

## October 1999 OAA Newsletter

### Editorial

*by Kathy Stagni*

It's fall again, and it seems to come faster every year. Melissa is settling into her new school and has made new friends, so all in all it's been a good change.

I am happy to again share family stories, and thanks to the internet, I am always amazed when I hear from families and physicians across the world. We are highlighting Isovaleric Acidemia this issue with an article from Dr. Jerry Vockley from the Mayo Clinic, as well as a couple of articles from Isovaleric patients. I hope you find these and the rest of the articles interesting.

I had the privilege to visit Dr. Charles Roe and Dr. Larry Sweetman at the Institute for Metabolic Disease in Dallas Texas in September. I toured the facility and received a tremendous education on the type of work being conducted there. I was most impressed with the Tandem Mass Spectrometer and how it operates to detect up to 30+ metabolic disorders.



The Institute is currently doing all screens for Baylor Hospital in Dallas and supplemental screening for various states. I also met with Diane Roe, another scientist (and Dr. Roe's wife) who gave me an overview of the Branched Chain amino acid structures and a tour of the lab where cells are cultured (fibroblast) for diagnosing new rare metabolic disorders.

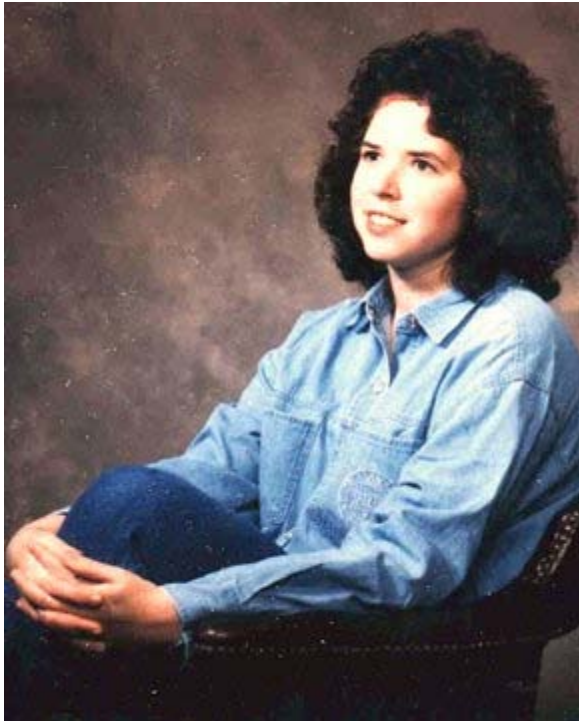
The Institute has created an Advisory Board that I have been asked to join. The mission of the Institute is to help families and children affected with metabolic disorders. Various other board members are undertaking fundraising activities for the Institute, mainly in the Dallas area.

What else is happening with OAA? Well have you had a chance to check out the website lately? We have revamped the questionnaire, and I also have taken a web design class and designed some of the web pages. I want to thank Kathy Kokkila from Comtrol Corporation for assisting me in keeping and maintaining OAA's website. If there are any members who want to help out with the website, please let me know!

We will be contacting the physicians on our Medical Advisory Board after the first of the year to make sure they would like to continue on our Board. Have a safe, healthy and warm holiday season!

# Audrian Ward

## *Isovaleric Acidemia, Age 23*



My name is Audrian Ward. I am 23 years old and have Isovaleric Acidemia (IVA), one of the more rare, genetic disorders. I was finally diagnosed when I was five years old, but by that time I had developed a unique, difficult to control seizure disorder which my neurologist believed to be a result of my chronic acidemic condition. I have since "outgrown" my seizure disorder, received a BA in English Literature, and am gainfully employed as a technical writer. However, I still have to drink my "formula" every day, and I must admit that I am not always as vigilant about drinking it as I want to be. Because my disorder is so rare and I do not have a support group, I too often ask, "Why me?" However, this past summer, I learned of a program that had been instituted by Emory University in Atlanta, Georgia four years ago.

The program is a weeklong summer metabolic camp designed for girls and young women. The original vision of the camp was to include all women with metabolic disorders. It has historically served Phenylketonuria (PKU) and Maple Syrup Urine Disease (MSUD) patients. In keeping with the vision, Dr. Rani Singh, the camp director, made a place for me this past June, the camp's

fifth year of operation.

To begin with, I was uncertain about the camp because I was using vacation time in order to go. However, in retrospect, I am very glad that I participated in the camp. Yes, I was the only IVA patient there, but all the girls and young women had so much in common that I started to see my own disorder in a more positive light.

We learned things such as the importance of drinking our formula and how to make low protein foods. We also discussed pregnancy and the impact it would have on us and what kinds of things we would need to do in order to have a healthy baby. We learned about the newest theories, developments, and research that is going on in the field of genetics. Not everything was just education though. We talked, played, watched movies, and visited several places of interest in the Atlanta area such as the Fernbank Museum, Stone Mountain, and White Water. We even went to Lenox Mall on a shopping spree.

As camp director, Dr. Singh envisions a camp that can include all organic disorders. Currently, the camp has a limited staff and is geared to PKU and MSUD patients. However, next year she would like to include more girls with IVA. If you are a girl or young woman with PKU, MSUD, or IVA who is at least ten years old and self-sufficient, then this camp is for you. You will meet other young women with similar disorders, and you will not feel alone with your genetic condition. For more information please contact Karen Crawford, metabolic camp coordinator, at Emory University in Atlanta Georgia - phone number (404-727-5651).

**Audrian Ward**  
4903 Champman Street  
Columbus, GA 31907

# Katie Foster

## *Propionic Acidemia (PA), Age 17*



December 13, 1998...Katie had a grand mal seizure. The seizure activity in her brain wouldn't stop. She was in a drug induced coma for 4 weeks. She was taken from Duluth to Minneapolis where a doctor tried a Propofol drip overnight. The next morning the drug was stopped and she woke up and I had my Katie back. Four days later she was home. She was weak and couldn't walk by herself, had no balance and kept falling down. Two weeks later she was back in school and back to swim practice. Katie is a member of the Proctor Special Olympics Swim Team.

On April 17, 1999, Katie won 2 Gold medals and 1 Silver medal at the Minnesota State Swim competition. I was so proud and thrilled. She has come a long way. Katie is also a member of the Proctor Special Olympics bowling team, which I coach. We had 10 team members this year and 6 kids went to state competition last November. I love being part of Special Olympics. The smallest thing, like knocking

down one pin or reaching the end of the pool in a race can make an athlete so excited.

This year, for the first time, our school acknowledged our athletes with a school send-off to state, complete with pep band, speeches, banner, flowers and balloons. The team got their picture in the yearbook. Regional and state competitions are always exciting for the athletes. They make new friends, receive awards for their hard work, have a great dinner and dance, and even get entertained by Elvis!

The world can sometimes be a cruel place for our kids. Special Olympics can build up their self-esteem and put them in the spotlight, if only for a short time. Get involved in your area, you'll be glad you did.

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# Adam Fulton

## *Long Chain 3-Hydroxyacyl CoA Dehydrogenase Deficiency, (LCHAD)*



Adam's story was first published in the OAA and FOD Newsletters in 12/93 and 6/95 respectively, and an update was published in both newsletters in 1996. It is hard to believe that he is now 8 years old. At the end of our last story we were starting to be concerned about long term effects of LCHAD.

Adam can only use a very small portion of the fat in his system for energy. He must eat frequent meals high in carbohydrates to supply most of his energy needs. If his carbohydrate supply becomes depleted or his system is under some type of unusual stress, his body will try to metabolize fat for energy. Since he does not have the enzyme to convert the fat to energy in the mitochondria of his cells, toxic substances are produced instead of energy. If this state is not quickly alleviated, his muscle tissue begins to break down in an attempt to provide an alternate energy source. The extreme symptom of this metabolic crisis is Myoglobinuria which is the breakdown of muscle tissue to such an extent that it can be measured in the urine. Since our last update in 1996, Adam has suffered many Myoglobinuria attacks which have resulted in hospitalization from 2-6 days.

There are several reasons why Adam develops Myoglobinuria. If he has even a slight viral infection his body seems to try to metabolize more fat than his cells can cope with. This also happens when he has a bacterial infection, or with any metabolic stress such as exercise, sunburn, altitude, cold or hot temperature or even emotional stress. Adam's body is very sensitive to dehydration and any of these metabolic stress situations can sometimes be reversed before myoglobinuria occurs if he is flooded with fluids. Under metabolic stress we give him 6-12 oz. per hour of fluids to rehydrate him.

The first sign we have that Adam is in metabolic stress is when he claims to have "hurty legs". This is severe aching in his legs that usually begins in his calves and works quickly up to his thighs and other parts of his body. Sometimes the onset of these symptoms is extremely sudden and very severe. Once, for example, we spent about one hour on a sunny but cool and windy afternoon at the ocean. After about an hour we went to a restaurant. Adam's legs began hurting as we seated ourselves. Although he drank some fluids, by the end of the meal he had severe muscle pain in his legs, arms, neck and chest. He complained it hurt to breathe and talk. At home we continued to hydrate him and he overcame this incident without hospitalization!

We are quite frustrated by the seemingly random "hurty leg" attacks that he gets. Sometimes when we expect them, they don't occur, and other times, out of the blue, he gets sick. This is very difficult for us, and even though we try to monitor his activities constantly, sometimes all of our attentiveness fails. We would very much like to hear from other people who cope with LCHAD and other diseases of fatty acid oxidation. We are concerned that if Adam's muscle tissue is so frequently breaking down, it is becoming weaker.

At this time we are particularly anxious because after a 15 minute aerobic exercise session at Occupational Therapy Adam complained of "hurty legs". One week when he was complaining particularly frequently I took him in for a CPK (liver enzyme) test to determine if his muscle tissue breakdown was worsening. We don't usually run to the lab for tests every "hurty leg" episode, but since it was the beginning of a 3 day weekend, I wanted to find out if he needed to be hospitalized while we could still communicate with his doctors. I don't know what the normal CPK is for Adam, but when he has been hospitalized before it has gone as high as 165,000 (normal CPK is about 0-100). Does anyone else have many unexplained incidents of "hurty legs" in their fatty acid oxidation children? We think some of Adam's attacks are just caused by sore muscles from exercise, but how do we tell the difference?

Another long-term LCHAD deficiency result is pigmentary retinopathy, which is gradual pigmentation changes in the retina causing severely impaired vision. Since 1996 Adam has been participating in a study through the Waisman Center at the University of Wisconsin, Madison, which provides DHA, a component in fish oil that is needed for retinal health. Taking fish oil directly would be bad for children with a severely fat-restricted diet. Martex Pharmaceuticals has taken the DHA out of the fish oil so fat-restricted diets can still have an essential element. Since abnormal retinal pigmentation was first observed in Adam's eyes in 1995, no further changes have occurred, and his vision is still within the normal range.

We know the least about the long-term LCHAD side effects of peripheral sensory-motor neuropathy. We only know about what we have read in research papers. From our understanding, this involves a gradual lessening response of sensory nerves and possibly skeletal muscle. Adam is a little delayed in gross and fine motor coordination which may be attributed to his first severe LCHAD episode when he did lose some muscle mass. We would be very interested in discussing this LCHAD symptom with older LCHAD patients or their doctors.

Adam has come a long way from the very sick 5 month old baby in May 1991. It is very encouraging that with a few modifications of diet and exercise he can do so well. We try as much as possible to let him be a "normal" little boy. He doesn't play soccer like his brother, but he does play baseball, is on a summer swim team, rides his bike, rollerblades, and participates in children's theater. His favorite activity is watching the Disney Channel while dressing up in costumes and making huge messes in every room where he is playing. We don't completely ban him from all very high fat foods. We let him try them so they won't be an enticing "no-no", but we always try to educate him as to what he can and can't eat and how much of each. He is allowed 20 grams of fat a day or 10% of his diet. We sometimes wonder about this because Adam is chubby. Maybe he is eating too much fat or just too much food. His favorite foods are Sushi (not raw fish but rice sometimes with fish on it), and plain white rice with Teriyaki sauce. There are so very few LCHAD individuals older than Adam because most his age and some even younger have died of severe LCHAD complications or weren't treated properly soon enough. We really don't know what Adam's long term prognosis is or what new problems may result as he grows up. We would like very much to talk to any LCHAD families, particularly those with older children, and LCHAD adults.

**Don and Valerie Fulton**  
**6594 Skyfarm Drive**  
**San Jose, CA 95120**  
**408-268-6818**

# Columbia University: Cardiomyopathy Update

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In previous newsletters, Dr. Bergmann has stated his need for patients with deficiencies of fatty acid metabolism to participate in a PET Scan study at Columbia University in New York City. Adam participated in this study in May 1998. Our family wants to act as a spokesman for this very necessary study analyzing the process of fat metabolism in the hearts of children with defects of fatty acid oxidation. It is very difficult for Dr. Daphne Hsu and Dr. Steven Bergmann to get participants in their study because most children who frequently have to experience invasive procedures aren't willing to voluntarily participate in yet another medical procedure. Adam may be an exception, but most medical procedures are no big deal to him. Maybe this because he has gone through so many, or maybe it's just his personality.

For Adam, the PET scan was really a simple test and Dr. Bergmann was wonderful in bringing us in the day before to explain the procedure and he let Adam 'play' with the equipment. Basically all that must be done is an IV administered with a very low radioactive solution and then the patient lays in a tube-like machine (like an MRI), while the metabolism is studied (about 1 hour). Adam fell asleep during the test. All he commented on was that his back became sweaty.

We stayed several days at Columbia University's expense at the beautiful Ronald McDonald House in New York City visiting such sites interesting to 7 year-old Adam as the Statue of Liberty, World Trade Center, Central Park, riding subways and taxis and of course, the plane ride there. Actually this turned out to be one of our favorite vacations and Columbia University was very kind to cover most of the expenses.

Any questions about the test from a parent's point of view you can call us:

**Don and Valerie Fulton**  
**phone: (408)268-6818**  
**[vallchadmom@yahoo.com](mailto:vallchadmom@yahoo.com)**

# Jacob Sachs

*(as told by his physician, Dr. Helmut Niederhoff)*

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Dr. Niederhoff from Freiburg University Hospital in Germany, wrote to OAA wanting to share this story of a patient that was recently diagnosed with Isovaleric Acidemia using the Tandem Mass Spectrometer, the newborn screening equipment necessary for early detection.)

This male infant by the name of Jakob Sachs was born on August 21, 1998. The routine general newborn screening for hypothyroidism and treatable inborn errors of metabolism was done on August 25 (5th day of life), the Guthrie-card with dried blood spots being sent to the Heidelberg University Children's Hospital screening lab. This lab, by the way, was set up in the late sixties by Professor Horst Bickel, one of the pioneers of the dietary treatment of PKU. That's why the Heidelberg lab has become the screening center for the state of Baden-Wuerttemberg to which Freiburg belongs. As a sort of further innovation this screening lab in Heidelberg started in 1998 to feed their tandem mass spectrometer with dried blood spots from the general newborn screening, in order to detect not only PKU, but also organic acidemias, before the baby becomes sick.

Prior to that, gas chromatography and mass spectrometry (GC-MS) had been used in the Heidelberg University Children's Hospital for selective screening in infants showing signs of a metabolic disease. This, however, is being done by several labs in our country, including our Freiburg University Children's Hospital.

The Sachs baby happened to be the first case of Isovaleric Acidemia (IVA) detected by this new routine of the Heidelberg lab. Thus Jakob and his mother were transferred on his 11th day of life from their maternity ward to our Children's Hospital in Freiburg. We confirmed this inborn metabolic disease by GC-MS while the newborn was still in good shape: a mature boy who did not show any sign of IVA other than the lab findings including an already slightly elevated value of blood ammonia!

That means, our therapy came just in time. Reduced intake of protein, particularly of its essential component leucine, supplemented with carnitine and glycine in order to support effectively the excretion of increased amounts of isovaleric acid and related metabolites. For these are the products which cause the untreated child's serious metabolic trouble, since the genetic defect of IVA is located in the pathway of leucine break down.

Within a few days we got Jakob on his special, calculated diet. At time of discharge mother gave 300 ml of her breast milk that was mixed with another 300 ml of a leucine-free amino acid mixture supplemented with vitamins, essential minerals, and trace elements per day. The blood ammonia level returned promptly to normal. Urinary organic acids and blood amino acids were kept within tolerable limits.

The hospital stay lasted only 7 days and no further admission to any hospital has been necessary so far. Minor illnesses at home have been handled by dietary adjustments. Jakob is now 12 months old. His development is quite normal and his growth curve is following the lower percentiles of normal.

Prerequisite for this favorable course, however, was teaching the parents all they have to know about IVA. They have been trained to cope with times of malaise and intercurrent disease with and without fever being supported by communication with our specialized pediatricians.

## **Cost Benefit Analysis**

*(according to hospital days in the Freiburg University Children's Hospital)*

Early diagnosed organic acidemia versus late diagnosed organic acidemia due to Tandem-MS (Example: Jakob Sachs with IVA):

Hospital Stay:	7 days
Subsequent admissions:	None
Outcome:	Normal development with special diet
Total of hospital days:	7
Costs per day:	US \$546.00
Total Costs:	US \$3,824.00

Late diagnosed organic acidemia due to clinical signs (a former infant with IVA):

Hospital Stay:	38 days
Subsequent admissions:	5 times with a total of 32 days
Outcome:	Moderately handicapped child with retarded development inspite of special diet.
Total hospital days:	70
Costs per day:	US \$546.00
Total Costs:	US \$38,242.00

In addition to this one has to add the costs for special rehabilitation by physiotherapist, etc.

You may also take this letter or parts of it as a contribution to the OAA newsletter. I asked Jakob's parents for permission beforehand.

I wish you all the best for continuing your work!

Yours sincerely

Helmut Niederhoff, M.D.

# New England Connection Metabolic Conference

*Saturday, March 18, 2000*

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Mark your calendars for **Saturday, March 18, 2000** for the New England Connection for PKU & Allied Disorders. Inc. Metabolic Parent/Professional Conference. The conference will be held at the Holiday Inn in Taunton, Massachusetts. The discounted rate of \$89/night has been offered to our families, and the cost of the conference will be \$25. Special invitation/registration forms will be mailed out after the first of the year. The families of the Organic Acidemia Association will be invited to attend this long-awaited conference. The conference pertains to the following disorders, Homocystinuria, MSUD, Organic Acidemias, PKU, Urea Cycle Disorders, and Tyrosinemia. The conference will be a day-long event, with a hors d'oeuvres/cash bar reception the Friday night before. All the speakers have not been confirmed as of yet, but normally the morning session has speakers common to all disorders with break-out sessions in the afternoon that are specific to each disorder. We have asked Dr. Charles Roe from Baylor to come and speak, as well as Dr. Richard Koch from Los Angeles Children's Hospital. We are currently looking into childcare activities/volunteers to help families during the conference. If you have any information that you can share, please contact the following parents who have volunteered to assist in planning our part of the conference:

**Doreen Dix 505-877-1684**

**Irene Osran 847-562-1551**

**Menta Pitre 504-798-5631**

**Lori Sanchez 303-933-3335**

**If you are interested in attending, please contact one of the mothers above, so we can get a head count on how many people will attend. Menta Pitre says "it's not too early to register, especially if you are seeking out sponsors or stipends to help you financially." "Some of these processes are sometimes difficult and lengthy, and we have a letter that you may send to agencies to justify attending. Hope to see you all in March."**

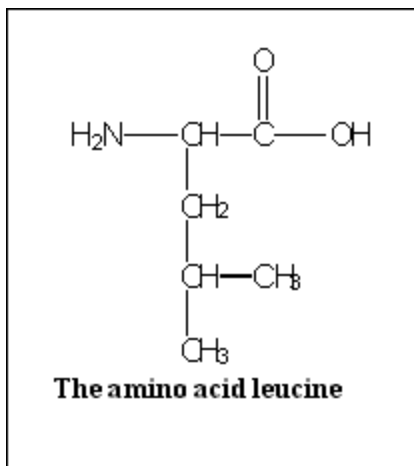
# Isovaleric Acidemia: A Treatable Disorder of Leucine Metabolism

*by Jerry Vockley, MD, Ph.D.*

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Isovaleric acidemia (IVA) is an inborn error of leucine metabolism caused by a deficiency of the enzyme isovaleryl-CoA dehydrogenase (IVD). Leucine, an amino acid building block of protein, is taken up from the blood stream by cells and transformed by several enzyme reactions into isovaleryl-CoA. When IVD function is impaired, isovaleryl-CoA accumulates to higher than normal levels in the blood and is converted to a number of other compounds in the blood and urine. One of these, isovaleric acid, is responsible for the characteristic odor exhibited by individuals with this disorder during times of poor metabolic control. These compounds are both directly toxic to cells and represent an excessive acid load to the body. Secondary inhibition of other chemical reactions in the body can cause a build-up of ammonia in the blood, which can lead to direct brain damage.



IVA can present in both an acute and chronic form. Approximately half of patients show symptoms within a few days of life consisting of acidosis with or without elevated blood ammonia levels. White cell and platelet counts can be low. Metabolic imbalance can be severe enough to lead to coma and death if a diagnosis is not made and therapy instituted. Left untreated, those infants who survive the newborn period are subsequently clinically indistinguishable from the remaining patients who present later in life. Late onset disease can present with a spectrum of severity including failure to thrive, developmental delay and intermittent episodes of acidosis. In its mildest form, late onset patients who are well until an acute episode of acidosis in adolescence have been described. The diagnosis of IVA is often first suspected because of the characteristic odor of isovaleric acid during acute episodes. This is similar to the smell of sweaty socks. The diagnosis is confirmed by demonstration of typical compounds in the urine by organic acid analysis. Specific

testing of IVD is available but typically requires establishing a culture of skin cells from a biopsy sample in the laboratory. Characterization of mutations in the IVD gene is possible, but only on a research basis. Prenatal diagnosis is possible when a pregnancy is known to be at risk for IVA. Amniotic fluid can be analyzed for the presence of isovalerylglycine, one of the compounds which accumulates to large amounts in this disorder. Enzyme analysis for IVD can be performed on cultured amniocytes. Regardless of the type of testing, it is vital that the lab be experienced in the techniques employed.

A great deal has been learned about the underlying genetic causes of IVA in recent years. IVA is an autosomal recessive (AR) disorder. We have two copies of every gene (the packages of genetic information) in our body. One member of each pair of genes is inherited from each parent, and only one copy of each gene is passed to a child. In an AR disorder, both copies of a gene must fail to function in order for a disease to occur. Thus, in IVA, both parents carry one functional IVD gene (which is enough to keep them from having symptoms) along with one defective copy. When both parents pass on the copy of the IVD gene that does not function, the child is left without a functional IVD gene, and IVA results. Molecular genetic techniques now allow direct analysis of the IVD gene in patients with IVA. Of the patients studied to date, roughly 60% have been demonstrated to have a defect in one copy of their IVD genes that leads to the production of an abnormal protein which fails to function properly (known as a point mutation). The remaining IVD genes tested show changes (mutations) that do not allow IVD to be

produced at all. It is sometimes possible to make a correlation between the mutation identified in a patient's IVD gene with clinical outcome. In these cases, the altered IVD protein can be shown to have some residual function, leading to milder symptoms. Most of the time, however, it is difficult to make such a correlation.

Treatment of IVA centers on decreasing the production of isovaleryl-CoA by the body, as well as enhancing the body's ability to eliminate it in non-toxic forms. The former is accomplished by reducing a patient's leucine intake. This consists of placing a patient on a diet low in natural protein calculated to provide the minimum recommended daily requirement of leucine. A typical level of intake of dietary protein is 1.5 grams for every kilogram of body weight, but this must be optimized for each patient. Additional protein requirements for growth can be met by the addition of a specialized metabolic formula to the diet. These formulae provide protein in the form of essential amino acids without leucine. While these formulae are usually viewed by health care providers and parents as being unpalatable, children treated with them since infancy appear to tolerate them well. Protein intake may need to be temporarily reduced or eliminated during times of illness due to production of leucine by catabolism. In this situation, carbohydrate calories should be provided along with IV fluids as necessary to support a patient through the initial phases of an illness. It is desirable (and usually possible) to re-institute the pre-illness diet within 24-48 hours.

Isovaleric acid is naturally bound to glycine by the body to form isovalerylglycine, a non-toxic compound that is excreted in the urine. It can also be bound to carnitine and excreted in urine. Glycine and/or carnitine can be given to patients with IVA to enhance the excretion of the increased amount of isovaleric acid that they produce. Glycine supplementation given at a dose of 200-300 milligrams per kilogram of body weight divided three or four times daily has typically been used for this purpose. Some concern has been raised that the high blood level of glycine achieved with this treatment might, itself, be toxic; however, there is no documented evidence for this. Aspirin may interfere with binding of isovaleric acid to glycine and should be avoided in patients with IVA. Carnitine supplementation at a dose of 100 milligrams per kilogram of body weight in three divided doses may be used as an alternative. The combination of the two may be more effective than either alone in patients in whom metabolic balance is particularly difficult to achieve.

Outcome in IVA depends in large part on the delay prior to initial diagnosis, and especially on the presence of any brain damage secondary to chronic acidosis or acute episodes of high blood ammonia levels. First affected children in a family are often more severely affected than subsequent affected siblings who are treated from birth. In the latter case, normal growth and development can be anticipated as long as metabolic control remains adequate. Treatment is lifelong, but the early childhood years and adolescence are particularly challenging times to manage due to the rapid metabolic changes occurring at these ages. A number of young women with IVA have successfully achieved pregnancies without apparent metabolic decompensation and delivered healthy infants. Careful consideration to maternal and fetal nutrition is vital in this setting.

There is reason to be optimistic in the face of a new diagnosis of IVA. Under the direction of an experienced specialist, it is usually possible to control the metabolic consequences of the disorder, especially when a prenatal diagnosis has been made. Every effort should be made to support patients through acute crises, and provide appropriate, long term care.

## **Free Patient Travel to Research and Treatment sites**

*(excerpt from the Alliance of Genetic Support Groups June, 1999  
newsletter)*

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**Call the National Patient Air Transport Helpline (NPATH) at 800-296-1217 for information about free transportation to research studies and treatment sites. NPATH is the source for information on individual flights to research and treatment, charitable ticket programs and coordinating transportation to research studies on your disease.**

The Air Care System is a national network of charitable air transportation resources, combining the resources of the corporate aviation sector, commercial airline sector and private aviation sector. The mission of this alliance is to ensure that no financially needy patient is denied access to distant specialized medical evaluation, diagnosis, treatment and on-going care. The resources of the entire Air Care System are coordinated in one place-the National Patient Assistance Center. The toll-free National Patient Air Transport Helpline (NPATH), 800-296-1217, provides access to information about all kinds of transportation assistance- from individual flights to large-scale programs to charitable ticket programs.

There are currently 43 VPOs, with 4,500 volunteer pilots, serving families in financial need. There is no expense to patients who use their services-pilots donate their time, fuel, landing fees and all related expenses. Since the aircraft used are small, private planes, they cannot fly more than 900 miles at a time and patients must be ambulatory. When a patient must travel more than 900 miles, VPOs in different regions work together to provide comprehensive service. A valuable resource to consumer organizations who are funding their own research, VPOs will sometimes make a commitment to handle all travel related to a research study or treatment protocol.

# Jordan Alaine Carlson

## *Methylmalonic Acidemia (MMA), Age 2*



This is an update on Jordan Alaine Carlson; she was born December 29th 1996. When I last submitted an article to the newsletter she was one year old, she is now two years old. Jordan was diagnosed with Methylmalonic Acidemia at 2 months of age. Since that time she has been treated with Carnitine, B-12 injections and followed as if she actually had MMA – although she doesn't. It was discovered after she had a skin fibroblast done in by Dr. David Rosenblatt in Montreal, Canada. He found her cells to be normal and did not have the genetic defect that would cause MMA. We were astonished by his discovery, as were the doctors in Pittsburgh that diagnosed her. They were not convinced she did not have the disease and were unsure of what the next step should be. So on November 18, 1997, the doctors in Pittsburgh along with Dr. Rosenblatt decided to take her off her daily B-12 injections, they kept her on the Carnitine though. They admitted her into the hospital to keep her under observation in case she should become acidotic. Jordan did not have a relapse, she stayed healthy and we took her home a couple days later.

Jordan's MMA level as well as the Homocysteine stayed with in normal ranges and she continued to progress. At this time we did not know what to think about the diagnosis, the doctors in Pittsburgh and Dr. Rosenblatt assumed she must have had a transient (short-term) case of MMA. They were not sure why or how it happened and were not able to say if we would ever know why it happened.

Dr. Harvey Levy in Boston phoned us after reading Jordan's story in the *OAA Newsletter* and saw she had been tested at birth for this disease through a newborn screening test done in Pennsylvania. He was trying to persuade the Dept. of Health expand newborn screenings to include MMA He asked us to either write a letter or come to Boston and testify at the public hearing that was to be held in January. After discussing this with my husband, we decided to go to Boston and appear at the hearing. Also, since Dr. Levy is familiar with metabolic disorders, I asked him if he could give Jordan a second opinion while we were there in Boston. He agreed.

In the meantime we had been trying to set up another appointment at Philadelphia Children's Hospital with Dr. Berry, another metabolic doctor. We finally got that appointment after numerous telephone conversations with our insurance company and doctors. What a hassle that can be. This managed care stuff is out of hand.

In January we headed for Boston, appeared at the public hearing and gave our testimony. It was a very eye-opening experience. I was very glad we decided to go, as far as I know it was a success and Massachusetts is going ahead with the expanded testing.

The day after the hearing we saw Dr. Levy and his team at the Children's Hospital. They looked over Jordan's medical records, took a full history from us and ran tests on her. We spent the whole day there; it was long, but well worth it. She also saw feeding therapists and other therapists whom assessed her development. Jordan had not eating anything orally. She was being fed by a G-J tube and had been since she was about 4 months old. At the end of the day they came to the conclusion her feeding problem was behavioral and that it seemed she did have some sort of *transient MMA*. They were not sure what exactly

had caused her problem, but that it was either nutritional or a problem caused by improper B12 transport. B-12 is what makes the enzyme work that breaks down the proteins in food. In children with genetic MMA, the enzyme is either totally non-functioning or is partially functioning. Jordan's enzyme is normal, but at some point the transport of B-12 was impaired and the enzyme did not work correctly, that is what caused her MMA and Homocystene to rise and almost took her life. This problem no longer seemed to be around since she was given the injections of B-12, well except for the feeding struggles. She still would not eat and was throwing-up regularly. This caused a lot of gastrointestinal discomfort for her and complications as well. We headed back to Erie, waiting for more tests results to arrive.

At her next appointment I asked her doctor in Pittsburgh if we could try taking her off the Carnitine, cited that the doctors in Boston could not see a necessity. Her levels were good and she did not have any fluctuations of the MMA or Homocystene. So they did decide to stop it and when we did Jordan's diarrhea and vomiting got better, she'd had loose stools ever since she started taking it. It did not make them go away altogether, but sure did make a difference. I was glad to see that.

After a month the test results came in on the transport defect of B-12 and Jordan did not seem to show any trouble with that. So that wasn't the cause, everything pointed to nutritional. Which did not make any sense. Usually when this happens the mother of the baby is a vegetarian and breast-feeds the baby exclusively. The baby then becomes deficient in B-12 because the mother is deficient. Being a vegetarian causes some people to be deficient because B-12 comes from milk, eggs, and meat primarily. It is important to take supplements to keep your level sufficient, especially if you are pregnant. When the baby is lacking the B-12 it can cause the enzyme to stop working that breaks down proteins in food. This then causes the MMA and possibly the Homocystene to rise.

So with this new information we waited for our appointment in Philadelphia. Dr. Berry asked a lot of questions about my husbands and my health. He took numerous of tests on Jordan, and myself, which I thought strange. This doctor seemed to think it had something to do with me. So he had agreed with the other doctors that Jordan did not have the genetic type of MMA and had to have been caused by a nutritional defect in B-12 metabolism. We were still not sure if this was good news or bad news. We wondered if she had something else worse.

Another upsetting news is that when Jordan was first was diagnosed, no one got a B-12 level for her or myself. This is very important to rule out B-12 deficiency. It should have been one in the very beginning. So when they finally tested myself and Jordan they found I was low in B-12 and her level was so high it was off the charts due to all her injections during the first year. I started to take an oral supplement of B-12 but it did not seem to rise as it should. It was slower than average. The Dr. in Philadelphia suggested I have a *Schilling* Test done to see if I properly absorb B-12. Well needless to say I was diagnosed with Pernicious Anemia which is a defect in metabolism of B-12. I don't have enough intrinsic factor in my gut, which is needed to transport B-12 through the intestine. I was found to only absorb 7% of the B-12 that goes in orally. That is a very small amount and explained why when I was pregnant with Jordan she became so deficient. She so far doesn't seem to have pernicious anemia, but she is still being monitored for it. We have Jordan's B-12 level taken monthly and I am on B-12 injections monthly. I was found to produce small amounts of MMA as well. The consequences that Jordan suffered going through this ordeal is, brain damage which is causing her feeding struggles and a motility disorder in her intestine.

Recently Jordan spent almost 3 months in the Children's Seashore House in Philadelphia; it is a rehabilitative hospital. It is connected with The Children's Hospital of Philadelphia, and has an intensive feeding therapy program. While she was going through the program they found Jordan had a colonic fistula connecting her stomach and colon together, which can lead to serious complications. They needed to perform surgery to take care of the situation and she recovered very quickly. She is now being fed through a G-tube versus the G-J tube.

The feeding therapists did a great job with Jordan and had her eating 5 ounces or pureed food before she was discharged. It is a very structured approach and parents are totally withdrawn for the initial training period. She was doing so well and wanted to eat everything in sight, even if she did not have all the skills required to do so. She even came off her feeding tube during the day and was only on night feedings, which was miraculous considering prior to this she had to be on feedings 24 hours a day. Her oral skills are

delayed and she is learning how to swallow, chew and drink for the first time. Jordan was doing great in the hospital and they warned us that things would be difficult at first at home but it would get better. Well since we brought Jordan home over a month ago, she has started to refuse her meals. It is very difficult trying to teach a child to eat who has never had to do so. We have run into some other complications, she is now down to two ounces at mealtime and back on the tube during the day at intervals. This is a pretty big setback considering where we were a month ago, but we are still working with her and at least she is eating something orally and not totally dependant on her tube feedings.

All in all, Jordan is very healthy and should be able to lead a long and fulfilling life. She has her setbacks, but there are so many others who do worse. We are excited that she is now walking alone. She is about 6 or 7 months delayed developmentally, but it never stops her from trying. She seems to keep right on progressing!

Well I will keep you updated and hope that this will enlighten some of you on transient MMA. I know we are not the only ones out there affected by this. I would love to hear from anyone else who has dealt with something like this.

One thing I do know for sure is that the newborn-screening (Tandem Mass Spectrometer) test caught my daughter's condition very early on. Without it I do believe she would not have made it.

**Carolyn Carlson**  
**Erie, Pennsylvania**  
**814-899-6646**

# Ashtyn Pitre

*MMA, cbl C, Age 4*



## **Development, Therapy and School:**

Ashtyn is now a 4-1/2 year old pre-school student who is very active and outgoing. This is her second year in Pre-K. Last year, she was placed in a Non Categorical Preschool (NCP) class; this year, she is in an inclusive Pre-K class. Her present school setting seems to benefit her special needs. Ashtyn likes to be with adults and is beginning to interact with her peers. She is parallel playing, imitating, verbalizing and using modified ASL (American Sign Language) with greater accuracy. Ashtyn learns best through multi-sensory activities and play. She receives OT, PT, speech, vision and APE (Adaptive Physical Education) services through our local public school. In addition, she also receives private OT, PT, and speech services every 2 weeks. Ashtyn has a mild/moderate motor deficit and is beginning to use a spoon independently. She is in the process of being toilet trained, and follows restroom routine with prompting and verbal cues. She is also beginning to follow simple directions, match like objects, identify colors and can sign some of them. Ashtyn can walk up steps utilizing hand railings or holding

another's hand. Her preference is using her left hand to do things such as writing, feeding and throwing. I think our biggest goal is to lengthen her attention span. I know one day it will come, and I will be ready when she is.

My daughter has come a long ways since I last wrote a story about her. I am proud of myself for allowing her to spread her wings and fly. It was super hard for me to leave her at school without me being there. It did take some time for me to be comfortable with leaving her, but I did it. There is no doubt in my mind that the school environment has been the best choice for her to accomplish her goals. There is so much exposure to multi-sensory activities, field trips and social gatherings. I would like to thank the Pre K staff and all the therapist (at Larose Lower Elementary) that are working with Ashtyn. You guys are doing an excellent job and I am very proud of you.

## **Her interest, likes and dislikes:**

Ashtyn loves music. Her favorite singer is Shania Twain. She also likes to listen to Cajun music. Ashtyn has many things she enjoys doing such as playing outside, taking a bath or swimming, and feeding her babies and Barney. Her absolute favorite is to ride a school bus. Some of her favorite foods are pasta, bread, grits, rice (especially with chicken gumbo sauce on top), Cheerios<sup>o</sup>, and popcorn. Ashtyn's dislikes are animals and quiet time. There are not many things that Ashtyn doesn't like. She is a very active, exciting, beautiful and loving child. I am truly blessed to have her as my daughter.

## **Current:**

Ashtyn is 54 months old. During her last physical examination, the following was recorded: height 91.3 cm; weight 11.22 kg (24 lbs. 12 oz.); head circumference 43cm.

## **Medicines, Vitamins and Diet:**

Ashtyn is currently on 1mg (1cc) of Hydroxocobalamin IM every day, 400 mg (4cc) of Carnitor twice a day and 1 tablet of One-A-Day Complete multi vitamin. I also give her fluoridated water as well. Her low protein diet, maintained daily, consists of a total of 16.5 grams of protein (2.0 grams/kg of body weight) and 15 Tbsp. of Pro-Phree and 3 Tbsp. of Propimix-2 in 8 oz of water.

## **Where tested and how often:**

Ashtyn's metabolic status is followed by the Hayward Genetics Center, which is located in the Tulane Medical Center in New Orleans. Her work-ups include monthly urine samples, blood serum screenings every 2 months and office visits every 3 months with a biochemical geneticist (Dr. Hans Anderson) and a metabolic nutritionist (Amy Cunningham).

## **Networking and Support:**

If anyone would like to share there experiences and network with other MMA families, please free to contact me (Menta) and I will do my best to help you in any way I can. My husband, Jamie, and I are planning to attend the New England's Connection Metabolic conference in Massachusetts on March 18, 2000. I'm looking forward to representing and meeting MMA families at the conference.

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# Joshua Lacey

## *Methylmalonic Acidemia (MMA), Age 6*

Hi everyone,



Since Mom is so busy around here with our family, I decided I'd better get this update out on me. In my last letter I had been taking Flagyl. It really brought my MMA level down at first. However, after several months my MMA level started going up again. My doctors thought my body was building up immunity to it so we went to a cycle of two weeks on Flagyl and two weeks off. We did this from Jan – May 98. Then we just stopped using it altogether because it wasn't doing any good anymore. I went back on 1 ml of B12 daily (via G-tube) too because it seemed to give me an energy boost. I continue to take 15 ml of Carnitine every day too.

My oldest brother Daniel and my little brother Jonathan broke out with "mosquito bites" in Feb 98. We couldn't figure out why they would get mosquito bites in February so Mom called Dr. Dinauer and we found out they had the chicken pox! I had to get 2 V-Zig shots to help my immune system since I was now exposed. About 2 weeks later my older brother Joel got the chicken pox and a week after him, I got them. I started using Acyclovir, which helped me not get such a bad case. But I did have them bad enough to get a natural immunity. I had a low-grade fever and lots of itches but my acid level didn't go up at all! Mom said she remembers back when I was first diagnosed with MMA that my doctors said if I ever got the chicken pox I would probably end up in the hospital in isolation. I'm so thankful that the Lord helped my body stay healthy and out of the hospital.

In May I had an MRI to see how my brain was doing. I didn't even have to be put under because I just lay very still the whole time. Mom and Dad stayed by my feet and I could only see their faces through a mirror above me. We all had earplugs because of the noisy machine. The medical people said I was the youngest person to have an MRI without being put under. My brain is doing well.

We moved from Maryland to Dayton, Ohio the summer of 1998. Dad is in the Air Force you see, so we have to move around a lot. Dr. Catherine Dinauer was on maternity leave but she came to see me before we left to make sure I was ready for the move. She and Kathy Camp, my dietician, were the best! Dad's getting his Master's of Engineering in Computer Science. It is a very hard school but he still finds time to play ball with me and my brothers. I love to hit the ball really hard way past my dad. Jonathan and I ride our new bikes with training wheels in our courtyard.

We just found out that after Daddy graduates in March 2000 his next assignment will be right here in Ohio. We are now house hunting because we need more space than we have in base housing.

Another milestone in my life... I'd been having trouble with my potty training. Mom and Dad had been working with me for a long time. They didn't know if poor muscle tone and having so much liquid day and night caused my problem or not. When Jonathan got potty trained before me, I decided I could do it too. Can't have a little brother showing me up now, can I? I was 5 years old; so don't give up out there.

It's been over 2 1/2 years since I've had to be in the hospital. I got a little sick last February and my ketones went to moderate, but Mom and Dad know just what to do to take care of me at home. They usually stop all extra protein but make sure I take all my Propimex and Prophree. They will split feed me and put the drip rate lower on my Kangaroo Pump. It takes me longer to get my strength back after I've been sick but before long I'm back going full force.

We used to have trouble with my *Mic-key* button leaking after only a couple weeks, but now Mom or Dad snip off half of the tip of the right angle adapter. This has solved that problem.

Dr. Miller, my genetic doctor, says I'm doing very well. I weigh 45 pounds and am 43 ½" tall. I'm consistent on my own growth curve. I don't eat a lot of foods by mouth, but I manage to eat 950 mg of Valine per day. I want to thank Dr. Miller, Kim Brubaker my dietician, and Dottie my check in-nurse. They are all great!

I'll be in kindergarten this year. Mom home schools us all, so she is always very busy. I love to work on my computer programs "Living Letters" and "Living Numbers." I also have other games I play.

Mom said I could tell you one more thing before I go. We are all very excited about another blessing from the Lord. Mom is going to have a baby sister for us. She is due around the middle of October. With 4 boys in the family, a little girl will be a nice change. We can't wait until she is here. After she is born we will find out if she has MMA like me.

Well, that's all I can think of to tell you. Mom will send a birth announcement later about my sister.

Love,

Joshua

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# Wing Size

## *Urea Cycle Disorder Lacking ASL Enzyme, Age 1*

**Hong Kong**



In August, 1998, I am excited to be the mother of my first baby. When I first saw her, she is so lovely and white in color. She is 2.9kg and healthy. When I took her back home and feed her the milk, it is unbelievable that she can drink 5 oz milk in just two weeks old. She is sleepy and getting more sleepy as time goes by.

When she is one month old, I took her to hospital to have the second dose of Hepatitis B Vaccine. Then she stopped drinking milk the next day. When we saw the doctor, he said because of some air trapped inside her stomach, she should be fine after taking some medicine. In next

morning, she started to shake her hands and her eyeballs were rolling back. I was very shocked and I then brought her back to the same hospital. The doctor told me it could be her reflex reaction. My baby stayed in the hospital and during the five days of examinations, they have checked the blood, ultra-sound on the head, nothing was found. Whenever she drank the milk, she shook. If only feeding her the glucose, she is fine but lying there pale and white.

On the fifth day, the doctor suspected the shaking might actually be a convulsion. So, my baby was transferred to a public hospital for further examination. On that day, it was found that my baby's liver was six times larger than normal, ammonia level was 412 and the shaking was actually a convulsion. So, she is preliminary confirmed suffering urea cycle defects and had the dialysis immediately. That night, she stayed in the intensive care unit and her ammonia level dropped to 100+ after a few hours of dialysis.

Now, we found that she is lacking the ASL enzymes and we feed her a restricted protein diet with 80056 supplements. However, as she got convulsions for a long time, the doctors said her brain may be damaged to certain extent. She is very poor feeding and we use the feeding tube to give her the milk. Also, she is very soft and delicate. We are having the physio--therapy, occupational therapy, speech therapy, pre-nursing education. She is getting better now and although she is just 9 months, she is already 9 kg. Although my heart before has dropped to the bottom when we understand her life-long disease, while I am getting better when I see her improvement. I hope that all parents can face the facts and help their child to get through all the difficulties.

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