taken, they could not determine the cause of her discomfort. I felt it was time to take Sanse in again for an evaluation.

We made an appointment with a physician at Kaiser Permanente (Sanse's HMO) for a consultation. The doctor thought she either had an ulcer or hiatal hernia and prescribed a medication for an ulcer. He did recommend that Sanse have an ultrasound to further check out the cause of her discomfort. After waiting for the appropriate appointments, an ultrasound was scheduled.

On Christmas eve, we received a telephone call from the doctor stating that Sanse had gallstones, and we needed to make an appointment with a surgeon. After the holidays, (January 2001) we scheduled an appointment with the surgeon at Kaiser. He was a delightful doctor, and assured us that he had removed many gallbladders. It would not be a problem - but, by the way, What is maple syrup urine disease?

We proceeded to tell him about MSUD and the metabolic complications. We were impressed with the surgeon because he asked, What is MSUD? and Who can I talk to in order to learn more about this disease?

I told him about the Inherited Metabolic Diseases Clinic (IMD) located here in Denver and also about Dr. Holmes Morton and the Clinic for Special Children. The present staff at the IMD Clinic in Denver had never been involved in a surgery for a MSUD patient. They were extremely busy, and the doctor did not return my telephone calls.

The Kaiser surgeon asked if it would be okay to call Dr. Morton. I told him I was sure Dr. Morton would discuss what was necessary for surgery involving MSUD. I immediately came home and faxed a letter to Dr. Morton. I told him about Sanse's problem and about the visit we had with the surgeon.

Within an hour, Dr. Morton called me back. He said it was interesting to hear about Sanse's gallstones because he had been discussing possible causes of gallstones in MSUD patients with a colleague that day.

Dr. Morton asked what Kaiser and Colorado were prepared to do to take care of Sanse during the surgery. I told him I don't think they know what to do. So the next day our Kaiser surgeon and Dr. Morton talked over the telephone. Our surgeon called us and said, It is in the best interest of your daughter to go to Pennsylvania for this surgery.

Dr. Morton was so kind to invite us to come. So the process began for approvals and making arrangements to go to Lancaster for Sanse's surgery. We were so thankful!

The surgery was set for February 7, 2001. We were all scared about facing surgery, but we knew we would get the very best medical care in the world. So we were thankful, but with tears running down our faces at the same time. What would happen?

Just before leaving, we had Sanse's blood levels run. They were the highest I had recorded since 1985. We knew we were in trouble. The valine was 388 µmol/l, the isoleucine was 189 µmol/l and leucine 1163 µmol/l. I think Sanse's levels were high because of the tremendous amount of stress and perhaps the diseased gallbladder.

Dr. Morton called that evening and said the leucine had to come down prior to surgery. Dr. Morton asked what our sick day regimen was. I told him we didn't have one. The only thing we knew was to push high caloric liquids, give bicarbonate of soda (if needed) and cut back on protein intake.

Dr. Morton gave us a recipe to make Sanse's formula which included increasing the grams of dry formula mix by 80 grams for a total of 200 grams, adding 50 cc of isoleucine and 60 cc of valine and increasing the water by 22 oz. The prescribed amounts made a total volume of formula of approximately 34 oz. (We had tried the valine and isoleucine supplements a number of years ago, but we must have done something wrong, because it did not work at that time.)

On Saturday, February 3, about noon, Sanse began drinking the formula made up according to Dr. Morton's instructions. She consumed her usual low protein diet. We left for Philadelphia on Monday morning, February 5. We went to the Clinic for Special Children on Tuesday. To our amazement, after 36 hours on the sick day regimen, Sanse's leucine levels had dropped 626 points to a leucine level of 537 µmol/l! We were absolutely amazed and thrilled. We had never experienced seeing Sanse's levels go down so far, so fast, and so easy. She wasn't even hooked up to an IV.

Sanse was admitted to the hospital on Tuesday, February 6, at approximately 4 p.m. Dr. Morton said he wanted to bring the levels down even lower to prepare Sanse for surgery. The nursing staff on the pediatric ward started the IVs according to Dr. Morton's instructions. Sanse had a light meal about 5 p.m., the evening prior to the surgery. Approximately 14 hours after Dr Morton's special TPN blend IVs were started, Sanse's leucine level was 42 µmol/l! We knew an absolute miracle had transpired before our eyes. In four days time, Sanse's levels went from 1163 to 42 µmol/l.

Sanse's laparoscopic gallbladder surgery was performed by Dr. Daleela Jarowenko about 8:30 a.m. the next morning, February 7. Dr. Jarowenko met with us after the surgery and told us the gallbladder was very inflamed and contained large gallstones. We were able to see the gallstones after surgery. They appeared to be about the size of olives, and there were at least six of them. Dr. Morton sent the gallstones to New Jersey for research.

After the surgery, Sanse did not vomit. Every time she had been in the hospital previously, we held the vomit tray under her chin most of the time. That was always a very bad sign - vomiting and then seizures. Scary! But not this time.

On Thursday after the surgery, what would her levels be with the trauma of surgery? Sanse's leucine levels were 99 µmol/l! On Friday, Sanse was dismissed from the hospital and her leucine level was 211 µmol/l. On Monday, we went to the Clinic for Special Children for levels. Sanse's leucine levels were 657 µmol/l. She burst into tears because the levels had gone up. She was reassured that it was okay.

Dr. Morton explained to Sanse the reasons why her leucine levels need to be much lower than they have been previously The levels for adults should range between 200 to 500 µmol/l [2.6 to 6.6 mg/dl].

Sanse understood Dr. Morton's explanations, and she is really trying hard to maintain much lower levels. Some of the things Dr. Morton taught Sanse were:

1. The high leucine levels block the other needed amino acids in her brain.
2. The lower leucine levels
3. Will help her to think better.
4. Will help prevent her mood swings.
5. Will help her sleep better.
6. Should help her hair to thicken. (Sanse's hair had become quite thin.)

On Wednesday, we went back to the Clinic. Sanse's leucine level was 432 µmol/l. Sanse was smiling again. More learning. The staff at the Clinic for Special Children was so kind and accommodating to us. The rural setting was so comfortable and comforting.
We went back to the Clinic for the last time on Friday, February 16. Sanse's leucine level was 406 µmol/l - another cheer!

We had heard about other parents using DNPH, but we had never been able to obtain it in Colorado. We asked Dr. Morton about DNPH, and he taught us how to use it and how to evaluate the results. It has really helped us to gauge Sanse's levels between blood tests. I hope we can obtain some DNPH in Colorado when we exhaust our supply. The DNPH does not replace the blood tests.

Sanse has been doing a great job of keeping her levels down since returning. There have been some days when they have elevated, but we have DNPH to help us see the degree of her elevation, and we use either well, modified, or sick day regimen.

Sanse has classic MSUD and our concerns and the management of this disease are not over, but we have learned so much from Dr. Morton it has been life changing. Sanse's levels still go up with stress, diet and illness, so it is not an easy path to follow. We know God will provide us with the strength we need for each day.

We are so very grateful to the Clinic for Special Children and especially to Dr. Morton. He has been a real blessing to so many families dealing with MSUD. We thank him so very, very much.

LAURA FROM BRAZIL

Details

Written by Giovanni Medeiros

Published: 20 July 2009

On July 17, 1998, Laura Brito Medeiros, our first daughter, was born. For us, a present, an expectation! Delivered by Caesarean childbirth, she weighed 3,780 kg [8.3 lb.] and measured 49 cm [19 in.] in length and seemed healthy. The first days of her life, she was fed mother's milk and baby formula (NAN 1).

About the fifth day, Laura started to exhibit a different behavior, characterized by irritability, vomits, inquietude, lack of appetite and sleepiness. So we sought a pediatrician in our city - Caic - /RN. This doctor suspected a urinary infection because of finding a strange scent in the urine. The result of the urinary exam was negative for infection. Laura's clinical picture became worse every minute.

At another doctor's opinion, we decided to take Laura to another city, Natal/RN. There the doctors have a larger patient load [more experience], more medical resources, and a hospital of superior quality. During this trip, approximately 300 kilometers, Laura presented convulsions. Upon arrival, she was admitted to UTI [ICU] showing sharp dispnéia, then she stopped breathing. Our daughter was maintained on a respirator for four days.

The medical team requested many exams, besides a screening test. When we received the results of the exams, Laura was already fifteen days old and had spent nine of those in a coma. The result of the chromatography of amino acids was the following: L-leucine: 2.083,5 µmol/L [27.3 mg/dl]; L-isoleucine 107,4 µmol/L [1.4 mg/dl]; and L-valine: 584,3 µmol/L [6.8 mg/dl] indicating that Laura had MSUD.
For us and for the medical team, it was a challenge; none of us had experience working with MSUD. One of the doctors on the team remembered that six months ago, another child (Jo V'tor) had the same diagnosis. We contacted the Fernandes family, and by phone learned about the geneticist, Dr. Ricardo Pires, who guided the medical team.The first procedure was completing peritoneal dialysis for 48 hours followed by glicoinsulinoterapia [insulin therapy]. We had access to formula - MSUD diet powder (Mead Johnson). We knew practically nothing about the disease, nor how to work with it.

At forty days of age, Laura left the hospital, but she vomited daily. We sought a gastric doctor who diagnosed hiatal hernia and began treatment with cisapride. During her first year of life, Laura had been hospitalized several times.

We still did not know how to work with the disease. It was through the Internet that we began to have access to information, not so much with Brazilians, but with foreigners. We began to learn about the disease through them.

We were always worried about Laura's health. Initially, following a neuro-pediatrician's instructions, Laura began a program of therapy. It consisted of strenuous stimulation for the invigoration of muscle tone, correct posture of the head, coordination for grasping and holding objects, and motor skill development.

When Laura reached eighteen months, she began to walk, achieving her freedom. Her speech began to be expressive by two years and four months. Today, Laura, is two years

and eight months and attending [nursery] school. She has been continuing reinforcement therapy since she was twelve months old.

Laura is an extremely affectionate child. And every day we have more certainty that she will have a better future, if God wants.

Our participation in the MSUD Symposium 2000 was very profitable. We learned a lot about the disease and how to work with it. The support that the MSUD Family Support Group has been giving, especially the Brubacher family, is something we don't know how to say thanks for.

Another important point of Symposium for us was making acquaintance personally with Dr. Morton and his teachings. It was a great learning time for us. We intend to attend the next events. And now we receive daily news through the MSUD eGroup. All this has been very gratifying.

A hug for all our MSUD friends from Laura, Aninha and Giovanni.