ACDA NOTES

From The Alveolar Capillary Dysplasia Association

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Dear Friends and Family,

All of us find ourselves at different stages in our grief. Some of you lost your baby so recently and are wondering how to cope on a daily basis. Some of us, including ourselves, have been blessed with a rich life since losing our baby but at times we still seem to struggle. No matter where you fit on this spectrum, it is our hope that the ACDA has given you a lifeline to grab hold of in whatever way you need or feel comfortable. If you would like to share how you have coped with your grief, please contact us. ACDA mom, Raquel Aida Smith, mom to Terrance, provides some helpful advice on page 4 that helped her navigate her grief and also in this edition, other ACDA parents share the songs that remind them of their baby.

Fondly,

Steve and Donna Hanson
Executive Directors, ACDA
Parents of Eric – June 7-17, 1997

INSIDE

Preliminary Data from ACD Survey

From Amelia Ashwell Lake, RD RPHNutr PhD and mom to David

Summarized below is a preliminary analysis of the on-line ACD questionnaire. The analysis is being completed by Amelia who is a full-time mum to son Auden. A more in depth analysis will follow in the near future.

- There were 66 complete responses to the questionnaire.
- Only 1 family (1.5%) had had more than one child affected by ACD. Thirty-four (51.5%) of infants were boys. The infant with ACD was the first-born child for 44% of respondents and the second child for 36% of respondents.
- Twenty-one (32%) had an abnormal ultrasound scan during their pregnancy with the ACD infant. The majority of individuals (64%) did not have any health related issues during their pregnancy.
- The majority (68%) of infants born with ACD were born by natural delivery and 38% were born by caesarian section. Of the infants born by caesarian section, the majority (68%) were done so on an elective rather than emergency basis.
- All but one of the infants with ACD were born in a hospital. Following delivery 46% followed the 'normal' route to a ward etc. However, 31% went straight to an intensive care unit and 11% to a neonatal observation ward. Twelve families (18%) took their infant home. Eight of these infants presented with

Continued on Page 3

Research News

By Diana Locke
ACDA Research Committee Chairperson

Thanks to Simon Ashwell, dad to David, for providing a layman's summary of recent ACD published articles:

Inversion Upstream of FOXF1 in a Case of Lethal Alveolar Capillary Dysplasia With Misalignment of Pulmonary Veins

Toshima Parris et al, American Journal of Medical Genetics 2013

This is a report of an infant with ACD in which a novel genetic abnormality is described. The abnormality was detected by karyotyping (see below). The infant was found to have a part of chromosome 16 inverted, close to the FOXF1 gene. The paper thus adds to the list of abnormalities of chromosome 16 that can cause ACD.

Novel *FOXF1* mutations in sporadic and familial cases of Alveolar Capillary Dysplasia with Misaligned Pulmonary Veins imply a role for its DNA binding domain

Partha Sen, Yaping Yang, Colby Navarro et al, Human Mutation 2013

This paper updates the publication by the same authors in 2009 in which they reported for the first time that abnormalities (mutations and deletions – see below) in the FOXF1 gene and the area of chromosome 16 around the gene are responsible for ACD. The 2009 paper found such abnormalities in 40% infants with ACD. Since this publication, material has been collected from a further 47 infants. Thirty new de novo (see below) mutations in FOXF1 are described. This means that of the 93 infants with ACD that Dr Sen's group has studied 61% have been found to have a mutation in FOXF1 or a deletion around FOXF1. This confirms the role of abnormalities in the FOXF1 gene as the major cause of ACD.

Two familial cases of ACD are described. These confirm that FOXF1 is subject to paternal imprinting. This means that the FOXF1 gene inherited by an infant from his or her father is inactivated, but the gene inherited from the mother is active and expressed. Thus if an abnormality in FOXF1 develops in the production of an egg by a female (which occurs when she is in utero), this is expressed and will result in an infant with ACD. However, if a similar abnormality occurs in the production of a sperm (by a mature man) the resulting infant will not have ACD as FOXF1 is inactivated. However, the individual will be a carrier of the abnormality and can pass it on to his or her offspring. A female carrier can pass the abnormality to her children, which will result in ACD.

The incidence of familial cases of ACD in Dr. Sen's combined series is approximately 2%. Dr. Sen mentions that his group is the only one in the world studying FOXF1 in relation to ACD and that they operate a service to detect FOXF1 mutations and deletions pre- or post-natally on a research basis.

A (brief) glossary of genetics:

Familial: A disease that runs in a family as one or both parents carry a genetic abnormality and can thus pass it to multiple offspring.

De Novo (or sporadic): The opposite of familial; a genetic abnormality that occurs for the first time in an individual and is not present in the parents of the affected individual.

Karyotyping: A test where an individual's chromosomes are inspected under a light microscope . It can be used to pick up large and obvious genetic abnormalities (e.g. Down's syndrome)

Mutation: A change in the DNA sequence of a gene. This results in a change to the protein that the gene is responsible for producing. These are usually small changes (e.g. a switch from one DNA unit to another.)

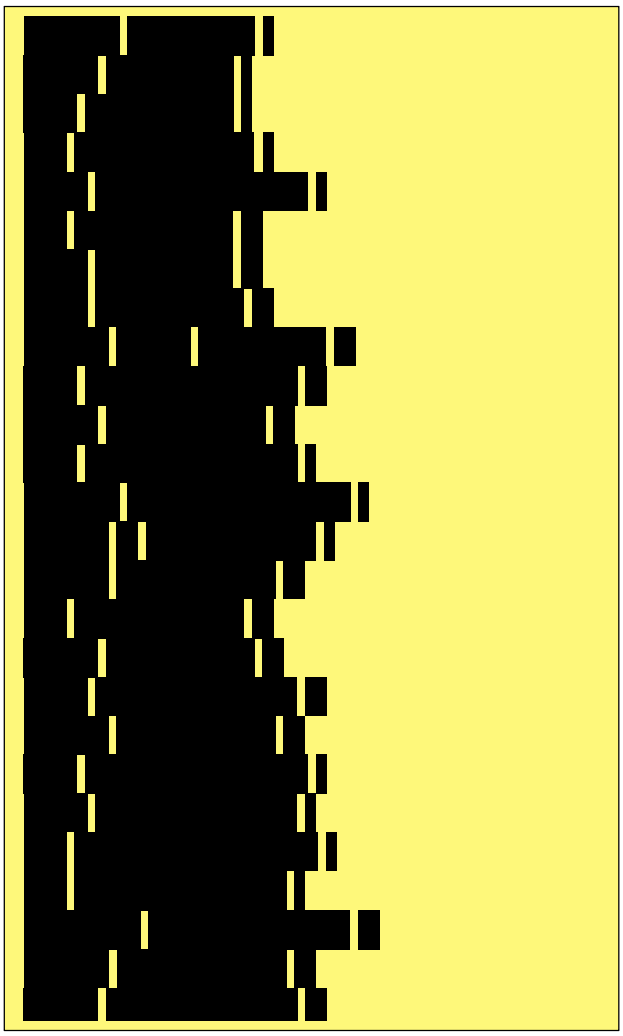
Deletion: The removal of a piece of genetic material. This can be a single DNA unit or a larger section of a chromosome.

ACD Survey Results: Continued from Page 1

symptoms at home, data on where the four presented with symptoms has yet to be analysed.

- Half of the infants with ACD had some other known defects.
- The diagnosis of ACD was discussed with 61% of families before the infant died. ACD was diagnosed by lung biopsy in 33% of infants and by post mortem in 58%. Lung transplantation was discussed in 20 cases (30%) and two infants were on a lung transplant list.
- Genetic analysis was performed in 24 (36%) of infants and NOT carried out in 28 (42%) of infants – there is no data on the rest (22%). Of those who had genetic analysis carried out 67% had mutation analysis of the FoxF1 gene and 50% had Chromosome 16 analysis (comparative genomic hybridisation) performed.
- Of those who had FoxF1 analysis done, 72% were normal and 28% were abnormal. Of those who had Chromosome 16 analysis done 50% were abnormal and 50% normal.
- Seven individuals (17%) had genetic testing done in subsequent pregnancies (i.e. amniocentesis or choronic villus sampling).
- Forty-two cases (65%) have taken part in the research being conducted at Baylor.

Thanks Amelia for this initial summary!



Family Support News

By Kim Anderson Bush
ACDA Family Support Committee Chairperson

Managing Your Grief

We have all experienced the overwhelming heartache of losing a baby and have wondered how we will manage the grief that is so unthinkable. The depth of our loss may be the same but we all grieve differently. There is no right or wrong nor is there a set timetable. In some ways, though, we all find a way to one day manage the grief and find peace with our loss.

If you would like to share what helped you through your grief, please send us an email. There may be another ACDA family that would find comfort in it also. Below, ACDA mom, [redacted], mom, to [redacted], shares her coping tips:

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For me, the two things that have helped me cope with the loss of our son is being as open, honest, and vocal about it as I needed to be and keeping only those who empathize, or understand, my grief close enough to listen to me express my feelings. Losing our baby was the worst pain I've ever felt, but hearing people say the wrong things or seeing them do the wrong things made me feel alone, even though I wasn't. THAT was the scariest part of grieving. When I felt alone, I felt no one cared. If no one cared, why should I? I became apathetic and apathy, for me, is one way to give up. I can't give up. I still have so much to give. So much love. It is probably as hard to hear (or read) as it is to say, but if you feel as if you can't talk about your baby around certain friends or family members without deeply regretting it, do not include them in your life while the pain is so raw. How long you've known them, what you've been through together, what your mom thinks- NONE of it matters if it is causing you pain. Find your cushy, warm, loving, peaceful, understanding community and hold on to it. They will help you through it, for as long as it takes.

Trigger Music

A number of parents on the ACD Parent Group on Facebook shared the songs that remind them of their child; songs that they listened to while pregnant, played at the baby's bedside or as part of their memorial service. The songs below have special meaning to ACD families:

Hand Built By Robots by Newton Faulkner - [This is] the album that I played non-stop while blissfully happily pregnant. It then became all I could listen to while we were in hospital. Every now and then I feel compelled to put it on let it consume me.

Chopin - I used to listen to Chopin. One day I was doing some cleaning and I noticed that music calmed him down. He was a non-stop kicker! So when he was really kicking hard I played Chopin and that would work. I haven't been able to listen to any Chopin in 14 months.

Continued on Page 5

We put a collection of songs to play at his funeral but the ones that get to me is *The First Time I Saw Your Face* and *One Sweet Day* by Mariah Carey and Boys II Men. It played as we were leaving the funeral home to go to the burial site. So whenever it comes over the radio I change the station.

The score to the Disney/Pixar film "Up". We watched that movie a lot during my pregnancy. I hummed the score and he calmed down as if to listen.

Hold Me Close by David Kitt - Played it at his funeral... There is a song by Athlete - *Wires* - about when his child was premature - played it loads... & I can't listen to it now.

I Never Told You by Colbie Caillat - The line "I miss those blue eyes" gets me every time. From the minute she was born we talked about her beautiful blue eyes that looked just like her dad's

All Through the Night by Yo Yo Ma - There are many different versions. They are all still beautiful. I love it because it is like she is sleeping and we sing her the lullaby. We had our guitarist from church sing and play it at her service. It was perfect. Just like my little girl.

More to come in the Summer Edition of ACDA Notes…..

Connect With Other Families On Facebook

For those of you on Facebook, we encourage you to "like" the ACDA's public page, which promotes ACD awareness and encourages families to contact the ACDA, (https://www.facebook.com/ACD.Association) and to encourage your friends and family to do the same. We're also happy to "like" the NICUs where your babies stayed in order to help promote the word about ACD.

We also encourage ACD parents to join the "ACD Parent Group" (https://www.facebook.com/ACD.Association#!/groups/168480916544514/). The ACD Parent Group is a closed group that provides support, information, and a place for families to share pictures and stories of their babies. Contact Emily Eschweiler for more information at Emily_Eschweiler@comcast.net (or search for Emily John Eschweiler on Facebook).

Fundraising News

By Emily & Tim Eschweiler
ACDA Fundraising Committee Chairpersons

Update from The David Ashwell Foundation

By Simon Ashwell and Amelia Ashwell Lake, Parents of David

Donations to ACD research via The David Ashwell Foundation have been continuing. Since March 2011, we have raised £104,969 ($161,001) for ACD Research. £33,118.00 ($52,053) was transferred in February 2012 to NORD and over £71,851 ($110,205) has been raised **since** that transfer. To have raised over £100,000 in memory of David and other babies is simply amazing and, as I have said before, really helps me in dealing with my loss of David (Amelia).

This amazing amount is the result of a great team effort from families across the UK and Europe. This year a lot of money has been raised in memory of other ACD babies –in particular Alexander, Alan and Noah, and we would like to thank these families for their huge efforts.

As you know Jo Taylor (mum of Alexander) nominated The David Ashwell Foundation as Thomson Airline's local charity. This donation route has now raised £24989.43 ($38,328.79)

In Scotland, Victoria and Andrew raised over £10,940 ($16,898) in memory of their son Alan. Andrew and 15 of his friends, Steven, Scott B, Callum, Scott M, Steph, Paul, Stewart, Kevin, David, Barrie, Graeme, Ross, Alan, Alan D, and Martin walked the 96 mile West Highland Way from Milngavie to Fort William. (See article below for more details)

Julie, a friend of Ellie Merritt and Nathan Flores (parents of Noah) ran the Brighton Marathon and raised over £539.00 ($832).

As you know we have The David Ashwell Foundation registered to 'The Giving Machine' which raises money as you shop. Karin Titze has very kindly set this up in Germany in memory of Janik.

In April, there was a coffee morning in aid of the charity in our area. A church whose hall we use for our Woman's Institute (WI) meetings heard about David and raised £650 ($1,003) in a lovely well-attended event. In May, in Northern Ireland, my mother, Vida, held a 'Craft and Coffee' Morning and raised over £500 ($772).

Stamp donations continue to come through! Thank you all for your contributions.

All UK and Europe based families are welcome to use The David Ashwell Foundation as a means of fundraising for ACD Research. If you live in the UK (and elsewhere), there are a number of options available for funding ACD research through The David Ashwell Foundation.

1. You can make a donation directly, using the Virgin Money giving website to gather donations for your fundraiser. http://David Ashwell Foundation
2. Fundraise while you shop (The Giving Machine) (a percentage of what you spend is donated)
3. Fundraise when you ebay (ebay for Charity).
4. Collect postage stamps http://David Ashwell Foundation

For additional information, please contact Simon and Amelia. http://David Ashwell Foundation
davidashwellfoundation@yahoo.co.uk
Amelia's mobile: 07855473686

We are more than happy to hear from other families who would like to use the charity to raise money for ACD Research. All money raised will be transferred to NORD.

Walking for Alan and ACD

By Andrew Kinchington, Dad to Alan
Scotland

We lost our son Alan last year at only 11 days old to ACD. To say it was worst time of our lives would be an understatement. I had never heard of ACD and couldn't believe how rare it was, which just added to how unfair and cruel it was to have our beautiful baby taken away from us for no good reason. I felt so helpless and guilty not being able to do anything to help Alan and I suppose I always will.

A friend and I decided to do a sponsored walk, the West Highland Way, in memory of Alan and thought it might interest a group of mates I grew up with. I was taken back when 15 of them all decided to do it with us, which meant taking time off work and away from their families as well as fundraising themselves. In total, we managed to raise an amazing £10,940.00 ($17,021) for the David Ashwell Foundation to go towards research into ACD.

The West Highland Way is a 96 mile hike over the Scottish highlands which we did over 6 days:

Day 1 - Milngavie to Rowerdennan - We walked around 20 miles the first day which ended with a hike up and over Conic Hill which was hard going but the thought of knowing there was a pub with a cold pint waiting for us kept us all going.

Day 2 - Rowerdennan to Inveranann - Another hard days walk of about 20 miles took us up by Loch Lomond with its amazing scenery. A few people were starting to struggle at this point with sore feet and we all soon split up into different groups, though all 16 of us made it..... eventually!

Day 3 - Inveranann to Tyndrum - A supposed easier half days walk of 12 miles, though didn't seem any easier as my feet were really starting to suffer with blisters! Competed plasters were out in force now!

Day 4 - Tyndrum to Glencoe - Around 19 miles, which took us though the Rannoch Moors, literally the middle of nowhere. One lad couldn't even walk over to get his photo took before the walk began as his feet were in such a mess, I told him he should maybe give this stretch a miss but he was having none of it and slowly but surely walked the 19 miles.

Day 5 - Glencoe to Kinlochleven - A half days walk which took us up the infamous Devils Staircase at the beginning, the walk down the other side was more painful on the blisters. I had on each of my toes now, each step an effort!

Day 6 - Kinlochleven to Fort William - The last day and everyone was still there. Lots of aches and pains but don't think anything short of a broken leg was going to stop anyone completing the final 16 miles. The good old Scottish weather of rain, wind and hail decided to keep us company for most of this stretch! We all eventually all made it to Fort William and crossed the finish line together which was nice and a little emotional. Lots of hugs and hi-fives all round!

Looking back I'm really glad I done the walk and thoroughly enjoyed it. Along with the rest of my friends, I feel it's something that will stay with us for the rest of our lives. To be able to do something no matter how small that has raised awareness of ACD and might one day help find a cure for ACD has left me with a sense of achievement.

Andrew and his walking mates; Andrew is in the first row, second from the left

Raising Awareness

Gene mutation analysis may point to imprinting in newborn lung disease

HOUSTON -- (May 1, 2013) -- For an unknown number of parents each year, a mutation or "misprint" or a deletion in a gene called FOXF1 results in an infant born with a dangerous and uniformly fatal lung disease called alveolar capillary dysplasia with misaligned pulmonary veins (ACD/MPV).

An international group of researchers led by those at Baylor College of Medicine (BCM) has analyzed the 42 mutations in FOXF1 in DNA from infants with the disorder and in a report that appears in the journal Human Mutation recommends that genetic testing be considered in infants with persistent pulmonary arterial hypertension with no known cause. This global collaboration involves samples from patients in 13 countries and 10 states. BCM is the prime institute involved in research related to this disorder and has the largest collection of DNA and tissue samples in the world.

"Most of the cases are spontaneous, meaning that they occur for the first time in the infant affected," said Dr. Partha Sen, an assistant professor of pediatrics - newborn at BCM and corresponding author of the report. However, reports on the rare cases in which the disease occurs in families can help understand the background of the disease, he said.

Many of the children with the disease can also have other anatomical problems involving organs of the gastrointestinal, cardiovascular and genitourinary systems.

In one family described by Sen and colleagues in a recent report in the European Journal of Human Genetics, five of six children died of the disorder soon after birth. Tests of DNA from three infants who died of the disorder showed that they had the same mutation in FOXF1 as did their mother. The healthy surviving sibling had a wild type gene (normal with no mutation) on chromosome 16. The mother had no evidence of the disease.

It appeared, said Sen, that the mutation was a new one (called de novo) that occurred on the chromosome the mother inherited from her father (the paternal chromosome). However, her affected children inherited the mutated chromosome from her - the maternal chromosome for them. The healthy child had the other chromosome 16 from his mother which she (mother) inherited from her mother (grandmother).

The affected children developed the disorder because of genomic imprinting of FOXF1 in human lung. In this case, the copy of the gene inherited from the father is silenced and the gene from the mother is the active copy - but it is a mutated copy.

In the exhaustive study of 42 new FOXF1 mutations in patients with this disorder, most were sporadic and not inherited from parents. However, among them were four familial cases and in three of those families, the infants inherited their mutated gene from the mother. Again, this buttresses the argument for genomic imprinting, said Sen.

BCM and the Texas Children's Hospital are centers of study for the disease, an interest that began when Dr. Claire Langston, distinguished service professor emeritus of pathology at BCM, first became interested in the disease many years ago. In 2009, Sen, Langston, and Dr. Pawel

Continued on Page 9

Stankiewicz, associate professor of molecular and human genetics at BCM were co-authors on a paper that first identified that alveolar capillary dysplasia with misaligned pulmonary veins results because of alterations (mutations and deletions) in FOXF1, a transcription factor, a protein that binds to specific DNA sequences, controlling how DNA is transcribed into messenger RNA - the first step in translating the information in a gene into a protein, the workhorse of the cell. They now estimate that alterations in this gene account for approximately 80 percent of the cases of the disorder.

While the disorder is not common, Sen is not convinced that it is as rare as it was thought to be previously.

"I get two to three requests each month from around the world, asking to have the test run and the rise in the number of patients is the result of awareness that has been brought by the research at BCM," he said. Sen concentrates on mutations in the gene and Stankiewicz on deletions. He acknowledges that their work is indebted to the Alveolar Capillary Dysplasia Association (ACDA), a parent organization that has helped in bringing awareness to this deadly neonatal disorder. ACDA has also raised substantial amount of funds to support research.

Very few infants have received lung transplants because they are difficult to perform and obtaining an organ for an infant who is five to six weeks is challenging.

BCM researchers who took part in these studies include Sen; Yaping Yang; Colby Navarro; Przemyslaw Szafranski; Avinash V. Dharmadhikari; Debra Kearney; Binoy Sivanna; Michael L. Baker; Langston; Stephen Welty; John Belmont and Stankiewicz. All of the physicians in this study also practice at Texas Children¹s Hospital.

Funding for this work came from the National Organization for Rare Disorders, a Pilot Project Award from Texas Children's Hospital to Sen, and the National Institutes of Health (NIH1R01HL101975-01) to Stankiewicz.

Written By Glenna Picton, Senior Communication Specialist
Baylor College of Medicine Office of Communications
For The Baylor College of Medicine News

ACD Gets Some Air Play

Thanks to Diana Locke, mom to Christopher, and Cami McGraw (in memory of her cousin's daughter, Bella Blehr) for their continued efforts to raise awareness of ACD! In March, Cami set up an interview on ACD with radio newsman Gordon Griffin, Diana and Dr. Becky Sharp, a physician in the Dallas/Fort Worth area. It aired three times over three different radio stations in the Dallas/Ft. Worth area.

You can listen to the interview by going to the link below. This is Diana's own recording of the interview and is not an official recording.

http://www.youtube.com/watch?v=M0vGR1uJhHo&feature=youtu.be

Many thanks to Diana and Cami!

Please Welcome Our New ACDA Families:

[redacted]

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[redacted]

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[redacted]

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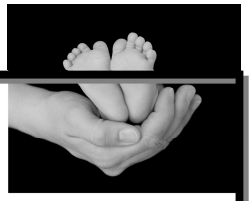
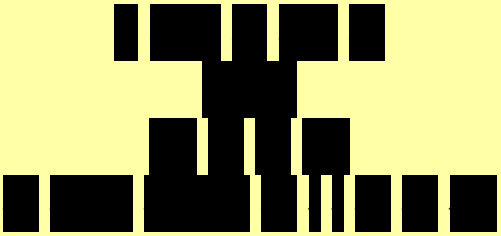
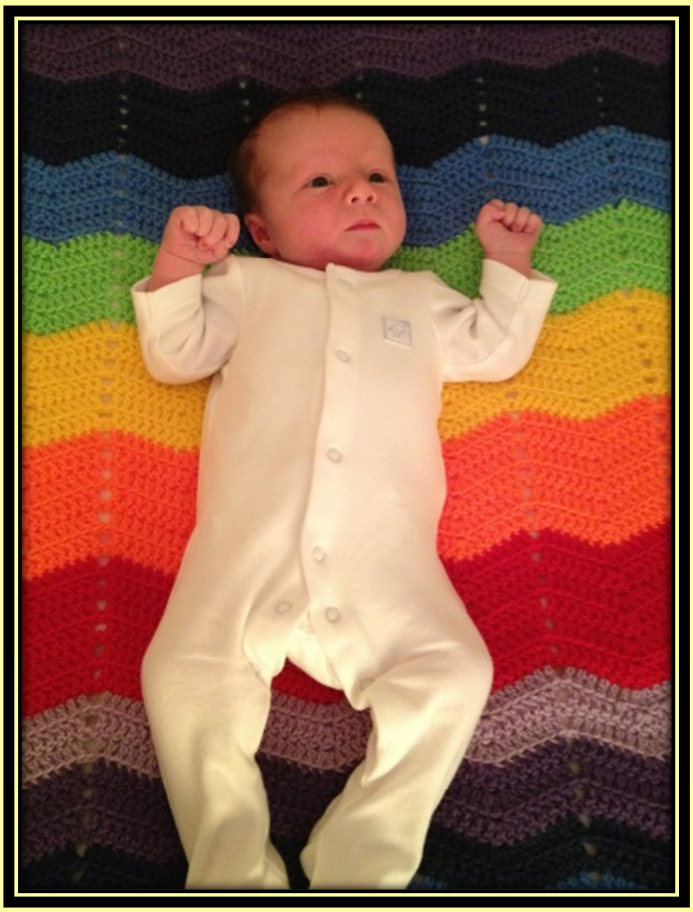
[redacted]

- If you have a skill or expertise that would help the ACDA, we'd like to know. We have started tracking those of you that have offered to help with graphics, legal advice and medical journal translation. We don't always need help but if you would like to add your name to our list to call on in case we need some assistance, please contact us.
- The current balance of our ACD Restricted Research Fund at NORD is $2,900.00.

Safe Arrivals







James lying on a rainbow blanket handmade by Amelia Ashwell Lake's mother, Vida.

Make a Tax-deductible Contribution for ACD Research

In the spring of 2002, the ACDA established an ACD Research Account at NORD. This means that your contribution to NORD can be earmarked specifically for ACD research. As stated below in *NORD's Rare Disease Clinical Research Program Policy*, NORD requires that a research account reach $33,500 before it will initiate the grant process to award research money to the medical community. Therefore, the goal of the ACDA is to raise more than $33,500 for research.

To make a tax-deductible contribution to NORD for ACD research either by mail or on the NORD website, please use one of the instructions:

***** Make a Donation by Mailing a Check *****

- **Please make your check payable to "NORD - Alveolar Capillary Dysplasia Restricted Research Fund" to earmark your donation for ACD research.**
- **In the memo section of the check or on a separate note attached to the check, state that the donation is "in memory of (name of child)."**
- **Your family and friends can attach a note to their check with your name and address and NORD with promptly notify you of their gift.**
- **Send your check to the following address:**

National Organization for Rare Disorders, Inc.
P.O. Box 1968
Danbury, CT 06813-1968 USA

The most critical part of this process is ensuring that your check is made out to "NORD - Alveolar Capillary Dysplasia Restricted Research Fund" to ensure that your donation is earmarked for our ACD Research Account.

***** Make a Donation on the NORD Website *****

Go to https://www.rarediseases.org/about/support/research-donations. Select "Alveolar Capillary Dysplasia" in the research fund pull-down menu and complete the rest of the form. In the "Additional Comments" box, type "Alveolar Capillary Dysplasia Restricted Research Account."

Special Information for Families Living Outside of the United States

NORD recommends that families living outside of the United States use a credit card to make a donation since it costs less to convert international currency when using a credit card. Use the NORD website at https://www.rarediseases.org/about/support/research-donations.

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