



**DIAMOND BLACKFAN ANEMIA
FOUNDATION, INC.**

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DBA NEWSLETTER

Diamond Blackfan Anemia

for patients...for families...for research



DIAMOND BLACKFAN ANEMIA
FOUNDATION, INC.

We are DBA!

Welcome to the 2012 Spring Edition of the DBA Newsletter! We hope you find it useful and entertaining, enlightening and informative. For your convenience we have compiled the DBA Facts into one spread for easy reference and listed the various clinical and research opportunities all together for you to consider for participation. The world of DBA *today* is an informed and connected one. We invite you to be a part of the progress.

Diamond Blackfan Anemia Foundation Funds \$246,253 in Research Projects... With a Little Help From Our Friends

American industrialist Henry Ford said, "Coming together is a beginning. Keeping together is progress. Working together is success." In 2011, DBA families have successfully come together, stuck together, and worked together to fund four very important DBA research projects in Sweden, Italy, and the United States. Thanks to the tireless efforts and generosity of our families and friends, the Diamond Blackfan Anemia Foundation (DBAF) is able to fulfill our mission of supporting DBA patients, families, and research. This past year, the DBAF has also come together with DBA Canada (DBAC) to collaborate on important initiatives and we look forward to our continued joint efforts.

\$50,000 to improve the treatment of DBA

In July 2011, Dr. Johan Flygare was awarded \$50,000 for his project titled: Identification of Genetic and Chemical Modifiers of Erythropoiesis in Diamond Blackfan Anemia. This grant marks the first collaboration of the DBAF and DBAC, as they generously contributed \$10,000 to this project. Dr. Flygare's project goal is to develop better treatments for DBA by identifying chemical compounds and molecular pathways that promote proliferation of RPS19-deficient erythroid progenitor cells.

This project has two parts: In the first part, Dr. Flygare will identify genes, which when down-regulated, allow RPS19-deficient erythroid progenitors to proliferate at normal levels. The findings of this study will increase the understanding of DBA pathogenesis and generate a list of genes and pathways that potentially can be targeted to treat DBA. In the second part, Dr. Flygare will use erythroid progenitors from a new and exciting Dox-inducible mouse model to screen for compounds that can rescue the RPS19-related erythroid defect. The chemical screens will lead to identification of compounds that rescue proliferation of RPS19-deficient erythroid progenitors. Such compounds will be potential compounds for the development of new drugs for DBA. By studying the mechanism by which these compounds influence the proliferation of RPS19-deficient erythroid progenitors, more will be learned about DBA pathogenesis.

The DBAF and DBAC are pleased and proud to be able to fund Dr. Flygare. This talented young investigator is well known to the DBA community, and has been supported by the DBAF throughout his career. Dr. Flygare stated, "During my ten years of scientific training I have focused on DBA-related research. This has been an excellent preparation for becoming an independent researcher with the long-term goal to develop novel treatments for DBA." Dr. Flygare has completed postdoctoral fellowships in Dr. Stefan Karlsson's lab in Lund University, Sweden and in Dr. Harvey Lodish's lab at The Whitehead Institute for Biomedical Research, Boston, MA. Dr. Flygare has established his own lab in Sweden and has earned the support and respect of many distinguished DBA researchers. We are grateful to Dr. Flygare for his continued interest in Diamond Blackfan Anemia and we wish him and his colleagues continued success.

An initial \$30,000 towards understanding remission

In August 2011, the DBAF funded two more prominent DBA researchers. Dr. Irma Dianzani, Professor, University of Eastern Piedmont, Novara, Italy was awarded an initial \$30,000 to begin work on her important research project entitled: Understanding the causes of remission in DBA patients, with the intent that the DBAF would consider funding an additional \$30,000 based on the progress of her findings and the availability of funds.

The DBAF is proud to continue our mission of supporting DBA patients, families and research. We are grateful for the support and involvement of many of our families, and we encourage all DBA families to partner with us as we strive to reach our goals.

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The goal of this project is to understand the molecular basis of remission in DBA patients. While remission occurs in approximately 20% of patients, the causes remain unknown. Dr. Dianzani proposes to identify genes that, when mutated, lead to remission in DBA patients. The identification of genetic and molecular alterations resulting in disease remission is anticipated to reveal novel genetic and/or molecular pathways that may be therapeutically targeted in DBA treatment. Buona fortuna Dr. Dianzani and team!

Another \$41,028 to identify mutations

At Camp Sunshine 2010, the DBAF presented Hanna Gazda, MD, Ph.D a check for \$51,512 towards her project entitled: New gene discoveries and biology of ribosomes in Diamond Blackfan Anemia. In August 2011, the DBAF was proud to once again support her continuing efforts on this important project and awarded Dr. Gazda, Instructor in Pediatrics, Harvard University, Children's Hospital Boston, \$41,028 to continue her efforts in identifying genes mutated in DBA patients. Dr. Gazda has played a major role in the identification of several of the known DBA genes. Further, her discoveries established DBA as a ribosomopathy, which has helped direct research efforts on many aspects of the disorder. We are grateful to Dr. Gazda for her commitment to Diamond Blackfan Anemia and wish her and her colleagues continued success!

Partnering with DBA Canada to fund alternate means of gene discovery

In December 2011, the DBAF announced the funding of Dr. Adrianna Vlachos' research project entitled, A Strategic Approach to Gene Discovery in DBA. We are pleased to fund this exciting project with the DBAC and appreciate their \$25,000 commitment towards this \$125,225 multi-centered project. The goal of this research project is to identify the affected genes in the approximately 30-40% of DBA patients in which their genes have not been identified by traditional sequencing of candidate ribosomal protein genes. Dr. Vlachos, Dr. Bodine, and a strong cadre of investigators at the National Genome Institute and John Hopkins University will employ state of the art technologies to further identify genes affected in DBA patients. The investigators will use comparative genome hybridization to identify genes deleted in DBA patients that may be responsible for the disease and interrogate the entire genome using whole exome sequencing. "We are so pleased to have DBAF's support and that of DBA Canada. We hope to continue to discover new genes and be able to genotype more and more patients," stated Dr. Vlachos.

Why it matters

Gene discovery not only has the potential to lead to new therapeutic treatments, it is also vital to patient care. Initially it was thought that the vast majority of the DBA cases reported to the DBAR were sporadic. However, with the discovery of 11 published DBA genes, family studies have identified a higher-than-expected proportion of individuals carrying the gene mutation – without ever being anemic or requiring treatment. These individuals may have mild, if any, hematologic manifestations with or without DBA-associated congenital anomalies. Identification, in a timely fashion, of inherited cases within a family is imperative so that appropriate reproductive and, when applicable, stem cell transplant choices can be made. For example, asymptomatic siblings or parents can be counseled as to the risk of having an affected offspring, and asymptomatic, yet genetically affected siblings would be identified as unacceptable stem cell transplant donors for DBA patients.

The DBA Foundation sincerely thanks all our families and friends that have made funding this project possible. The researchers also appreciate your efforts. Dr. David Bodine stated, "I promise to make this money count. It will allow us to move much faster in our search for DBA mutations. We are all grateful to the families and contributors for their confidence in us."

Without our families' support, we would not be able to fund these exciting projects. As you can see, these worldwide research projects have the potential to answer questions, to identify genes, to unlock the mystery of remission, and to provide insights into therapeutic agents. These projects also represent the hopes of all of us for a better understanding, better treatment options, and possibly a cure for our "orphan disorder." Please help us to continue funding critical research.



In the spirit of working together, Jack Pereira and Andie Morrison present Dr. David Bodine a check representing DBAC's contribution to a DBAF approved gene discovery research project.



Dear DBA Family,

The Diamond Blackfan Anemia Foundation, Inc. (DBAF) is proud to announce our eighth national family retreat. This retreat will take place during the week

of July 8-13, 2012 at Camp Sunshine, which is located at Lake Sebago, Maine. Air carriers fly into Portland, Maine. Ground transportation is provided by Camp Sunshine to the campsite.

Camp Sunshine has proven to be an unforgettable experience for the families that have attended. We are grateful to Camp Sunshine for extending an invitation to us once again this year. Lodging and three meals daily are provided. Camp also plans daily activities for the entire family, and offers parents an opportunity to share their experiences and exchange information. Aside from the benefit of meeting other families, the DBAF has also obtained commitments from experts in the medical field to come and share their expertise and to update us on current research.

Please visit www.campsunshine.org to learn more about Camp Sunshine.

Applications are now available at

http://www.campsunshine.org/programs/family_application/index.php.

Final selection of families chosen to attend is determined by Camp Sunshine. Completed applications and physical examination forms should be returned to Camp Sunshine as soon as possible, due to the limited availability of family accommodations. Travel expenses are the families' responsibility. If you have any questions or concerns regarding Camp, please contact Dawn Baumgardner at 716.674.2818. We are looking forward to seeing many of you this summer!

It Was the Best of Times; It Was the Worst of Times

by Tommie Lelia Wilkins

Most probably recognize this opening statement of Charles Dickens's novel, 'A Tale of Two Cities.' How can something be the best and the worst at the same time? Sixteen years ago I would have deemed such a declaration the essence of an oxymoron. But that was before my experience with Diamond-Blackfan Anemia-- which is certainly the best and worst thing that has ever entered my life.

When I discussed writing this article with my fifteen year old son, Ty, I tried to solicit a quote from him on what it is like to live with DBA. His knee jerk response... "It sucks!!!" After giving him my motherly 'watch your mouth' eyes and explaining to him that I believe the intent is for us to submit something a little more inspirational, he changed his response to, "Fine, it sucks, but you get used to it." My 'watch your mouth' eyes don't carry the weight with him they once did! Those who know Ty are accustomed to his dry sense of humor and his no-fluff, short answer responses. I contemplated not sharing such a blunt response or at least modifying it but I thought better of it. After all, I am writing this for our DBA family to read. There is no need for me to sugar coat what I feel sure most of us have felt at some time or another.

So how do you learn to live with it? How do you get past the anguish and frustration, the why my child or why me, the anger... how do you get past the fear? If only there were a one size fits all answer.

However like DBA, everyone's journey may start on similar paths, but our destinations vary. There are variables; variables in the roads DBA unfolds for us and variables in how we adapt. For every moment of anguish, frustration, questions, and anger; I have experienced even more moments of amazement, happiness, certainty, and calmness. Just when I have thought fear would consume me, my hope has been restored. It takes a conscious effort every day to choose which aspects of DBA need to be focused on... otherwise, it can engulf you. Ty's motto seems to be... 'I will not allow DBA to rob me of any more of life than is absolutely necessary.'

We may have little control over how much time we spend dealing with the day to day DBA maintenance; but we don't have to allow it to saturate our every thought.

The fact that Ty has a mutation in his RPS19 gene has understandably weakened his body, but it has also served to strengthen his spirit. I feel the need to elaborate on the previous quote from Ty. It is only fair that I share the setting. When I asked him the question about what it is like to live with DBA, I did so after returning home from a doctor appointment day... you know the ones... when you try to consecutively squeeze in a couple of specialist follow-ups since your day will be shot anyway. We had not received the best of news on this day; not terrible news but not what Ty wanted to hear. So for that moment, for that day, that quote is exactly how he felt about DBA. There have been plenty of times when he has felt that way. But Ty is an overcomer and his spirit always prevails. Let me share another quote-- one I did not solicit. "Mom, if I had not been born with DBA, I probably would not have as close of a relationship as I do with Christ." He then went on to tell me how he has to lean on Him to get "me through the rough times." With a recent struggle, when Ty had been suffering for months, I told him how proud I was of him for keeping his sense of humor through it all. He informed me, "Mom, I have to keep up my sense of humor or all of this would make me crazy." That is how he copes.

Coping takes on a different form for every one of us. My coping skills consist of prayer, organizing, and being pro-active-- while squeezing in as much laughter as I can. My survival techniques have changed over the years.

At first, I could only handle reading bits of DBA information at one time before the fear would rush in. I later coped by studying anything I could get my hands on, which in those days wasn't much. When Ty was in remission at a young age, I ignored DBA for months... didn't want to think about it, deal with it, or even remember it. It was like the dark cloud I had felt over my son for years was lifted. Then there was the emotional crash I experienced when he slipped out of remission... I handled it by becoming a fighter... I would no longer succumb to the apprehension of DBA taking my son from me. I spent years managing but feeling so alone in this world. In spite of the many good people I was surrounded with, I never felt anyone could truly understand.

Then I found the DBA Foundation, I found Dawn, and I found you-- my DBA family. You "get it"... even those of you who have completely different coping skills, spiritual beliefs, or opinions from mine. As different as we all are, there is a common thread that binds us.

Ty isn't as vocal or active among our group as I am. Unlike years ago, there is a lot of information at our fingertips. Information is power, but it can also stimulate stress and unnecessary concern. So, I filter Ty's exposure to it. After all, at Ty's age, he only wants to deal with DBA when he is forced to. Nonetheless, he feels the connection. He has become close to several in our DBA family, and I trust they realize how essential their friendship is to his emotional well-being.

That brings me to Camp Sunshine-- hands down one of the most amazing experiences of our life. To come into contact with so many on the same journey as us-- that are fighting the same battle. I felt as though I had spent years treading water and, metaphorically, the support we received at Camp Sunshine became our life boat. It is impossible to put in to words the impact that week had on me. Ty spent his week connecting with those who live with DBA in some form or another. When we would discuss who he enjoyed interacting with, I would ask the question, "Does he/she have DBA?" and more times than not Ty would say, "I don't know, we didn't talk about that."

Yet he felt a connection, the kind that doesn't need words... the kind that silently screams... I get it, I understand, and you are not alone. It reaches a depth that is far beyond mortality; it fortifies his spirit.

It is the worst of times; it is the best of times. DBA breaks you. It pulls you to your knees. It shakes your very soul. Then through the battles, through those times when DBA has you at your weakest; you overcome and it strengthens you. You learn to appreciate life, to savor the moments, to find the joy through it all. DBA makes you a better person... it accelerates your spiritual growth. Once you have lived with DBA in any form, you will never be the same.

Ty asked me to include this quote. "It is the tough things I have gone through with DBA-- that have made me the man I am."

Yes son, you are quite the young man. You are my best of times.



Marcus "Ty" Wilkins is the Star-ranked patrol leader of Troop 174. He is shown here just before being awarded four new merit badges for Auto Maintenance, Citizenship in the Nation, Environmental Science, and Reading. Ty will make Life on 4/15/12 and then will only be six months away from Eagle. He plans to do a Swim-a-thon fundraiser for DBAF as his Eagle project.



Steven Ellis, PhD
DBAF Research Director

The 12th Diamond Blackfan Anemia International Consensus Conference was held March 17-19th in Battery Park in New York City. The conference began with a kickoff dinner held in a restaurant club room which was actually an old vault in a former bank in lower Manhattan. The intimate setting set the stage for a meeting known for its blend of physicians, scientists and other interested parties who freely exchange ideas in a highly collaborative environment. The keynote speaker at the dinner was Jeff Bond, father of four-year old Angus

Bond, who was diagnosed with DBA at 8 weeks of age. Like many, Mr. Bond told of the initial anguish he and his wife Jessica had in trying to understand his son's diagnosis and how from this experience the seeds were sown for the Captain Courageous Foundation of Australia, one of a growing number of international foundations supporting research on Diamond Blackfan anemia. The Bonds were warmly welcomed into the broader DBA community.

Sunday, March 18th

Plenary Session "Assessment of iron loading in Diamond Blackfan anemia".

This session was particularly timely given recent deaths in the DBA community from complications of iron overload in transfusion dependent patients.

Dr. Thomas Coates (Los Angeles) gave the first of two talks on iron loading relying on his considerable experience with thalassemia patients. He described studies indicating that certain tissues, like the heart, take up iron by mechanisms different from that in the bone marrow and the liver, and the rates at which tissues accumulate iron also differ. **Consequently, a surrogate measure for tissue iron like serum ferritin is a totally unsatisfactory way to monitor iron content of different tissues.** Instead, new imaging technologies are improving the way iron content in individual tissues can be monitored allowing much better assessment of the effectiveness of chelation therapies. Adherence to treatment regimes continues to be a major problem in older patients. Effective iron monitoring and close cooperation between patients, parents, and physicians is essential for reducing mortality.

His talk was followed by Dr. Ellis Neufeld (Boston) who spoke on the strengths and weaknesses of current chelation therapies. He indicated that there is still a need for improved chemical chelation therapies. He provided some encouraging data on a new chelator currently undergoing early phases of testing.

[Note: the ICC also had a session where research was presented in a poster format. I will not discuss the posters separately, but instead describe them briefly if they complement one of the session talks. Posters will be presented in *italic*.]

Dr. Josu de la Fuente (London) reiterated themes raised by Drs. Coates and Neufeld in his poster on iron loading in the UK DBA population. He showed data indicating a number of patients had clinically significant iron overload even though their ferritin measurements indicated adequate iron chelation. Again, these data indicate the need for more effective means of monitoring tissue iron content in DBA patients receiving transfusion therapy.

Developmental Biology - This session focused on the timing of DBA presentation during mammalian development.

Dr. Lydie Da Costa (Paris) gave a talk on DBA presentation in a developing fetus. One of the more puzzling aspects of DBA is why it typically presents in the first year of life, or in other words, why it doesn't present in the developing fetus. Previously, published studies on fetal deaths thought to be as a result of DBA lacked a definitive genetic diagnosis. Dr. Da Costa's study provided the first documented evidence of a ribosomal protein mutation associated with signs of anemia in the developing fetus. These studies indicate that DBA should be considered in cases where there is evidence of fetal anemia, but also raise the

question of why many DBA patients escape anemia during fetal development and present after birth.

Dr. Johnson Liu (New York) spoke on work using mouse embryonic stem cell models of DBA comparing the differentiation of two cell lines each of which was mutated in a different mouse gene known to be affected in DBA. The results presented indicated that depending on the gene mutated there could be different effects on differentiation, providing a potential rationale for the heterogeneous clinical presentation in humans affected in DBA. Trying to link clinical features of DBA with the underlying genetic defect has been a holy grail in DBA research. Dr. Liu's presentation gave a very nice segue into the session on genetics which followed.

Genetics - This session focused on gene discovery, new approaches to gene discovery in DBA, and the identification of genes that may modify the manner in which DBA presents and responds to therapy in different patients.

Dr. Hanna Gazda (Boston) began this session by describing the first DBA gene that does not encode a ribosomal protein. As has been the case in all my meeting reports, I am unable to go into too much detail on the talks given as unpublished work is frequently presented. Suffice it to say, that this discovery raised quite a stir and set the stage for large scale projects interrogating the entire genomes of DBA patients for possible causative genes. One of the questions after Dr. Gazda's talk was whether this new gene somehow links in to the ribosome defect in other DBA patients representing some type of biological continuum in disease pathophysiology or whether this represents a distinct subclass of DBA. The answer to these questions awaits further study.

Dr. Jason Farrar (Baltimore) presented his work on scanning the genomes of DBA patients for larger deletions containing genes whose loss would have been missed by traditional DNA sequencing technology. One of the more fascinating aspects of his study was finding that in some of these patients these deletions were found in mosaic cell populations where some of the cells had the deletion and others not. This mosaicism appears to be linked to remission in certain DBA patients.

Dr. Adrianna Vlachos (New York) presented another outgrowth of the deletion studies described by Dr. Farrar. One of the deletions indicated that a patient originally diagnosed with classic DBA in fact had a more non-classical form of DBA that can be effectively managed with a novel treatment. These studies illustrated the power of defining the underlying genes affected in all DBA patients, pointing out that gene discovery is not simply an academic exercise.

Dr. Paula Quarello (Turin) presented work on gene deletions in the Italian DBA population supporting the view that gene deletions are a relatively frequent occurrence in DBA patients.

Dr. Elizabeth Chao (Aliso Viejo) presented work on the diagnostic testing Ambry Genetics has begun offering to DBA patients in its CLIA (Clinical Laboratory Improvement Amendments) lab. Ambry Genetics currently offers testing for 11 possible DBA genes in a cost effective manner.

Dr. Annarita Migliaccio (New York) presented work on the tremendous amount of structural variation in the glucocorticoid receptor in humans. Since this receptor mediates many of the biological and clinical effects of steroid hormones, their laboratory is currently investigating whether these sequence variants might somehow be linked to the different ways in which DBA patients respond to steroid therapy. Thus, it may be possible someday to be able to predict a patient's response to steroids depending on the nature of their glucocorticoid receptor gene.

This session ended with a talk by Dr. Marcin Wlodarski (Freiburg) who described their studies on the genetics of DBA in the German DBA Registry. He, like others described above, is using various whole genome interrogation methods to identify genes affected in DBA patients. Clearly, these are very exciting times in the gene discovery field.

Basic Mechanisms and Translation - this session explored the molecular mechanisms whereby defects in ribosome synthesis influence cell death signaling pathways and how these pathways may be targeted in developing more effective therapies for DBA.

Dr. Teng Teng (Cincinnati) presented work on how reducing expression of the DBA protein Rpl11 influences how cells divide. Previous studies have reported that Rpl11 plays a central role in p53 activation in response to ribosome stress. Therefore, it came as somewhat of a surprise when RPL11 was identified as a DBA gene. The studies reported here indicate that alternative mechanisms may come into play in cells depleted of Rpl11.

Dr. Alan Warren (Cambridge) discussed what he feels may be a more primordial form of ribosome stress signaling in *Drosophila* which he plans to exploit in a strategy to identify therapeutics that target elements of this pathway.

Dr. Akiko Shimamura (Seattle) presented a poster that suggested additional complexity in signaling pathways responding to ribosome stress.

Dr. Pierre-Emmanuel Gleizes (Toulouse) outlined his studies on a newly identified DBA gene which appears to regulate p53 activity through various mechanisms. As I'm sure the reader is by now aware, there appear to be numerous mechanisms operating in terms of signaling ribosome stress to cell growth and death signaling pathways. This should come as no surprise however, given the ubiquitous and fundamental role the ribosome plays in all cell types.

Dr. Fabrizio Loreni (Rome) presented studies on one of these additional signaling pathways that appears to integrate aspects of cellular energy metabolism with ribosome stress and how it may be relevant to DBA.

Nadia Danilova (Palo Alto) presented work on how small molecule effectors of energy metabolism pathways influence phenotypes in their zebrafish model of DBA.

Dr. Alison Taylor (Boston) backed into one of these alternative signaling pathways when she was screening chemicals that reversed a DBA-like phenotype in her zebrafish model of DBA. These studies have obvious implications for potential therapeutic development.

Dr. Lingbo Zhang (Boston) discussed his work on a protein that is required for the ability of glucocorticoids to stimulate erythropoiesis. Identification of factors critical for the effects of glucocorticoids may ultimately lead to alternative strategies to influence the activity of these factors with less toxic therapeutics.

Dr. Janice Abkowitz (Seattle) presented her work on the role of heme toxicity as a potential mediator of the erythroid selective nature of DBA clinical presentation. Her work is based on the DBA-like phenotypes in mouse where the heme exporter FLVCR is knocked out.

Two posters presented from the laboratory of Dr. Chetankumar Tailor linked ribosomal protein mutations to defective expression of FLVCR through an effect on RNA splicing. These studies again might relate to the continuum whereby defective ribosome synthesis can influence other cellular processes that ultimately give rise to the distinct clinical features of DBA.

Along these same lines, Dr. Marieke von Lindern (Rotterdam) presented her work on two genes that influence erythroid development whose expression is preferentially affected by ribosomal protein haploinsufficiency. Dr. Irma Dianzani (Novara) presented work on various transcriptional regulatory pathways that appear to be affected in cells expressing suboptimal amounts of ribosomal proteins.

Finally, Dr. Adrianna Vlachos (New York) closed out the session with her analysis of cancer incidence in the North American DBA Registry. While DBA appears to be a cancer predisposition syndrome, the cancer risk appears lower than with other bone marrow failure syndromes. While Dr. Vlachos' talk at first blush may appear out of context with all the other talks in this session on different signaling mechanisms, it is worth pointing out that many of the signaling pathways that appear to be involved in DBA pathophysiology also play important roles in tumorigenesis.

Monday, March 19th

Clinical Treatment and Drug Development - this session focused on translating basic science discoveries into more effective treatments for DBA.

Dr. Anu Narla (Boston) presented her work on the effects of leucine in reversing phenotypes in zebrafish and human cellular models of DBA.

Dr. Dagmar Pospislova (Olomouc) presented a poster on her encouraging work on the effects of leucine in the Czech DBA population and Pekka Jakko (Lund) presented a poster on the effects of leucine in his mouse model of DBA.

Ms. Sara Sjögren (Lund) presented two high throughput strategies for DBA therapeutic development currently underway in the laboratory of Dr. Johan Flygare.

Dr. Johnson Liu (New York) described a new clinical trial for adult patients with DBA evaluating a drug initially developed for osteoporosis which had the undesirable side effect (at least in non-anemic patient populations) of stimulating red cell production. The safety and efficacy of this drug will be evaluated in this study. This fascinating drug is also undergoing clinical trials to stimulate red cell production in patients receiving cancer chemotherapy.

The last scientific talk of the meeting was given by Dr. Carol Mercer (Cincinnati) who discussed her work on the effects of a p53 inhibitor in a mouse model of DBA.

Summary

This was another outstanding DBA conference! I hope you can tell from the foregoing discussion that I think we have really turned the corner on potentially identifying genes affected in all DBA patients, which in turn will dramatically influence our ability to correlate clinical features of the disease with underlying genetic changes. The basic science discoveries of the past few years also appear to be leading to many different and novel approaches to therapeutic development. We hope that the fruits of the endeavors reported here will soon lead to improving the lives of patients and families affected by DBA.

Acknowledgements

Many thanks go out to Marie Arturi and Lauren Carroll for all the work they put into setting up the meeting and making sure everything ran smoothly. Thanks also go out to the Daniella Maria Arturi Foundation who sponsored the meeting and to Celgene, FerroKin BioSciences, Ambrey Genetics, and the Diamond Blackfan Anemia Foundation for their meeting support.



2012 DBA International Consensus Conference Attendees

The Love, Hate Relationship with Desferal

by Kathi Vroman

Desferal, for us, has always been a bit of a love/hate relationship. I hate poking both our boys once, and sometimes, twice a day. I hate bringing syringes and needles on vacations. I hate that our high school senior has a tube running into his front pocket of his khakis at school. I hate the sore spots on our boys' tummies and the fact that their skin is getting tough. However, I love that this horribly inconvenient and complicated drug keeps our boys alive. And this fact, all by itself, trumps everything else. End of discussion.

Chelation therapy with desferal has been part of our lives for 14 years now. We've done lots of things to disguise the ugliness of chelation and make it a less traumatic part of our life. We keep supplies in a charming brass and wood chest in our bedroom and gave the pump "cute" names when the boys were small – calling it a "Power Rangers Power Pack" so that it didn't make the boys feel "weird" or "unusual".

Eventually chelation was no longer the traumatic part of our day that made me literally hyperventilate the first time I did it. And we learned to go about our routines, only having to think about chelation at night. None of us loved it and we all continued to pray for a cure so that the boys wouldn't need to deal with it forever. But it was doable and part of our life.

Then the unthinkable happened. The DBA Community began to lose vibrant, beautiful, young people to complications from iron overload. Children we knew. Children from families we had spent time with at Camp. Children our children played with.

This horrible feeling began to nag at us. We had watched the boys' ferritin levels creep up and up, albeit slowly, and we realized that the false sense of security we had was dangerous – perhaps even critically so. With great encouragement from Dawn Baumgardner we pursued getting a T2-Star for both boys. Our 13 year old's values were somewhat elevated but our 17 year old's were staggeringly high. We heard the news we dreaded: our 17 year old would need to chelate at the maximum dose 24 hours a day, 7 days a week. How would we ever break this news to our son who was the drumline captain for his marching band?

DBA has humbled us and taught us many things – one of which is how all of the children afflicted with DBA have astounded us repeatedly with a courage and wisdom often beyond their years. So we presented him with the facts. We told him what round-the-clock chelation would entail and what we would have to do. We told him that if we didn't do this he would die young. We told him we could live with anything in this world – but that. Not if we could do something about it now. We told him 24/7 chelation wouldn't be forever. We told him we'd figure out how to work this into his drumline schedule.

He, in turn, had only one question: "If I do this will I die young from iron overload?" We told him the doctor told us this was the best way to prevent it. He shrugged his shoulders and said "then I don't have a choice."

That was a year and a half ago. Along the way we've continually prayed for him to have the peace to accept this treatment and have dealt with emerging issues – working around the schedule for things like drumline competitions and the prom. He's slowly learning how to "hook himself up" and to remind us when his pump is out and needs to be re-attached. But his iron levels are coming down. Not as fast as we would all like, but we are making progress. We probably have another year or so to go before he can go back to evening only chelation.

But, we are all living with it, and his teachers understand why his school uniform can't be tucked in and that the unusual "whirring" noise in class is his pump, not his cell phone. And all his friends know. When they learned, they looked at his pump and said profound things like "huh" and "wow, that sucks". That's it.

I guess my message is this: I hate chelation and DBA, but I love that I can kiss my boys goodnight every night. Get your children's livers checked... for real. Don't rely on the false security of ferritin levels. INSIST to your hematologist that a T2 Star or Ferriscan be done. Don't take no for an answer. If your hospital doesn't have the equipment to do either scan on site, bug your doctor to find a facility that does. Call the office of the DBA Foundation to ask for help. Ask what normal values are for iron levels and take ACTIVE steps. Don't push it to the back of your mind because you're afraid of how your children will react. They probably will surprise you.



Chris Vroman has been section leader for the past two seasons for his high school's drumline. He's been able to juggle being "hooked up 24/7" with support from his band director and bandmates. His drumline placed first 3 times in its class already this year!

Mission Fruition

Your Contributions Allow the DBAF to Continue to Provide Support for DBA Patients, Families and Research.

The key to the success of Diamond Blackfan Anemia Foundation (DBAF) lies in our ability to provide funding for approved research studies, scientific meetings and collaborations, various patient education materials and family supportive measures. It is imperative that YOU, the very families that need these important resources, commit to this shared responsibility in whatever capacity you are able as the majority of these services are derived from charitable donations.

The DBAF realizes that the commitment to fundraise puts additional burden on the very people that are struggling to manage the demands of living with a rare disorder; however, it is crucial that you understand that without this revenue, the DBAF will be unable to fulfill every objective of our mission. This article reminds our readers about the various ways to financially support the DBAF through charitable contributions.

Three Ways to Make a Charitable Donation

The type of asset you give and the way you transfer it to DBAF will determine the tax and financial benefits resulting from your gift. It pays to plan your gift in order to secure maximum benefits.

Gifts of Cash

A gift of cash is the simplest and most direct way to contribute to charity. You may designate your gift for a specific purpose, or you may choose to leave your gift undesignated so it will be used to fulfill areas of greatest need.

Gifts of Appreciated Securities

An alternative to a gift of cash that deserves careful consideration is a gift of appreciated securities (that have been owned for more than one year). Substantially greater tax benefits may result from this gift by avoiding the taxation associated with capital gain.

Gifts of Life Insurance Policies

Life insurance is an asset that is frequently overlooked. If the original need for which a policy was purchased no longer exists, a gift of this asset can be very rewarding, particularly if the policy is fully paid up.

Two Ways to Make a Gift and Receive Income for Life

A life-income gift plan with the DBAF is an arrangement under which you make a gift of cash or property (stocks, bonds, real estate) in exchange for a stream of income for life. Life-income gifts may be made in the form of trusts and gift annuities.

Gifts in Trusts

In its simplest terms, a trust is an arrangement under which an individual transfers legal title of property to another, the trustee, who manages the property for the benefit of the individuals and/or organization (i.e. DBAF) specified in the trust agreement.

A Word From the Board

by Dawn Baumgardner, Executive Director, DBAF, DBA Mom

As parents of a child with DBA, I think each of us can vividly remember our version of those unforgettable words, "We think your child has Diamond Blackfan Anemia." Diamond what...? And so began our journey into a world we never knew existed. A journey filled with twists, turns, fears, passion, determination, and progress. My family's DBA story began over two decades ago in a much different world. A world where computer access was limited, medical information was retrieved from the dusty books on a top shelf of a medical library, and connecting with other DBA families or doctors was not a Google search or Facebook page away. Being diagnosed with a rare condition was an extremely scary and isolated place to be thrown.

Flashback 20 years ago: Our oldest son's diagnosis came out of the mouths of the highly esteemed Dr. Blanche Alter, respected attending physician, Dr. Jeffrey Lipton, and their very young fellow, Dr. Adrianna Vlachos. I remember standing in the procedure room, clutching my sweet, happy, unsuspecting toddler (and I was 8 1/2 months pregnant, I might add), asking Dr. Vlachos if she had ever performed a bone marrow biopsy and if she knew what she was doing! I insisted that one of the "real doctors" be in the room with us! Who knew that decades later, these three incredible physicians would still be such an integral part of our lives? Who knew the baby I was carrying also had DBA? Who knew that dreaded June afternoon would be the start of the Diamond Blackfan Anemia Foundation?

Months after the diagnosis, I became obsessed with learning as much as I could about DBA. I read, I questioned and then I read and questioned some more. I used every possible resource to educate myself about DBA. As the mother of three young boys under the age of five, my days were filled with love, giggles, Star Wars, baseball, hospital visits, and diapers. My nights were spent between the stacks of medical libraries or harassing overseas doctors on the phone. Then my focus turned to finding other patients and families with DBA. Surely, there were other parents who would do whatever it takes to cure our children. In my heart, I knew that I would not rest until my boys were DBA free. I promised them, I promised myself, I would not stop until a cure was found. I drove everyone around me crazy... except for my husband! He knew my determination (stubbornness) and that my heart would not allow me to stop until I was doing something to make this better for my family and for others. He was smart enough to support me and continues to be the "man behind the DBAF." Throughout the beginning years, I was privileged to meet other families who shared my goals. Together, we formed the Diamond Blackfan Anemia Foundation in 1994. While the faces of the DBAF's board members have changed, our mission remains the same. "The mission of the Diamond Blackfan Anemia Foundation, Inc. (DBAF) is to collectively and actively generate funds for the charitable and scientific purpose of furthering, by clinical study, laboratory research, publication and teaching, the knowledge of the disorder known as Diamond Blackfan Anemia (DBA). Our intentions are to share this knowledge, to inform, to lend support, and to communicate with all families of DBA patients."

Trusts that make lifetime payments to the specified beneficiaries and benefit a charity are known as charitable remainder trusts.

Charitable Gift Annuities

The gift annuity is perhaps the simplest and most popular charitable life-income arrangement. A gift annuity is a contract between the donor and the charity in which fixed payments are guaranteed to the donor in exchange for a gift of cash or marketable securities.

Please consider making a charitable contribution to the DBAF, so we can bring our shared mission to fruition.

And so it began... and so it grew. From nineteen families to over 700; from helping to fund one DBA project to funding numerous projects every year; from a one page newsletter to a 16 page newsletter, monthly e-newsletters, web based support groups and family meetings; from virtually no (zero, none, nadda) information to resources and opportunities I could have only dreamed about. And all of this...because of families just like yours and mine! It has been a great honor and an immense privilege to be a part of the DBA Foundation since its inception. Over the past 18 years, I have volunteered as the treasurer, secretary, or president. It has been a true blessing to be a part of my DBA family. My passion and dedication to find better treatment options, a cure, and to inform and lend support grows stronger and deeper with each passing day. I want something more... something better... for my sons and for all our patients and families. We need your help.

It is because of you that the DBA Foundation continues to exist. Your donations and fundraising efforts have allowed the DBAF to provide funding for major research projects that have resulted in the establishment of the DBA National Registry (DBAR), the discovery of defective "DBA genes," a better understanding of DBA on both the molecular and genetic levels, advances in creating animal models, novel approaches to less toxic treatments, and promising advances towards successful therapeutic cures. We have sponsored international scientific meetings, national family conferences and retreats and provided our families with informational materials and support. Fortunately, the DBA Foundation's successes and responsibilities continue to evolve. Our exponential growth and exciting plans for the future has recently been addressed by the Board. The current board members have recognized the need for a full time Executive Director and offered me the position. I am pleased to accept this opportunity and excited about the prospects.

This new opportunity is another chapter in my DBA story. More blank pages to fill with DBA advances and DBAF accomplishments, and more blank pages to fill with families' faces and stories. I pledge to work hard and tirelessly to serve our families and the DBA Foundation. I am sincerely grateful to the board members (past and present) for their commitment and hard work, to our DBA families and friends for their dedication to our mission, and to my family who has embraced the fact that curing DBA and supporting our families is my life's passion. I encourage each of you to call me and get involved with the DBA Foundation. I enthusiastically welcome your ideas, questions, and input. With your continued support, my sincere hope... my sincere prayer is that together we can find a cure and together we can write "The End" to all our DBA stories.

Thank you for allowing me to be a part of your lives.

Steroids Treatment Tips

What is a corticosteroid? How will it affect a DBA patient? What things should I know when taking steroids?

A **corticosteroid** is a powerful drug that is commonly used to treat many conditions including allergic reactions and inflammation. Corticosteroids can also help some DBA patients make more red blood cells. This is often one of the first types of treatments for those with DBA. It is not known exactly why steroids work, but 80% of people with DBA who take corticosteroids are able to increase the production of red blood cells to some degree. The goal in using steroid therapy is to maintain a healthy hemoglobin level of 9 g/dL or higher (equivalent to a hematocrit of approximately 30%).

When **considering a steroid treatment**, it is important to discuss the basic guidelines of this therapy with your physician, taking under consideration the patient's current hematologic status and overall well-being. The main goal in using steroid therapy is to stimulate red blood cell production while balancing the side effect profile typical of steroid therapy so to allow the DBA patient to make their own red blood cells while having as "normal" of a life as possible. Initial treatment consists of a high dose (2 mg/kg/day) of the steroid for several weeks. Upon a response to steroids resulting in a rise in hemoglobin, the physician will slowly and carefully titrate the initial dose over the next 2 to 4 weeks. Over the course of several weeks and months hemoglobin levels will be tested and the steroid dose will be adjusted accordingly. The goal is to maintain a level of hemoglobin that allows for normal daily functioning at the lowest dose possible while successfully managing side effects. Currently, it is believed that achieving the goal dose of 0.5 mg/kg/day allows patients to avoid many of the long-term side effects related to steroid therapy. Ideally a dose of 1 mg/kg every other day is even better to allow for the adrenal glands to continue working.

Pregnancy and increased growth may warrant an adjustment in steroid dose, and for reasons that are not fully understood, some patients experience unexpected declines in hemoglobin levels and require adjustments to their dose. Colds and bacterial infections may also result in dips in hemoglobin which can be temporary or permanent. Some people experience automatic recovery while others require dose adjustment to kick start red blood cell production. Others may have to rely upon a blood transfusion to return their hemoglobin to a safe level while waiting for the boosted steroid dose to take effect. Remission is a possibility for patients on steroids and those on blood transfusion therapy. Not all treatments and therapies are alike just as all DBA patients are not all alike.

Side effects, both short and long-term, are common when taking steroids. However, by closely working with your doctor these side effects can be avoided or managed. A low dose of corticosteroids may be adequate to maintain a normal hemoglobin with few side effects. High doses over a prolonged period can cause serious side effects; therefore patients taking high doses of steroids should be carefully monitored. Your physician may suggest other treatment options if serious side effects develop.

Possible side effects of **short-term** use:

- upset stomach
- increased blood sugar
- increased hunger
- behavior changes, trouble sleeping, irritability
- increased risk of pneumonia, thrush (white coating in the mouth) and other infections
- weight gain, salt and water retention
- high blood pressure
- increased fat on the face (rounded face), upper back and belly
- stretch marks on the skin, acne, poor wound healing, increased and unusual hair growth

Possible side effects of **long-term** use (3 months or longer):

- all short-term side effects
- poor growth in children (can be severe)
- osteoporosis (bones break easily, problems with hips and shoulder joints)
- muscle weakness
- diabetes
- increased risk of developing cataracts

- increased risk of developing stomach ulcers
- the adrenal gland may shut off, making it impossible to produce cortisol during emergencies (this is what speeds up your heart rate and gives that 'adrenaline rush'), such as a car accident or surgery (it may be necessary to 'stress dose' during these times).

Patients who take steroids should be aware of other **necessary precautions**. Certain medications may be taken to avoid or treat specific side effects, and your doctor may suggest additional monitoring while on steroid therapy. While on corticosteroid therapy, patients should call their doctors if they have a fever of 100.5°F more than once, or a fever of 101.0 °F even once. Talk to your doctor about your concerns including stomach issues, growth retardation and bone health. Following these medical recommendations and taking care of yourself will help to ensure that you are doing all you can to prevent the pitfalls that come with steroid therapy.

It may be required to stay on hydrocortisone if your doctor determines you no longer need steroid treatments. This is due to the adrenal glands not producing cortisol after depending on the steroids for so long. This can be determined by measuring an am cortisol level.

Other medications:

- Antibiotics – a prophylactic dose of an antibiotic can help ensure that the patient does not contract certain types of pneumonia while taking high doses of steroids for long periods of time and if white blood counts are low at start of therapy.
- Anti-fungal – may be helpful in treating yeast-based diaper rash or thrush and should only be taken as needed
- Acid reflux medication – may help in relieving and sometimes preventing stomach problems
- Vaccines – patients on high doses of steroids SHOULD NOT GET LIVE VACCINES Re-vaccination may be necessary if steroids were started before completion of the initial series of immunization.

Recommended on-going medical care:

- Monitor CBC monthly once a steady dose is attained
- Measure height routinely. A 'steroid break' may be needed if growth has fallen below the growth curve for age, especially during the first year of life and during puberty
- Annual vision check
- Dental visits twice a year
- Baseline dexascan (x-ray to determine the strength of the bones)
- Endocrinology referral - This doctor can be helpful with growth and development issues as well as discussing side effects from short term steroid usage and long-term use.
- Yearly flu shot
- Try to avoid anyone who has viral infections.
- Careful monitoring should be considered during puberty. Both the chemical and physical changes that take place during this time can affect DBA patients and his/her treatment.
- Women who become pregnant while on steroids should be carefully monitored. It may be necessary to go to transfusion therapy during pregnancy. It is important to include your hematologist in family-planning discussions prior to becoming pregnant if at all possible.
- You cannot commence steroid therapy 'cold turkey'. You must be weaned over a period of time as you can experience steroid withdrawal.

Some people on long-term steroid therapy wear a bracelet or necklace engraved with the patient's medical and personal information to ensure that the response team will be able to provide proper treatment in the event you are unable to communicate.

DBA patients taking corticosteroids can testify that this treatment plan comes with certain side effects and risks. Working closely with your team of physicians to meet recommended treatment guidelines and to obtain appropriate on-going medical care will help to make steroid treatment therapy a useful option for living with DBA.



The DBAF is very lucky to have the expertise and services of a nurse specifically dedicated to DBA. Ellen Muir, RN, BSN, CNS has graciously taken the time to write up some "DBA Facts" and has posted them to our Facebook page as well as submitted them to our monthly e-newsletter. We have compiled them here so that our families can conveniently keep them in one place for easy reference. Look for more DBA Facts coming your way!

DBA Fact #1: REMISSION

Approximately 20% of those affected with DBA have a chance of going into spontaneous remission. These can be long lasting. It is possible to go into and out of remission at any point of your life. Remission for DBA is when no treatment (steroids or transfusion) are required for 6 months or more.

DBA Fact #2: IRON CONTENT

One unit of blood contains 200mg of iron, which would be the same amount of iron as eating 69 lean 3oz steaks. One 3oz steak contains 2.9mg of iron.

Food restrictions of iron are unnecessary in preventing iron overload, however supplemental vitamins should be avoided. (Women's One a Day vitamin contains 18mg iron/ Men's One a Day vitamin contains 0mg iron)

DBA Fact #3: RED BLOOD CELL PRODUCTION AND MEDICATION

Red blood cells (RBCs) are produced in the bone marrow. The RBCs carry hemoglobin to all the cells of the body, providing oxygen for function.

Reticulocytes (retics) are immature red blood cells. The % will tell us how hard the bone marrow is working. It is not uncommon in a bone marrow failure syndrome such as DBA to have a retic of less than 1%.

Drugs which have been studied to improve red blood cell production include:

Corticosteroids (prednisone, predlone, prednisolone) have been the standard drugs for treating DBA with a response rate of 80%. Many side effects with long term use, or at high doses, include: growth stunting, high blood pressure, cataracts, diabetes, and osteoporosis to name a few. With an initial trial of high doses, there is a risk of infection, especially a serious form of pneumonia. Bactrim, an antibiotic, can be given to prevent this from happening. If there is a response in hemoglobin and retics, the dose is tapered to a more tolerable, lower dose (ideally 0.5 mg/kg every other day).

Cyclosporine A (CSA) and Antithymocyte Globulin (ATG) have been studied in DBA patients with limited success. An NIH-sponsored protocol combining CSA and ATG closed due to poor responses. These drugs are associated with serious side effects, including compromising the immune system and kidney failure.

Epogen (procrit, epo, erythropoietin). Erythropoietin is produced naturally by the kidney to help improve production of RBCs. It can be supplemented by injection for low levels in the system. Patients with DBA have no problem with RBC production, in fact, they usually have very high levels. Even giving high doses of erythropoietin has been proven not to increase RBC production in DBA.

Metoclopramide (Reglan). This drug commonly used to treat reflux has shown to be somewhat effective in the treatment of DBA. A small group of patients with DBA using metoclopramide showed a 33% hematologic response rate. Metoclopramide induces the release of prolactin from the pituitary gland, thereby increasing prolactin levels. It has been proposed that prolactin may improve erythropoiesis by stimulating cells in the microenvironment of erythroblasts. Unfortunately, other studies in the US and Europe showed only a 10% response rate therefore not confirming these results of the small study.

Leucine (L-leucine). Leucine is a branched chain amino acid (BCAA) used by muscles for energy. Amino acids are the building blocks of protein and are commonly found in food. Recently, leucine has been cited in the literature as associated with the complete response (discontinuation of transfusions) in

one DBA patient. In unpublished data, five more patients have been placed on a leucine trial with partial responses occurring in 4 of the 5 patients (either decreased need for treatment or discontinuation of treatment). Recently, funding has been secured from the Department of Defense (DOD) with the help of the DMAF to study the safety and possibility of giving leucine to 50 DBA transfusion-dependent patients. This study will open once the protocol goes through the approval processes of the DOD, FDA and hospital review board.

Other drugs undergoing investigation presently or in the near future are: *lenalidomide* (Revlimid), and drugs used for cancer treatment with a side effect of increased hemoglobin. No results are available yet.

DBA Fact #4: MANAGEMENT OF IRON WITH TRANSFUSION

Criteria for starting chelation: After receiving 10-20 transfusions, begin regularly measuring serum ferritin. If at this time serum ferritin is greater than 1000- 1500 ng/ml on two separate occasions (a month apart), start chelation. Note: **ferritin levels are elevated with any stress on the body...**the flu, a cold, virus, etc... It is considered "an acute phase reactant". Trends in ferritin should be monitored so that the gradual upwards or downward changes are considered—not the jumps likely associated with body stressors. Before starting chelation, individuals should have a baseline and yearly echocardiogram and EKG as well as hearing and vision testing.

If ferritin is high for the patient's age or in relation to the number of transfusions received, patients should be tested for the hemochromatosis gene (HFE). This disorder, unrelated to DBA, in which the body retains ingested iron can also cause serious iron overload issues and would greatly exacerbate the problems resulting from transfusions.

Iron Overload is a serious health condition that does not present with symptoms until it is too late. Some complications include: cirrhosis or fibrosis of the liver, potentially lethal cardiac arrhythmias, diabetes, reproductive organ failure, growth stunting, endocrine failure affecting the thyroid, and others. Many of the effects of iron overload are reversible, even including cardiac issues, however diabetes and reproductive failure may not be reversed.

- Dosing of **Desferal** (Deferoxamine, DFO): 40mg/kg 7 nights a week, then may taper to 5 nights a week.

A Desferal challenge may be done before starting DFO. This test requires hospital admission so that urine can be collected for 24 hours to measure iron prior to DFO therapy and again for 24 hours after DFO therapy is started to allow for iron quantification. If not enough iron is being excreted, the patient may be advised to hold off starting DFO due to high possibility of toxicity from DFO that can occur when not enough iron is present for chelation.

Desferal only works while it is being infused. Once it is disconnected, the free iron has nothing to bind to in order to be eliminated from the body. Some doctors like to use vitamin C with chelation. This can only be done with extreme caution because the vitamin C pulls iron from the tissues into circulation. If there is no DFO present in the circulation for the vitamin C to attach to, the iron will be deposited somewhere else- possibly the heart! Vitamin C should not be taken when DFO is not being infused!!!

- **Exjade** (deferasirox) dosing is 20 mg/kg and may be escalated to 40 mg/kg (maximum dose). Exjade works well to maintain iron balance, but it does not bring ferritin levels down very quickly. Exjade may be used at the same time as DFO (i.e. DFO 12 hrs over night, then Exjade in the morning).

DBA Fact #5: WHAT YOU SHOULD CONSIDER BEFORE SCT (stem cell transplantation/bone marrow transplant):

Determine what your reasons are for considering a transplant. Is it because you **want** it? Are you sick and tired of transfusions and chelation or steroid therapies so that your quality of life is significantly diminished? Or is it because you **need** it? Maybe you have developed antibodies, making it impossible to find a compatible blood donor and you are resistant to steroids therefore removing them as a treatment option. Maybe you have developed aplastic anemia or myelodysplastic syndrome (MDS) - other bone marrow failure syndromes affecting red cells, white cells and platelets. Maybe you are limited to transfusion therapy because steroids do not work for you however you also have the hemochromatosis gene, thereby compounding your iron loading issues.

You should talk with someone who has been through the transplant process and absolutely speak to your hematologist in detail. Please call the DBAR (877-DBA-NURSe), as we have the most experience and information about the outcomes of these types of transplants. Dr. Vlachos has spoken to transplant doctors in other states and has even stopped transplants from taking place as she felt it was too much of a risk. More information regarding transplants can be found at www.marrows.org.

The benefits must outweigh the risks.

Risks:

Death may occur due to complications of GVH, rejection, and infection.

Graft vs. Host Disease (GVHD) - the donor cells can actually attack different parts of the recipient's body. It is the body's natural defense to fight the donor marrow as it is seen as "foreign." GVH of the skin can cause a rash, discoloration, peeling and sloughing. GVH of the gastrointestinal system can cause the GI tract (from the mouth to the anus) to slough off causing sores and diarrhea.

Rejection can occur when the recipient immune system is strong enough to reject the donor cells. This happens sometimes in "mini transplants."

Infections may be severe and can even be life-threatening if the patient contracts a simple cold or virus. For a time after transplant, caution must be taken to ensure that all food is well-cooked and the patient may need to temporarily avoid fresh fruits or vegetables and fast food until the immune system recovers completely.

Having DBA carries a slightly increased risk of cancer. In that a transplant requires chemotherapy, which is associated with later cancers, an individual undergoing transplant may increase their cancer risk. Chemotherapy can also cause the inability of the reproductive organs to work correctly possibly resulting in infertility.

Donors need to be carefully screened. In the past, there have been rare incidents of individuals unknowingly receiving donor cells from relatives who have "silent" DBA resulting in the return of DBA following transplant. The donors had the same gene as the patients, but were asymptomatic meaning that the donors were not anemic and did not have the congenital anomalies sometimes associated with DBA therefore they did not know that they also had DBA at the time of transplant. A transplant of this nature is not successful.

Benefits:

A successful transplant eliminates the ongoing need for transfusions and steroids for the treatment of anemia. It does not eliminate the 50% possibility of passing it on to offspring or the other risks associated with DBA. DBA is in every gene of the body. A transplant "fixes" the bone marrow production of red blood cells, but does NOT "cure" all aspects of DBA.

DBA Fact #6: RECOMMENDED LABS FOR CHRONICALLY TRANSFUSED PATIENTS:

Endocrinologist, Dr. Irwin Klein, at the Feinstein Institute for Medical Research, has done extensive research studying heart disease in relation to thyroid dysfunction. In that DBA patients who are chronically transfused have thyroid issues due to iron overload, Dr. Klein has taken an interest in working with us to prevent thyroid disease as well as cardiac failure due to thyroid dysfunction. As we know, other endocrine organs besides the thyroid are also affected by iron overload including the pancreas, gonads and pituitary. Linear height is also affected by iron overload.

Labs recommended to monitor and prevent the devastating effects of iron overload in the thyroid and heart and to monitor for the effects of diabetes:

- **total T3**
- **total T4**
- **TSH**
- **T3 uptake** (instead of free T4)
- **IGF-1** (monitors acute fluctuations in insulin action and determines inadequate insulin treatment or poor control of dietary intake)
- **NT-proBNP** (aids in diagnosis of left ventricular dysfunction in heart failure)
- **Antithyroid Abs** (Antithyroglobulin and AntiThyroperoxidase)
- **Fructosamine** (useful in situations where the A1C cannot be reliably measured - as with transfused persons)
- **Vitamin D**

DBA Fact #7: THE BONE MARROW EXAMINATION - WHAT IS IT AND WHY SHOULD IT BE DONE

The bone marrow is the "factory" where hematopoiesis (the production of the red blood cells, white blood cells and platelets) takes place. A bone marrow examination is a test that looks at the cells in the bone marrow, to determine how many there are and what they look like. The bone marrow is found in the center of the bones and is made up of both spongy bone and liquid marrow.

Most of the time, the information from the bone marrow exam can be useful in diagnosing DBA and may help rule out other disorders which may cause a change in the marrow (such as leukemia, aplastic anemia or myelodysplastic syndrome (MDS)). A bone marrow examination is usually done to make the initial diagnosis of DBA. If this hasn't been done, it is recommended before starting steroids as the medicine can change the appearance of the cells. Aplastic anemia, acute leukemia and MDS have been reported in individuals with DBA. For this reason, we perform a bone marrow evaluation if there has been a change in blood counts seen on the complete blood counts (CBC), such as a steady decrease in white blood cell count or platelet count. We do not perform routine yearly bone marrow exams in patients whose blood counts are stable and have not changed.

A Bone Marrow Aspirate is usually done from the posterior (back) hip (iliac) bone. Rarely it can be done from the anterior (front) hip bone or the chest bone (sternum). The area to be used is numbed with a topical anesthetic, usually lidocaine. The area is then sterilized and a needle is placed into the bone. Liquid marrow is removed with a syringe and sent for the following tests:

Morphology of the bone marrow is usually done by the hematologist, the pathologist or both. This is where the bone marrow is spread on a slide and stained with special stains that will "color" the blood cells making them easier to identify under the microscope. The cells are counted and viewed for their appearance. Abnormalities in the number of cells can give information about the potential of aplastic anemia (too few cells of all three cell lines) and abnormalities in their shapes or sizes can be important in diagnosing myelodysplastic syndrome or leukemia.

Cytogenetics is the study of the structure of DNA within the cell nucleus. This is done in two parts: karyotyping provides information about the number of chromosomes. A normal person has 23 pairs of chromosomes; one of those pairs is XX (female) or XY (male). An extra chromosome (trisomy) or a missing chromosome (monosomy) will indicate a disease process (for example, an extra chromosome 21 is associated with Down Syndrome). Fluorescence in situ hybridization (FISH) provides researchers with a way to see and map the genetic material in an individual's cells, including specific chromosomes or portions of chromosomes.

A bone marrow biopsy can be done at the same time as the bone marrow aspirate. A piece of the spongy bone is removed, usually using the same needle and puncture area. The biopsy specimen is removed and sent to pathology for testing to determine:

Cellularity – the percentage of cells in the specimen. Bone marrow contains hematopoietic stem cells and fat cells. If a sample is hypocellular it has fewer than the expected number of hematopoietic cells (cells that mature into red blood cells, white blood cells and platelets). If a sample is hypercellular it has more than the expected number of hematopoietic cells. Cellularity is age dependent. In newborns all marrow is hematopoietic (shows 100% cellularity). With aging, hematopoiesis (the number of cells) decreases and the amount of fat increases. Normal cellularity of an adult bone marrow ranges between 30-70% and changes under pathological conditions. Marrow is reported as hypercellular (over 70%), normocellular (30-70%) or hypocellular (under 30%).

DBA Fact #8: PORTS

Some things to consider when having a port placed:

A port is a small medical device placed under the skin and is used to infuse fluids for medical treatment into the blood stream and to also withdraw blood from a large vein. It is accessed with a special needle, in usually one stick. Its parts include a reservoir with a septum (area where the needle is inserted) and catheter. The special needle used to access it is called a 'huber' needle. It has a 90 degree bend so it is comfortable when in use and is 'non coring,' which means it won't leave a hole when the needle is removed.

A port may sometimes be referred to as a port-a-cath, mediport, or passport. The name varies depending on the manufacturer as does the size and materials it is made of. Most port reservoirs are made of stainless steel, titanium or plastic.

For anyone who may need to have a cardiac MRI to look for iron overload, we recommend a plastic port so it does not interfere with the results. If it cannot be plastic, placement outside the scanning field is recommended (such as right side of chest). If your hospital does not use plastic ports, they can be special ordered.

The reservoir has a silicone septum which allows it to be punctured with a special needle-- hundreds of times. It is self sealing so it does not leak when the needle is taken out. The catheter, which attaches to the reservoir, is made of a soft, bendable silicone or polyurethane. The surgeon must make a pocket for the reservoir under the skin, usually in the chest area. Speak to your surgeon to decide on the area that is best for you. Your options for placement are upper chest, over the ribs (under the breast), or sometimes in the forearm. The catheter is then threaded through a major vein and ends at the superior vena cava of the heart.

Poor IV access when receiving monthly blood transfusion is one reason for placing any type of central venous access device (CVAD). Other reasons may be for delivery of chemotherapy, IV nutrition, antibiotics or dialysis. A Broviac (Hickman, Groshong) is another type of CVAD in which the access point is outside of the body. This type of 'tunneled catheter' is what is used during stem cell transplantation. A peripherally inserted central catheter (PICC) is another type of external catheter that is used for temporary IV access.

Benefits:

IV's can be started quickly and relatively easily without repeated needle sticks. You can continue to bathe and even swim with a port once the surgical incision has healed. A numbing cream can be applied to the port site 30 minutes before accessing it to avoid feeling the pinch.

Some homecare agencies will not provide 24/7 Desferal therapy if the individual has an IV that is not a central line.

Possible Complications:

Infection – a severe bacterial infection can compromise the device, require its surgical removal, and seriously jeopardize health. To prevent infection, these ports are accessed using a sterile technique, and the needle should be changed once a week. An individual experiencing a fever should seek medical attention immediately so blood cultures can be obtained (sometimes from the port and from a vein in the arm). Antibiotics need to be given through the port right away to prevent sepsis- a serious life threatening blood infection. If receiving 24/7 IV therapy, the dressing must stay dry, and the needle should be changed weekly to prevent any bacteria from growing.

Thrombosis – is a formation of a blood clot in the catheter which may clog the port. To prevent clotting, the port should be flushed with saline and heparin after being used for treatment or a blood draw by a nurse, other medical professional or by the patient or family member that has been properly trained. The port should be flushed at least once every four weeks if not being used.

If a *thrombin sheath* forms at the tip of the catheter (forms a kind of flap) blood is not able to be withdrawn. The catheter can still infuse because the flap is pushed away by the pressure of the fluid. In the future, this may become a complete blockage or become a source of infection.

Mechanical failure – sometimes when withdrawing blood, the tip of the catheter is pulled against the wall of the vein and no blood is able to be withdrawn as a result of too much suction. The catheter can still infuse as it is pushed away from the vein wall with the pressure of the fluid.

Infiltration – if the needle is not placed through the port septum, the infused fluid can leak and cause pain, swelling and sometimes redness in the area surrounding the port.

Age – If the device is put into a child, the child will eventually grow to render the catheter too short as the end of the tubing moves away from the superior vena cava. The port will need to be removed or replaced.

Complications can occur during surgery, so be sure to speak to your surgeon and anesthesiologist about your medical history. Always weigh the risks and the benefits of any medical intervention.

When deciding which port is right for your needs, patients are advised to contact Ellen so that she may provide guidance on a more personal level.

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Research in Progress... Opportunities for Patient Participation

The DBA Registry: A Vital Tool for the Study of DBA – The Feinstein Institute for Medical Research, Manhasset, NY and the Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY

1. Entity

The Diamond Blackfan Anemia Registry (DBAR) has been led by Dr. Adrianna Vlachos, pediatric hematologist, since its inception in 1991. It is housed at the Feinstein Institute for Medical Research and the Steven and Alexandra Cohen Children's Medical Center of New York. Joining Dr. Vlachos in the data management and analysis are Dr. Jeffrey Lipton, also a pediatric hematologist, and Eva Atsidaftos, CCRC, the clinical research coordinator. The DBAR has been instrumental in better describing DBA, studying responses to various therapies, evaluating the outcomes of stem cell transplants, and investigating remission occurrence, cancer predisposition, birth defects and gene discovery. Reports of transplant outcomes, the rate of remission and cancer predisposition using data from the Registry data have been presented at national meetings and published in prominent journals. Over the past 7 years the DBAR has been funded by the National Heart, Lung and Blood Institute of the Institutes of Health.

The DBA DNA Biorepository was established in 2006 and all 80 ribosomal protein genes were studied in the first 75 patients enrolled through a grant from the DNA Resequencing and Genotyping Service of the National Heart, Lung and

Blood Institute. Blood samples collected from the DBAR patients were essential for the discovery of 9 of the published genes. To date there are over 135 patient samples in the Biorepository. The samples for which no gene mutation was found were then included in the next gene discovery studies. The DBAR and its research colleagues (Drs. Jason Farrar and Robert Arceci of Johns Hopkins and Dr. David Bodine of the National Human Genome Research Institute) were the first to describe gene deletions in areas of ribosomal protein genes. This has accounted for a total of 70-75% of gene mutations and deletions found in the DBA population. A new study (described below and sponsored by the DBA Foundation) will proceed with whole exome sequencing of those remaining 25-30% of patients who do not have a defined gene mutation or deletion. The goal is to identify more genes that are responsible for DBA and its symptoms.

2. Patient benefits

Although there may be no direct benefits to the patient for participating, being part of the DBAR and sharing medical information allows the researchers to learn more about this very rare disease and may ultimately lead to better treatment options for all those affected.

3. Criteria for admission

All patients with Diamond Blackfan Anemia are eligible for enrollment into the DBAR. There is no age requirement or limit. Patients can be enrolled at diagnosis or anytime thereafter, even into adulthood. Parents of pediatric patients

Continued on Page 12

will sign consent on behalf of their child. At the age of 18 years, patients will be asked to consent for themselves. Enrollment involves signing consent for participation and completing a comprehensive questionnaire. The DBAR will accept medical records and will assist the patient/parent/physician in completing the questionnaire. All members of a family with DBA will complete their own questionnaire. There is no cost to participate in the DBAR.

4. Contact information

Eva Atsidaftos, CCRC

c/o Vlachos Lab

Diamond Blackfan Anemia Registry

Feinstein Institute for Medical Research

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Manhasset, NY 11030

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eatsidaf@nshs.edu

A Strategic Approach to Gene Discovery in Diamond Blackfan Anemia – The Feinstein Institute for Medical Research, Manhasset, NY and the Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY

1. Entity

The DBA Foundation awarded a grant to the DBAR and the National Human Genome Research Institute to continue with the gene discovery project as noted above. Patients for whom no gene mutation has been identified by commercial or research means are eligible for deletion testing using new SNP array technologies. If a gene deletion is not identified, then the patient becomes eligible for the next part of the study using whole exome sequencing technology. The DBAR is trying to make observations connecting symptoms and response to therapy with specific DBA genes.

2. Patient benefits

Direct patient benefits are to identify all members of the family with DBA by gene mutation/deletion identification. This can assist with choosing appropriate transplant donors, making reproductive choices as well as identifying possible 'silent' family members with a DBA gene mutation that do not have signs of anemia.

3. Criteria for admission

All patients with Diamond Blackfan Anemia that do not have an identified gene mutation are eligible for enrollment into this study. There is no age requirement or limit. There is no cost to participate.

4. Contact information

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Phase I/II, Open-Label Study to Determine Safety and Efficacy of Sotatercept (ACE-011) in Adults with Red Blood Cell Transfusion-Dependent Diamond Blackfan Anemia – The Feinstein Institute for Medical Research, Manhasset, NY and the Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY

1. Entity

Patients with DBA are usually treated with red cell transfusions or corticosteroids, however the DBAR is searching for new potential treatments for DBA. Sotatercept is a drug that has been shown to increase bone mass, however its side effect of increasing hemoglobin levels poises it to be a investigational treatment for DBA. A new clinical trial (sponsored by Celgene Corp.) has opened to investigate the safety and dose-efficacy of sotatercept in adult transfusion-

dependent patients with DBA. The patients will be monitored for a complete response (defined as transfusion-independence and hemoglobin >9 gm/dl) or a partial response (defined as an increase in transfusion interval from baseline, and hemoglobin < 9gm/dl with an increase in reticulocyte count). Patients will also be monitored for safety of the drug by assessment of adverse events and relationship to sotatercept, time to response and duration of response. The drug sotatercept will be given as a subcutaneous (under the skin) injection once every 4 weeks for 4 months.

Estimated Enrollment: 20

Study Start Date: March 2012

Estimated Study Completion Date: March 2013

2. Patient Benefits

The patient may benefit by becoming transfusion independent or by requiring fewer transfusions. There is no guarantee that the anemia will improve as a result of your participation in this study. The anemia may stay the same or potentially get worse during the study.

3. Criteria for admission

Inclusion Criteria:

- Must be 18 years of age or older and diagnosed with Diamond Blackfan Anemia
- PRBC transfusion-dependent (defined as ≥ 10 cc/kg of RBC per 28 days average)
- Use birth control (if a female of childbearing potential) or use a latex condom (if a male) during any sexual contact with females of childbearing potential during study participation and for 112 days following the last dose of sotatercept

Exclusion Criteria:

- Evidence of renal impairment or hepatic failure
- Evidence of heart disease or significant history of uncontrolled hypertension
- Currently responsive to corticosteroids for treatment of Diamond Blackfan anemia
- Treatment with another investigational drug or device <56 days pre-study entry
- Pregnant or lactating females
- Cancer

4. Contact information

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The Use of Novel Therapies to Reconstitute Blood Cell Production and Promote Organ Performance, using Bone Marrow Failure as a Model – The Feinstein Institute for Medical Research, Manhasset, NY and the Steven and Alexandra Cohen Children's Medical Center of New York, New Hyde Park, NY

1. Entity

As mentioned, patients with DBA are usually treated with red cell transfusions or corticosteroids. The DBAR is searching for new potential treatments for DBA. Another potential drug treatment for DBA is Leucine. Leucine, one of the branched chain amino acids, is used as a protein supplement by athletes for muscle building. It has been used in the Czech Republic in a few patients with one patient attaining a remission and the others able to increase their transfusion interval, or decrease their steroid doses. It has been used in patients with other diseases without toxicity when given orally.

The DBAR has secured funding from the Department of Defense for a clinical trial for the use of Leucine in patients with DBA who are transfusion dependent. The goal is to determine safety and effectiveness of Leucine in DBA patients. The patients will be monitored for a complete response (defined as transfusion-independence and hemoglobin >9 gm/dl) or a partial response (defined as an increase in transfusion interval from baseline, and hemoglobin < 9gm/dl with an increase in reticulocyte count). Patients will also be monitored for safety of the drug by assessment of adverse events and relationship to leucine, time to response and duration of response. Leucine will be given orally three times a day for 9 months.

2. Patient Benefits

Leucine may increase hemoglobin and red blood cell production which may or may not affect your standard treatment for DBA (for example, less frequent transfusions or no need for transfusions). The duration of any effects and the chances of response are unknown. We cannot and do not guarantee or promise that you will receive any benefits from this study.

Estimated Enrollment: 50
 Study Start Date: Spring 2012
 Estimated Study Completion Date: Summer 2013

3. Criteria for admission

Inclusion Criteria:

- At least 2 years of age and be diagnosed with Diamond Blackfan anemia
- PRBC transfusion-dependent (defined as ≥ 10 cc/kg of RBC per 28 days average)
- Remain on his/her transfusion schedule for the duration of this study without any other DBA medications. Iron chelation medications will be allowed.
- Adequate renal function.
- Negative serum pregnancy test if the patient is a menstruating female and documentation of adequate contraception.

Exclusion Criteria:

- Known hypersensitivity to branched chain amino acids
- Evidence of renal impairment or hepatic failure
- Pregnancy, or plans to become pregnant during duration of trial

4. Contact information

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New Gene Discoveries and Biology of Ribosomes in DBA – Children’s Hospital, Boston, MA

1. Entity

As part of The Manton Center for Orphan Disease Research at Children’s Hospital Boston, Dr. Hanna Gazda and her team are conducting research to identify and understand the genes involved in Diamond-Blackfan Anemia (DBA). Dr. Gazda’s lab has screened 79 ribosomal protein (RP) genes for mutations in DBA and identified mutations in seven of the ten RP genes (RPS24, RPL5, RPL11, RPS7, RPS10, RPS26 and RPL26) which cause DBA. In collaboration with the group from Johns Hopkins, they also found mutations in the eighth ribosomal protein gene, RPL35A. Recently, they have started using an advanced technology called whole exome sequencing (in collaboration with the Broad Institute in Cambridge, MA) to screen all known genes and identify the remaining DBA genes. Dr. Gazda’s lab also plans to perform screening to identify modifier genes. These are genes which affect the clinical features of DBA and cause patients with the same mutations to have different clinical symptoms. All families with DBA, whether or not they have a known mutation, are welcome to participate.

The Refrigerator Door



Tyler Green, age 10, shares his inspirational artwork.



Trevor Mancuso’s artwork entitled, “Best Friends”.

2. Patient benefits

- Participants are screened for the 10 genes known to be associated with DBA. Approximately 55% of individuals with DBA will have a mutation identified in one of these genes.
- If a mutation is not identified on the initial screening, the lab is using advanced technology, including whole exome sequencing, which tests all of the person’s genes, in hopes of identifying the remaining genes associated with DBA.
- Knowing the mutated gene can be beneficial for reproductive choices, stem cell transplantation, and in the future for better treatments.
- Even if a mutation in a gene causing DBA has been identified either through clinical testing or by Dr. Gazda’s lab, there are still benefits to participating. For example, participants’ samples are used to study modifier genes which affect the clinical features of DBA and response to treatments.

3. Criteria for admission

Eligible participants include individuals with DBA and their family members. As mentioned, this includes those who have a known mutation in a DBA gene or those who are participating in other research studies. There is no cost to participate in our study and travel is not required.

4. Contact information

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 www.childrenshospital.org

Etiologic Investigation of Cancer Susceptibility in Inherited Bone Marrow Failure Syndromes (IBMFS) – Rockville, MD

1. Entity

A team of specialists, led by Dr. Blanche Alter, are studying bone marrow failure disorders at the National Cancer Institute’s Clinical Genetics Branch - a Division of Cancer Epidemiology and Genetics at the National Institutes of Health.

2. Patient benefits

- The patient and his/her family members may be invited to spend a week at the NIH where they will meet with various specialists experienced in the study and treatment of DBA.
- The entire immediate family will undergo comprehensive evaluation including clinical evaluation and laboratory testing, cancer screening and epidemiologic studies.
- The affected patient will also participate in bone marrow studies.
- Gene identification, mutation analysis and genetic counseling services are included.

- Treatment is not provided, however advice about proper management is offered.

3. Criteria for admission

Patients with DBA that have been diagnosed by molecular and/or clinical exam are eligible to participate in this study.

4. Contact information

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Research Nurse and Study Coordinator

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www.marrowsfailure.cancer.gov

A Pilot Study of Lenalidomide (Revlimid) in Adult Patients with Red Blood Cell Transfusion – Dependent Anemia- Stanford University Medical Center, Palo Alto, CA

1. Entity:

The rationale for evaluating lenalidomide in DBA comes from the study of an acquired form of bone marrow failure named myelodysplastic syndrome (MDS). Although DBA is inherited, and MDS usually develops in older adults, they share several clinical and laboratory features: poor production of red blood cells often leading to a need for frequent blood transfusions, and a somewhat increased risk of developing acute leukemia. Iron overload from chronic red blood cell transfusions is a common and serious problem. Mutations in more than 10 ribosomal proteins have now been identified in greater than 50% of DBA patients and are now implicated as the cause of the disease. In a very important report published in Nature in 2008, Dr. Benjamin Ebert and colleagues at Harvard discovered that loss of the gene encoding ribosomal protein S14 was critical to the cause of a form of MDS called 5q- syndrome. In this subtype of MDS, a region of the long arm of chromosome 5 is missing, and ribosomal protein gene S14 is located in this missing segment. This was an unexpected and important finding, since it was the first time that a common biologic link was found between DBA and MDS.

2. Patient benefits

In patients with 5q- MDS who depend on red blood cell transfusions, the oral medication lenalidomide (Revlimid) can eliminate the need for transfusions in 70% of subjects. Given the outstanding red blood cell response rate to lenalidomide in 5q- MDS in which loss of ribosomal protein S14 has emerged as an important discovery, there is a strong reason for investigating lenalidomide in DBA in which ribosomal protein deficiency is also linked to impaired red blood cell production.

3. Criteria for admission

Inclusion criteria:

- Age ≥ 18 years at the time of signing the informed consent form.
- Red blood cell transfusion-dependent with a requirement of at least one unit of RBCs per month for the 2 months prior to study enrollment (e.g. 2 units/8 weeks)
- If applicable, ongoing therapy with a stable or decreasing dose of prednisone < 60 mg/d or corticosteroid equivalent, for which there has been no treatment-related improvement in RBC transfusion requirements for at least 2 months prior to study entry
- Laboratory test results within these ranges:
 - Absolute neutrophil count $\geq 1000/\text{mm}^3$
 - Platelet count $\geq 100,000/\text{mm}^3$
 - Serum creatinine ≤ 2.0 mg/dL
 - Direct bilirubin ≤ 1.5 mg/dL
 - AST (SGOT) and ALT (SGPT) ≤ 2.5 x upper limit of normal
 - Disease free of prior malignancies for ≥ 5 years with exception of currently treated basal cell, squamous cell carcinoma of the skin, or carcinoma "in-situ" of the cervix or breast.
- Females of childbearing potential must have a negative serum or urine pregnancy test.
- Able to take aspirin (81 - 325 mg) daily as prophylactic anticoagulation (patients intolerant to ASA may use warfarin or low molecular weight heparin).

Exclusion criteria:

- Pregnant or breast feeding females. (Lactating females must agree not to breast feed while taking lenalidomide).
- Use of any other experimental drug or therapy (excluding steroids) specifically used for DBA within 28 days of baseline including metoclopramide, leucine, danazol, or other hormonal therapy.
- Clinically significant anemia due to factors such as iron, B12, folate deficiencies, autoimmune or hereditary hemolysis, or gastrointestinal bleeding.
- Known hypersensitivity to thalidomide.
- Concurrent use of other anti-cancer agents or treatments.
- Known positive for HIV or infectious hepatitis, type A, B or C.

Please refer to the website link: <http://www.clinicaltrials.gov> and enter the search term "Diamond-Blackfan Anemia and lenalidomide" for full eligibility criteria and additional trial information.

NOTE: BECAUSE THIS STUDY IS CURRENTLY ONLY BEING CONDUCTED AT STANFORD, WE HAVE FUNDS TO COVER PATIENT TRAVEL EXPENSES.

4. Contact Information:

Principal Investigator: Dr. Jason Gotlib, Stanford University School of Medicine

Co-Investigator: Dr. Bertil Glader, Stanford University School of Medicine

Scientific Co-Investigators: Dr. Hanna Gazda, Boston Children's Hospital/Harvard and Dr. Benjamin Ebert, Brigham and Women's Hospital/Harvard

Please contact our study nurse, Andrea Linder:

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Email: alinder@stanford.edu

Also, feel free to contact Dr. Gotlib by email: jason.gotlib@stanford.edu

"Heritable diseases of Hematopoiesis: Evaluation of cell function and creation of induced Pluripotent Stem (iPS) cells for disease modeling and design of treatment strategies." – Children's Hospital of Alabama, Birmingham, AL

1. Entity:

Drs. Fred Goldman and Tim Townes from Children's Hospital of Alabama and the Stem Cell Institute at the University of Alabama, Birmingham are inviting DBA patients and their family members to participate in an IRB-approved research project entitled "Heritable diseases of Hematopoiesis: Evaluation of cell function and creation of induced Pluripotent Stem (iPS) cells for disease modeling and design of treatment strategies."

2. Benefits to patients:

The ultimate goal of this project is to find a safer way to treat and potentially cure DBA. The current pre-clinical studies are designed to identify consequences of RPS gene mutations in red blood cell development, and to follow erythroid development in stem cells that have correction of their mutated gene.

3. Criteria Admission:

All DBA patients are eligible to participate, though preference will be for those that have known RPS gene mutations. Eligible patients and family members will be asked to undergo a small punch skin biopsy and a blood sample will also be obtained.

4. Contact Info:

For further information, please contact Dr. Goldman's research nurse, Brandy Reeve, by email at breeve@peds.uab.edu.

Welcome to the DBA Fundraising Group



Jacob & Scarlett Buckmaster hosted a "Run/Walk for DBA."



Lily Soto shows off her bodyart at the blood drive and craft sale her family organized to support the DBAF.



John & Emi Shannon do their parts to fulfill our mission by asking friends and relatives to donate to the DBAF each year instead of buying them gifts for their birthdays.



Brandi Adams is pictured with a friend at their annual "DBA Fishing Journey".



Christopher Vroman poses with star host, Matthew Pulnik, at the 2nd Annual "Fun Day for DBA."

We invite you to share ideas, post photos, announce fundraising events, and celebrate fundraising for DBA successes.

<https://www.facebook.com/groups/381623081865086/>

Our Inspiration

by The Mancuso family

Throughout the last five years, people have often asked us why we hold fundraisers to which we logically answered, "because our son has DBA." We never really thought much more about it until July of 2010 when my family and I experienced Camp Sunshine for the first time and our whole idea of what DBA meant to us was turned upside down! We were a family of five from Cleveland who had treated DBA simply as a "pill to swallow" until we came face to face with 53 other families who gathered to support and educate each other on how to navigate the bumpy road that is DBA. Initially, we felt to be outsiders as we observed the diverse emotions in that room.

We witnessed heads, held high... a sign of the toughened exteriors used to protect bullied hearts... others crying cheers of joy for reconnections made... all eyes filled with wonder about what Camp would hold for them this time...

Throughout the week we found ourselves unexpectedly conflicted. Our son had his ups and downs but never had he gone through what some of these families face on a daily basis. And then one day during Camp it hit us as we were working through a wide range of emotions... We don't fundraise just for Trevor... We do it for ALL OF THESE PEOPLE, TOO!

I realized that the children and adults who had traveled from near and far to meet on common ground - to share stories, laughter and tears - also benefit from all the work put into planning our event. Some families scraped, pinched and saved to be able to make the trip, hoping to seek comfort from the only other people in the world who "get it." They came to learn about the latest treatment recommendations, about what grants are being funded and who is working on what research to find a cure! These, also, became our reasons to fundraise.

At camp we realized that knowing that you are doing some good is one thing. But actually seeing the people you are doing good for is quite another.

As Jim and I prepare for yet another golf outing, we are filled with frustration, fear and exhaustion - enough so that Jim, every year, swears "to never do this again" ... until the day of the event, that is, when we look out upon our supporters and donors, our friends and family, and know that this is good and that this is right. Fundraising is a humbling experience that gives us a sense of pride and accomplishment and creates an overwhelming feeling of gratitude for those who support our family through our son's journey with DBA.

Fundraising is a personal matter and one that can be done in so many different ways. Jim and I choose to host a golf outing and silent auction every September. This is what works for us. What works for you may be something entirely different.

All of our families wish for a cure for DBA; mine is no different. Sadly, however, this is not a gift. First must come the shared responsibility of funding the search for a cure. And this is why we are excited to announce that the 6th Annual Friends of DBA Golf Outing and Silent Auction will take place on Saturday, September 15, 2012!

So now, when asked why we fundraise we can reflect on that first trip to Camp Sunshine and all those wonderful families - our DBA family - and say, "How can we not fundraise?"

To share thoughts and ideas about fundraising, join our group "Fundraising for Diamond Blackfan Anemia."

<https://www.facebook.com/groups/381623081865086/>

DBA National Resource Centers

Steven and Alexandra Cohen Children's Medical Center of New York Adrianna Vlachos, MD

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Hematology/Oncology and Stem Cell Transplantation
Director, Diamond Blackfan Anemia Registry
Surveillance and Awareness Program
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Ellen Muir, RN, MSN
Clinical Nurse Specialist
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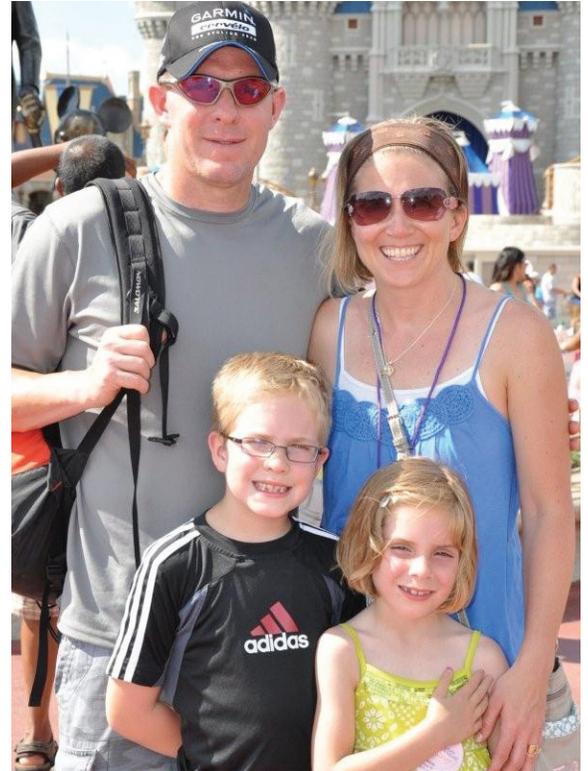
Children's Hospital Boston Colin A. Sieff, MB.BCh, FRCPath

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Children's Hospital Boston
Associate Professor of Pediatrics
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Kudos



Shelly Marquer, Kendra Kofron, Ruby Swanson, Josh Hollingsworth, Ed Fields & Kelsey Fields attended DBA Day in Seattle.



The Lamb family regularly host various fundraisers to benefit the DBAF!



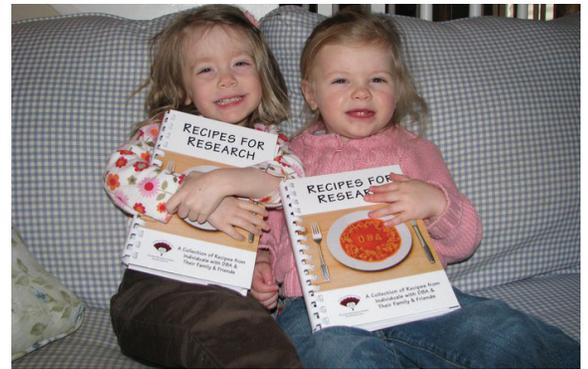
Dylan & Lena Nape enjoy DisneyWorld as part of their Make A Wish Trip!



Millidge Sisemore poses with a pig to advertise for his family's unique event held to raise money to support the DBAF's mission!



Together, the Luddy family of Vienna, VA took the ice cold plunge into Lake Anne, Veston, VA., while 2 year old DBA patient, Eliza, loved getting her little feet wet in the Chicken Dip! Hand in hand, mom, dad, brother, sisters, and cousins participated in the Virginia Polar Dip to raise money to send a DBA family to Camp Sunshine this year.



Bailey Lightner and her friend, Addison, are the DBA Foundation's cutest, most irresistible cookbook "salesladies!"



Jack Sargeant's Aunt Donna surfed a wave at 17 beaches throughout Sydney, Australia on their "Wave for a Cure" fundraiser that raised awareness \$6000 awareness for DBA! Three-year old Jack joined her on the last wave and loved it!



Logan Allen, age 5, rides a sheep at the Spokane Interstate Fair!

Scientific Advisory Board

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Workplace Giving

The Diamond Blackfan Anemia Foundation relies on the support of our friends and families to continue our mission of supporting DBA patients, families, and research.

Once again we are asking for your help. Many employers and companies offer their employees an opportunity to donate to an organization through a payroll deduction program or participate in a matching gift program. The payroll deduction programs and United Way payroll designation programs make donating easy. The matching gift programs are a great way to double your contribution! The DBA Foundation is a 501(c)(3) organization and is eligible to take advantage of these generous company-based programs.

To find out if your employer participates in a charitable giving program, it's as easy as visiting your Human Resources Department or checking the company's website. The DBAF is happy to assist you in filling out the necessary paperwork.

Over the last few years, donations received through payroll deductions and matched gifts have markedly increased. We are grateful to our donors and their employers for their continued support. We encourage everyone to take advantage of these workplace options to help maximize your charitable giving.

Please contact the DBA Foundation for further information at
DBAFoundation@juno.com

THANK YOU!

Thank You to Our Families and Friends

The Diamond Blackfan Anemia Foundation, Inc. is proud of our many accomplishments in 2011. We are grateful for the commitment and hard work of the families and friends of the following DBA patients who have supported the DBAF in 2011. Together, our wonderful families have provided the DBAF the opportunity to accomplish our mission.

We strongly encourage ALL our families to get involved. We need your partnership to continue to support ongoing research and initiatives. If you would like to make a donation, please send your tax-deductible contribution to: Diamond Blackfan Anemia Foundation, Inc. PO Box 1092 West Seneca, NY 14224. If you would like to organize a fundraiser, or would like more information, please contact Dawn Baumgardner at 716.674.2818. THANK YOU!

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* denotes deceased

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