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Diamond Blackfan Anemia Registry

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Diamond Blackfan Anemia Foundation, Inc.

DBA NEWSLETTER

Diamond Blackfan Anemia for patients...for families...for research

The Irony of Iron: Can't Live Without Enough of It. Can't Live With Too Much of It.

If the DBA community were to entitle the year 2010, "THE DBAF vs. IRON OVERLOAD" would rank superior. In fact, people are still talking about Dr. Lawrence Wolfe's direct and somewhat unsettling description of the way that extra iron, when left unchecked, utilizes a sneak attack that leaves the noncompliant begging for a second chance. Dr. Wolfe strategically used his dramatic yet effective version of the "physician scare tactic" to grab his audience by the throat, forcing even the sleepiest camper to stand to attention. For those of you who weren't able to witness his lecture in person, here is the take home message:

IRON OVERLOAD KILLS… CHELATION RESCUES.

In planning for Camp Sunshine this past summer as well as the contents of this publication, the DBAF Board purposely put *Iron Overload Education* as a top priority… the victims were far too many and the losses of late to this silent killer were almost too much to stomach. It seemed that a coup was overdue.

So with an introduction that may be a bit over-the-top, welcome to this edition of the DBA Newsletter. Prepare to be enlightened.

Kevin's Legacy

by Sally Thompson Gately

I am writing this to all DBA parents and patients, both young and old. I want you all to know what can and will happen if you get severely iron-overloaded. Hopefully you can compare the experiences our family went through with the inconvenience of keeping up with your chelation every day. If I can spare even one person the agony we went through and are still feeling, then Kevin's life will not have been in vain.

I just returned from a walk in the woods with my dogs, during which I continued to ask myself "why?", "how?" and "what could we have done differently?" --constantly. My son, Kevin Gately died on July 26, 2010 from complications of DBA and iron overload. He was 29.

He was diagnosed on October 19, 1981 at the age of three months by Dr. Jeffrey Lipton with whom some of you may be familiar. After initially being stabilized by transfusions, he was put on prednisone at diagnosis and remained on steroids until the age of 18 mos. He then returned to transfusions for a year to allow his growth to catch up, then was transitioned back to prednisone until the age of 11. At this time he was very obviously on high doses of prednisone (overweight, moon face, etc.), so in preparation for entering middle school, the doctors decided that the side-effects of transfusions would be less than those of the steroids and started him on transfusions again. He was given three units of blood every three weeks for the rest of his life.

Chelation was always a struggle for Kevin. It was as if he seemed so normal that we struggled with how anything really serious could be happening inside him. He was on desferal until Exjade became available a few years ago. On desferal he had to insert a needle in his stomach which was connected to a pump, supposedly for ten hours a night. I remember some weeks the desferal cartridge sat in the paper delivery bag untouched. We were happy when he was able to get onto Exjade. "Wow", we thought, "just a drink in the morning, and off you go not to worry about it for the rest of the day".

Continued on Page 2

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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Kevin's Legacy *Continued from Page 1*

But that wasn't the case for Kevin. He had awful diarrhea from it about a half hour after taking it and for most of the day. He said that he would take it at night but then night came around and he was busy or with his girlfriend, and it was put off until the next day, etc.

When he was young my husband or I were always with him at his transfusions. We would drive him in to the hospital in Boston the day before for the clot (cross-match) to be drawn, then arrive at the clinic the next morning and stay until around 5:00 pm when the last bag was done. He was always wiped out on the ride home but would rally soon after. I remember how we would both hold his hands when he slept in his car seat between us. He never complained. In fact, when he was really little he would even say "thank you" after the nurse put his IV in. Kevin was always very open to talking to people about his DBA. At the age of 5 he even explained all about it to our new neighbors.

He was so normal in every other way. He played little league, was in a golf clinic every summer at my parent's club, and was in a bowling league from the age of 5 from which he made great lifelong friends.

While Kevin was still living at home we could keep at him, get on his case about keeping up with his meds. We could not force it down him. Ultimately, it became up to just him to do his chelation. Kevin moved out a few times for a year or two at a time. It was difficult ceding control of being with him at transfusions to his girlfriend of the moment, but he was an adult. What can you do but teach them right from wrong and send them out into the world? I assumed that he would continue to keep watch on his ferritin counts and chelate faithfully. When we asked about it, he would always say that it was "a little high" or "it's down from last time".

Kevin's descent was quite rapid. The last weekend of June he went to New York to visit some new-found relatives around his age that he had met at family reunion last year. They eagerly drove to Times Square, but that night Kevin was so weak he had to stop and sit down every 100 yards or so. He slogged through the weekend and managed to drive himself home. He told us he felt really weak, had gained 6 pounds rapidly without eating much, and couldn't lie flat without having difficulty breathing. He tried to go to work that Monday but called to tell me he wanted to go to the emergency room (at Tufts Medical Center in Boston, his usual place) and was worried about my car- whether he should drive home and get me first. It was so like him- always concerned about others before himself. At this point he had broken up with his fiancé (another story for another day) and was living back with us. They found that he was diabetic and had a weak heart, so he was admitted. The plan was to get the fluid out of his body and start him on diuretics and a heart-healthy diet. Imagine my shock when his hematologist told me that when he had transferred from pediatrics to the adult section a few years ago, he came to them with a ferritin count of over 7000 and now it was even higher! They sent him home after six days on all kinds of drugs with strict orders not to skip a chelation. He developed a bad cough due to the heart medicine but kept up with it for 13 days until his regularly scheduled transfusion. That was July 14th.

He was admitted again because his condition had not improved with the treatment but had, in fact, deteriorated. Another echocardiogram was performed which showed that his heart was pumping much more weakly than just two weeks prior. He was extremely weak and uncomfortable and had been unable to lie flat and even sleep for many days prior. This time he was placed in the cardiac section of the hospital. The decision to be more aggressive in getting the fluid off of him was complicated by the worry that his kidneys "would not like it" if done too quickly. We were shocked to hear that Kevin might need an artificial heart "down the road".

I knew that Kevin's pediatric hematologist had threatened him with hospitalization and 24/7 high doses of desferal if he didn't get his ferritin down. Naturally, I wondered why this never happened. I'm still wondering, but that is a fight for another day. Losing confidence with the treatment in Boston, I placed a call to Dr. Lipton who is now at Long Island Jewish Hospital in New York. He told me that Kevin should be on a new protocol which is only approved in the US for certain clinics which supposedly has shown to actually remove iron from the heart. I ran it by his Boston hematologist who had already begun the process to get Kevin on it at her practice. Thinking that Kevin could get on it quicker if we got him to LIJ, she agreed that we should bring him there as soon as he was stable enough to travel.

July 21 was Kevin's 29th birthday. We convinced the doctors at Tufts to let him go home for one night, his birthday. He so missed his dog, Remy, and his family. All his cousins showed up that night to wish him a happy birthday, but he was so weak and uncomfortable that he really couldn't enjoy it. That was the last time his cousins saw him alive. We moved the recliner into his bedroom because he still could not lie flat, and, alarmingly, he stopped passing urine that night. Later he moved to a kitchen chair which was more upright. It broke my heart seeing him suffering while sitting in that kitchen chair. Eventually he went back to the recliner for a while. We decided to just get up and go around 5:00 a.m. Shortly after that, we heard him fall in the kitchen and found him lying there gasping for breath. We managed to get him onto the couch and try to get some food into him, but it was difficult. I wanted to just take him back to Boston, but he pleaded to go on to New York. That was the last time he left home.

So we made the 4.5-hour drive and arrived at LIJ at 11:00 a.m., armed with all the medical records and scans and doctor's notes that I could get my hands on. We had a nice reunion with the doctors in the emergency room. The doctor who had taken care of Kevin in pedi/hemonc for all those years, Dr. Larry Wolfe, now works with Dr. Lipton at LIJ and knew he was coming. He was moved to the Cardiac Intensive Care Unit–where our nightmare began.

They found that his levels of all kinds of things were not right and realized that he was going into kidney failure along with the heart failure. He needed to have a catheter inserted from his groin into his heart and had to lie flat for it to work. In order for him to lie flat they needed to intubate him by inserting a breathing tube down his throat. He never spoke to us again.

After they brought him back from the catheter lab they told us that they couldn't keep him sedated like they would normally do because the sedation would slow his heart even more. So, they kept him awake and gave him a small pad of paper to write on in order to communicate. The first thing he wrote to me was, "I feel so much better!"

When it became apparent that Kevin was much worse off than we ever imagined he would be, the doctors encouraged me to "gather the family". My husband, George, and son, Will, drove to the hospital and arrived around 2:30 a.m. I feel sure that when Kevin saw them there he knew something bad was up, but he kept the notes upbeat nevertheless. I will never part with that notebook. One note to my husband read, "you are the best man I know, equal with Pa". (Pa being George's father). Another, to me, read "don't cry" with a smiley face.

Kevin continued to get worse during that awful night. They tried to get him on kidney dialysis, but it wouldn't work due to his blood clotting up. We were told that they would have to insert some kind of artificial heart device to even get him through the night; but, eventually, they were able to somewhat stabilize him.

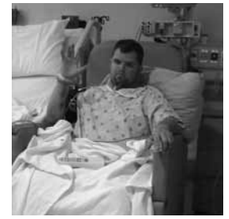
The device he really needed was not available at LIJ but was available at Mt. Sinai Hospital in Manhattan, N.Y. Due to amazing efforts from the staff at LIJ, we were able to transfer him by ambulance, still on all those machines, to Mt. Sinai the afternoon of the next day, July 23. That evening we met with the heart surgeon who told us how horrible that artificial device was going to be, but at least he would be able to leave the hospital at some point.

We told Kevin they were going to let him sleep awhile in order to get him more stable before surgery- probably within the next 48 hours- and that we were going to a nearby hotel to wash and rest up and would be back in the morning. He motioned for us to get out and take care of ourselves, which we did. It was the last time we saw him awake, and he was thinking of us.

We were awakened by a phone call at 4:20 the next morning. The surgeon wanted to know Kevin's wishes because he probably would not make it through the weekend, maybe the night, without emergency surgery. We told him to do whatever it took to keep him alive, so he was rushed to the operating room. Early that afternoon the surgeon finally gave us the news. His heart had stopped on the way to surgery, but they were able to bring him back. He was in Thoracic CICU on a heart bypass machine, kidney dialysis machine and was still intubated for breathing. He had also been on blood thinners which were making it very difficult to control the bleeding, so they were giving him blood constantly. There was no way of knowing whether he had suffered brain damage due to extended lack of oxygen. They couldn't wake him up because he would have been in too much pain, and the doctor told us that his heart had the consistency of wet cardboard.

I had been crying for days and could not stop. I could feel him slipping away from us. The next day, Sunday, was worse; they had to add an oxygenator to the bypass machine and put him on a lung machine. So at this point everything was being run by machines. We could hardly find a place to touch him as there were so many tubes in him, and his fingers and toes were getting blue due to lack of oxygen. We stayed with him as long as they would let us.

The next day, July 26, 2010, was the day he died. When we saw him we knew he was no longer with us. All of his hands and feet were blue by now. We asked for a priest to give him last rites and also to talk to his doctor. Our question to him was, "how can anyone ever recover from this?" and the answer was, "they can't". He would have never left the hospital even if he was ever able to wake up. So, we had to make the decision to stop the machines. He died a few minutes after they were turned off, feeling no pain.

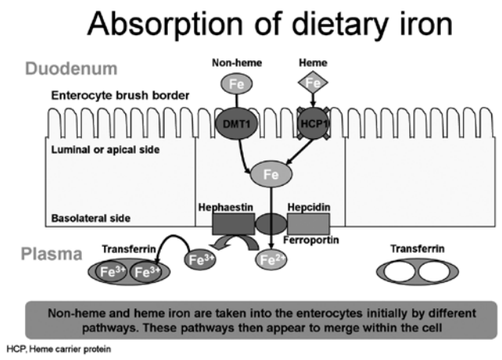


Editor's note: Inspired by love and motivated by a desire to memorialize Kevin's life and tragic death, his family and friends have established the Kevin J. Gately Foundation **(www.kjgfoundation.org)**. Their mission is to support Kevin's charitable interests and to raise awareness of DBA and the importance of compliance to treatments. We applaud their efforts, appreciate their generous support, and mourn with them in their loss.

Iron Overload 101

by Lawrence Wolfe, M.D.

This cartoon shows the absorption of iron and the shuttles and controls involved (see article below for details):



Duodenum is the inside of the tube running between stomach and intestine where iron is taken into the body

Plasma is the fraction of the blood the iron is sent to.

Non-heme and heme refer to iron from meat (heme) or from other foods (non-heme)

DMT1 and HCP1 are shuttles (guards)

Ferroportin is the door that lets iron into the blood-It is controlled by Hepcidin made in the liver.

Transferrin accompanies iron in the blood

Iron is an essential cofactor for life. It is contained in the hemoglobin molecule of red cells that transport oxygen around the body, aids in the removal of waste and is involved in a host of other processes in the body. Interestingly, despite the fact that it is absolutely essential, the body constantly surrounds iron and controls it chemically as if it were a dangerous criminal in a maximum-security prison.

The iron in our diet enters the digestive system through the intestines. It is accompanied by a shuttle and must pass by a border guard, ferroportin. Ferroportin takes its orders from a chemical made in the liver that, through a series of complex processes, dictates how much iron can enter. Controlling the amount of iron that is introduced by food is the body's mechanism to manage iron load. This system is tightly guarded as it is the only way that one's iron level can be affected. Said another way, **Key point #1: The body controls the amount of iron coming in because it is completely unable to get any iron to leave the body.**

Iron is carried throughout the body by a molecule called transferrin. Storage areas for iron are vital to provide some reserve in the case of the absence of iron-containing food or to offset iron losses from bleeding episodes (such as menstrual periods). The major form of iron storage is through a molecule called ferritin.

DBA and Stem Cell Transplants at a Glance

Dr. Adrianna Vlachos, M.D. presented statistics from the DBAR at a lecture at Camp Sunshine this past summer.

According to the literature, as of 2009, there have been approximately 100 stem cell transplants (SCT) in DBA patients, and 54 of these patients have reported to the DBAR enabling their clinical data to be analyzed. Thirty-two of these received donor cells from a matched sibling and twenty-two had alternate donors. Matching a donor to the recipient is done by attaining blood samples in which HLA (human leukocytic antigens) found on chromosome 6 are analyzed. A full match is when all 10 donor and recipient HLA are identical. Within a family, there is a 25% chance that one child will match another (10/10). If a sibling donor is not available, possible options to find a potential donor include bone marrow and cord blood registries.

The majority of DBA transplants were myeloablative meaning that full, traditional doses of chemotherapy were used to condition patients. There have also been six non-myeloablative (reduced-intensity) SCTs recorded by the DBAR. Reduced-intensity SCTs often result in a greater likelihood of graft rejection, thus they are reserved only for those patients who are older or are unable to withstand a traditional preparatory regimen.

Survival rates of related sibling donor transplants are broken down to those under nine years old (94%) and for those older than nine (55%). Historically, matched sibling donors were far more successful, however much improvement has been made in unrelated donor transplants since the year 2000 where survivability has reached 86% (for all ages).

The four major factors that go into a successful SCT include achieving a stable engraftment of donor marrow, preventing graft vs. host disease (GVHD), restoring normal immunity and establishing graft tolerance. Achievement of these milestones takes years in which some typical problems related to SCT can be life-threatening including: graft rejection, opportunistic infections, GVHD, therapy-associated toxicities and recurrent malignancy.

In regards to minimizing the risk of infection, transplant centers focus heavily on prevention by installing laminar air flow systems or HEPA filters, enforcing a clean/sterile environment, requiring the patient to perform regular mouthcare and observe gut decontamination measures through a restricted and cooked diet. Another important factor in avoiding infection is the prophylactic use of antibiotics, antifungals and antivirals.

GVHD, can occur in the skin, liver and/or GI tract and can be of the acute (onset within 30 days of transplant) or chronic form (appears 2-12 months post transplant). Prevention of GVHD is attempted by using the best match possible preferably from a young donor, maintaining the patient in a protective environment, and effective immunosuppression of the donor cells to allow the recipient to become "trained" to accept the donor cells. Another measure, T cell depletion, is being performed in some centers where a portion of the T cells from the donor cells are removed prior to transplantation in hopes of reducing the risk of GVHD.

The main therapy-associated toxicities include veno-occlusive disease (VOD) of the liver, idiopathic interstitial pneumonitis, infertility, endocrine failure (possibly resulting in gonadal dysfunction, thyroid and growth hormone deficiencies and diabetes) and recurrent malignancies (cancers caused by chemotherapy treatment). DBA patients, due to the likelihood of building antibodies as a result of chronic blood transfusions, have a potentially increased risk of graft rejection as well as an increased risk of developing VOD due to iron overload in the liver.

Editor's Note: *This article is not meant to be comprehensive or to replace conversations with experienced physicians but is meant to provide an overview of the SCT process so to help to prepare families for discussions with medical professionals.*

DBA and Cancer

Those present at Camp Sunshine were fortunate to receive up-to-date information on the relationship between DBA and cancer occurrence from the NIH.

Dr. Blanche Alter from the National Cancer Institute of the National Institute of Health reports cumulative cancer risk data as collected from DBA patients from 1936-2009 as "better than we first believed". According to the literature pertaining to DBA and cancer occurrence during this time period, of the 967 DBA patients, 31 cases of cancer (30 persons, one of which had 2 types of cancer) have been reported for a crude rate of 3.1%. It is noteworthy to mention that those DBA patients who developed cancer did so at a younger than average age as compared with the general population.

Historically, case reports have led researchers to believe that the rate of MDS and AML as well as solid tumors in DBA patients would be higher—as is seen in other inherited bone marrow syndromes (IBMFS). Dr. Alter's NCI cohort data provides the first direct comparison of Diamond-Blackfan anemia with Fanconi anemia (FA), dyskeratosis congenita (DC), and Shwachman-Diamond syndrome (SDS) in a single cohort by the same investigators, consultants, laboratories, outcomes, and statistical analysis. The data showed that persons with DBA might have a slightly increased risk of cancer but not as high of a risk as the other IBMFS. The relative risk in DBA compared with the general population was 3-fold, compared with 11-fold in DC and 39-fold in FA. However, because of the small number of neoplasms in DBA, the data are not statistically significant. Alter admits that bias still exists as many cases of cancer do not get reported to the NCI, especially those types that are less prevalent. Also limiting is the small enrollment number of DBA patients as well as the fact that many persons who have DBA in a milder form or those not requiring treatment are not as likely to join studies such as this. Additionally, data from children with DBA who present with cancer at children's hospitals are likely to be included in the cohorts at their corresponding centers and not referred to the NCI study.

Dr. Alter also reported on the data that exist at the NCI examining the possible link between DBA, cancer and the use of growth hormone. Based on limited data, of the 6 DBA patients reported in the literature who presented with osteosarcoma, half had a history of growth hormone use. Though the data is inconclusive, Alter advised that extreme caution be exercised when investigating this option, as both the Growth Hormone Research Society and the American Academy of Clinical Endocrinologists post warnings to the use of growth hormone. Certain patient groups seem to have a high intrinsic risk of malignancies in which the use of replacement growth hormone may complicate the interpretation of these risks.

The DBAF would like to thank all of our DBA families who have enrolled in this NCI study. Without your participation, the relationship between DBA and cancer will continue to be misunderstood. Dr. Alter frequently referred to how the small cohort affected the interpretation of this very important data, so it is our hope that more of our families will enroll in studies such as this so that we all might benefit. Knowledge is power.

Iron Overload 101 *Continued from Page 3*

The transfusions many patients with DBA receive contain large amounts of iron. Each full unit of blood contains approximately 200mg of iron. As mentioned, the body can only control the dietary intake of iron. **Key point #2: The act of blood transfusions, although life-giving, circumvents the body's only means of control over the accumulation of iron.** After the body has accumulated many grams of iron, it begins to run out of prison cells to hold the iron (ferritin in the liver and spleen) and corrections officers to escort iron when it leaves its prison (transferrin). Subsequently, a condition known as iron overload occurs.

Iron overload damages the body in a number of ways. The iron that breaks out of prison and is no longer escorted in the blood stream travels in the body unguarded and is referred to as Non-Transferrin Bound Iron (NTBI) and enters other organs including the master gland (pituitary), the pancreas, the liver, joints and the heart. Upon entering each cell, a chemical reaction called the Fenton Reaction occurs that begins a process of injury to individual cells, which, if untreated, leads to dysfunction, failure of organs and the death of the patient. **Key point #3: Failure to prevent or treat ongoing iron overload always leads to organ damage, organ dysfunction and death.**

The organ systems involved include: the heart- leading to heart failure, the liver- leading to cirrhosis and liver failure, and the pancreas- leading to difficult-to-treat diabetes, infertility and glandular disturbances (such as low thyroid hormone, problems with calcium and bone metabolism and low sex hormone levels).

Since many patients with DBA need chronic transfusion therapy to survive, determining iron status as well as investigating the options available to remove iron from the body is necessary. Currently the following modalities provide markers of iron status: saturation of transferrin (are there enough corrections officers?), serum ferritin (are the prisoners breaking out of jail?), liver iron concentration which is obtained by biopsy or indirectly by imaging and, finally, iron distribution in the liver, pancreas and heart as determined by MRI-magnetic resonance imaging.

Most physicians rely on serum ferritin obtained from a blood sample to determine the presence of iron overload. A correlation exists, allbeit crude, that a ferritin greater than 1000 nanograms/ml is indicative of iron overload. Monitoring serum ferritin proves valuable to determine when to initiate treatment for iron overload. This marker is also a useful way to analyze trends in a patient's iron load. Utilizing ferritin values as an indicator has been validated over time, but it has drawbacks as well. Ferritin is affected by a number of factors; and there is a small group of patients with low ferritin levels who present with significant iron-loading in their organs. Deciding when to initiate treatment to remove iron involves a number of factors including the total amount of blood transfused, and the serum transferrin and ferritin levels (ferritin levels up to 2500ng/ml is moderate overload, greater than 2500ng/ml severe). More complicated is determining if the treatment program is effective. For this reason, and because of all the extraneous factors that can influence serum ferritin, other forms of testing have evolved.

The gold standard of iron testing is through a liver biopsy, a course of action which should be considered in patients with borderline ferritin levels or evidence of liver injury. A biopsy can also give a true picture of the extent of organ damage as well as iron content. In addition to the invasive procedure of liver biopsy, less invasive methods are now available. Magnetic technology, the most widely available being Magnetic Resonance Imaging, used to evaluate the target organs (heart, pancreas and liver) is a reliable means of monitoring iron load. **Key point #4: Non invasive testing has developed to the point where an MRI of the liver and pancreas and a special MRI of the heart can actually predict a patient's risk of organ dysfunction or death from iron overload.**

For patients at high risk for organ damage or death there are aggressive treatment programs (even for patients who have not received or complied with proper treatment), which can successfully reverse some of these toxicities. **Key point #5: Although treatment exists for patients who have become seriously iron overloaded, it is critical to prevent transfusion-induced iron overload, rather than try to treat it after severe iron loading has occurred.** However, one should never give up on a patient in heart failure. Although patients in heart failure are very likely to succumb, the approach of supporting the heart by all means available while chelating aggressively has salvaged many patients.

The means in which iron overloaded patients are treated is to give them a medicine that will cause iron to leave the body- by chelation. These medicines capture the iron, hold it tight, and accompany it out of the body via the urine or feces. The first chelator, the gold standard, is a drug called deferroxamine (Desferal). It is given subcutaneously or intravenously and is a safe and efficacious chelator that has been shown to decrease iron levels in the body. It is only effective at grabbing the iron floating around without a guard, NTBI, while it is in the body thus, if it is not used around the clock, iron remains free and can cause trouble. Although a very effective and safe agent, the fact that Desferal has to be given into the skin or through an IV (for 10 or more hours each day) makes it difficult for patients to remain compliant. Introduced in 2005, deferasirox (Exjade) is an effective oral iron chelator, which works especially well for patients who are mildly overloaded or to prevent iron overload. This chelator not only removes iron from the body, but it also stays in the body for 24 hours gathering up the NTBI which serves to protect the organs from harm. Exjade has some side effects, but a physician familiar with its use should be able to maintain the vast majority of transfused patients on this drug with an excellent quality of life and few problems. Exjade works best when used to maintain a low to moderate ferritin and is less effective when it is brought on board when a patient already has significant iron load (ferritin>2500ng/ml).

Other chelators are available but tend to have higher side effect profiles.

Key point #6: Most children on chronic transfusions will usually have accumulated enough iron to begin preventative chelation by age 2-3. Patients and parents need to advocate for aggressive chelation, the monitoring of serum ferritin and the use of liver biopsy or non-invasive measures when the serum ferritin continues to rise or is difficult to interpret.

Little Disease, Little Town, Little Boy -- Huge Heart

This article by Christine Quirk originally appeared in the Times & Courier, Clinton, Mass. It is being reproduced with her permission.

When Christopher Vroman was diagnosed with Diamond Blackfan Anemia, or DBA, Matthew Pulnik wasn't yet born.

But their grandmothers, Dot Grady and Dot Kilcoyne, are best friends, and over the years, Matthew became aware of Christopher and his brother, another Matthew, who were fighting a disease with little awareness and even less funding.

"It's a little underdog disease," Kathi Vroman, Christopher and Matthew's mom, said. "It doesn't get a lot of attention in the media, and it doesn't have enough notoriety for big corporations or celebrities to donate to it or endorse it."

But DBA does have Pulnik, a Clinton third-grader who has spent the last few years selling lemonade, collecting cans, and soliciting donations to benefit the national DBA foundation.

"It feels good," he said. "It feels like I'm helping people … because I am."

Matthew's mother, Julie Grady, explained that it all started in 2005 with Hurricane Katrina.

"He came home from preschool and wanted to do a lemonade stand," she said. "[The neighbors] were collecting money for Katrina so we decided to do that. Then, the next year, we asked him what charity he'd like to do, and he said DBA because of Dot and Ray [Kilcoyne's] grandchildren."

Matthew wanted to add popcorn to the menu and the Kilcoynes bought him a popcorn maker. He and his parents built a sturdy stand and he sets up in front of his Wilson Street home and takes donations in exchange for lemonade and popcorn. Some folks, he said, leave $20 bills.

Several area businesses also have donated money; Matthew sends a personal thank you note to each donor. Nypro has agreed to match his donations, he said.

Matthew's on-going project is a can drive. Cans can be left at his house at 396 Wilson St., or he (with the help of his mom, dad and grandparents) will come and pick them up.

Matthew said he usually takes the cans to Apple Country Market because there's no limit on how many he can cash in. One of the employees there offered to do the transaction for him, as did Matthew's grandmother, but he politely declined, saying he likes to do it himself.

Matthew is also planning a summer movie night, where, for a $3 donation to DBA, participants can sit outdoors, watch a movie on the side of the house, and get – what else? -- popcorn and lemonade.

One hundred percent of what Matthew collects in donations goes to The DBA Foundation. The Pulnik-Grady family donates all the materials so there's no overhead. His "fiscal year" runs June to June and so far this year, he has raised more than $1,100 in donations.

"We support him, (his brother) Nathaniel helps, but Matthew is the force raising the money," Grady said.

The face of the disease

DBA is considered a "pure red cell aplasia," Kathi Vroman explained, with aplasia being the absence of an organ or tissue or the defective development of the usual restoration process.

"In laymen's terms, children with this disease do not manufacture red cells on their own," Vroman said. "It is a very rare disease and typically there are only 20 to 30 new cases world- wide each year."

Vroman's older son, Christopher, was diagnosed when he was just 7 weeks old.

"The pediatrician discovered he was literally running out of blood," she said. "He only had fetal blood remaining at that time."

Matthew came home from China at age 2. Already diagnosed with DBA, he stood a slim chance of being adopted and would likely not live long.

"We were the perfect family for him," she said. "We knew this disease, how to handle it and were not afraid of it. It was easy. Any family in our situation would have made the same decision."

Now 16 and 12, the boys receive regular blood transfusions of three bags of packed red blood cells at each appointment

Vroman said there is no way to express her gratitude to Matthew Pulnik, and added the most amazing part of their story is that, since the Vromans have lived in Georgia for the past 15 years, they have never met.

"I cannot put for you in words and do justice to what Matthew does in terms of what it means to us," Vroman said. "I sit on the board of directors of the Diamond Blackfan Anemia Foundation and can tell you that every dollar raised for research is raised by families and people like Matthew."

Matthew said he wants to be a teacher when he grows up, partly because he loves school so much, although Grady and Vroman joke that he will one day be the CEO of the DBA Foundation.

"Matthew is our gift from God -- and that is so true since the name Matthew means 'gift from God,'" Vroman said. "I just keep thinking … little disease, little town, little boy -- huge hearts."

Kristine Gunderson primes the tubing with Desferal, loads the syringe into the pump and inserts the needle into her arm.

Paige's Page

Dream…Believe…Achieve

I rush around the house trying to find my chelating pump. I look in my bedroom, the bathroom, and my parent's room. I finally find it on the kitchen table by the rest of my chelating items. For a few seconds, I think about how much of a hassle chelating is.

Then, I remember it saves my life.

From the age of 7 I have been transfusion dependent, and along with transfusions comes desferal or Exjade. I tried both and finally stuck with desferal. When I first started chelating, I was attached to my pump five nights a week for about a year. During this time, desferal became a part of my nightly routine and as natural as brushing my teeth. Now, I have gotten to the point where I can chelate less because I don't get transfused as much and don't have as much iron stored. This is nice, but it might not last if I get transfused more. When I have more iron stored, I will chelate more.

"There are only two ways to live your life. One is as though nothing is a miracle. The other is as though everything is a miracle." Albert Einstein.

Kevin Gately's family inspired me to have a positive attitude towards chelation. When I was diagnosed with DBA, Kevin's mother was the first person my mom spoke with about DBA. She shared with my mom that when she went to the hospital she saw children with cancer and in much worse conditions than Kevin and I. She told my mom to consider herself lucky. DBA is not cancer. Kevin was a DBA warrior and lived his life to the fullest. He lived an awesome life.

"Every man dies- Not every man really lives," --a quote by William Ross Wallace.

Chelating allows me to live my life to the fullest. Without chelation, iron would build up in my organs; this would be fatal to my health. If someone thinks negatively, they will never see the good in things. Like the Gatelys, do not view DBA as a negative thing; it isn't. Conditions could be much worse. We are lucky.

"Life is like a game of cards. The hand that is dealt you represents determinism; the way you play it is free will." Jawaharal Nehru.

Make yourself have the determination and will power to chelate. Life is meant to be enjoyed. Do everything you can to enjoy it. Chelating will help you.

Life is short; don't shorten it.

Paige's Page will be a regular column written from a teenager's point-of-view. Paige goes to school, she gets blood transfusions, she chelates, she conquers. If you have any encouraging thoughts, quotes, stories or questions, send them to paige@dbafoundation.com, and they may be incorporated into the next DBA newsletter. Requests for anonymity are respected.

Update on Chelators

Dr. Carole Paley, M.D., is the Executive Medical Director of Oncology at Novartis Pharmaceuticals. Dr. Paley worked with Dr. Lipton and Dr. Vlachos managing the care of DBA patients before moving to Novartis to direct research on Desferal and Exjade. She has provided our families with the following important updates:

Exjade administration
The current mode of administration for Exjade is with water, apple juice or orange juice on an empty stomach. This can be challenging and many have asked if Exjade can be taken with food and other liquids. In order to answer this question, Novartis has conducted a study in which Exjade was given with different food and beverage combinations. The study has completed enrollment and data will be available in the near future.

Combination of Exjade with Desferal
Another question that is being addressed is the role of combination therapy. Treatment therapies that combine two iron chelators may enhance chelation efficiency by improving access to different tissue iron stores and control of the toxic iron pools. The combination of two chelators may reduce toxicity through averting the need for high doses of a single drug, but it is essential to establish the safety of such therapies. Two combination therapy trials have been conducted. One has completed enrollment the other is more than half enrolled.

Exjade safety
Based on an ongoing review of safety data, the Exjade label was updated earlier this year. Key changes included the addition of a boxed warning and changes to the contraindications. The boxed warning states that Exjade may cause serious renal and hepatic impairment (including failures) and gastrointestinal hemorrhages; some with a fatal outcome, and identifies specific patient populations at increased risk (patients with advanced age, high-risk MDS, underlying renal or hepatic impairment or low platelet counts (50 x 109/L).

New contraindications include patients with:

- baseline creatinine clearance of <40mL/min or serum creatinine >2 times the age-appropriate upper limit of normal*
- poor performance status and high-risk MDS or advanced malignancies.
- platelet counts less than 50 x 109/L

The goal of the label update is to further clarify which patients with chronic iron overload due to blood transfusions are appropriate for treatment with Exjade.

Thanks to YOU, the DBAF Funds More Research!

Paul de Figuieredo, Ph.D., Assistant Professor, Texas A&M University, was awarded a $43,256 grant from the DBAF for the project "Discovering therapeutics for DBA ." The long-term goal of this study is to develop small molecule therapeutics for Diamond Blackfan Anemia (DBA), by screening for molecules that overcome growth defects associated with decreased expression of ribosomal protein S19 in a yeast model of DBA. Yeast are remarkably versatile microorganisms that share many aspects of ribosome biology with humans. Due to their small size and ease of growth, they are readily amenable to high throughput drug screens where thousands of compounds can be assessed for their effects on cell growth. The Figuieredo lab will screen 25,000 chemical compounds for their ability to reverse the effects of reduced expression of Rps19 on cell growth. Any compounds identified in the yeast screen will be examined for their ability to compensate for reduced expression of Rps19 in human cell lines. Dr. Figuieredo has had substantial success using a similar approach to identify lead compounds for therapeutic development in another ribosome-related bone marrow failure syndrome, Shwachman Diamond syndrome (SDS).

Hanna T. Gazda, M.D., Instructor in Pediatrics Harvard Medical School, was awarded $51,512 from the DBAF to continue her efforts in identifying genes mutated in patients with DBA. Dr. Gazda has played a major role in the identification of most of the 11 known DBA genes. Her discoveries have clearly established DBA as a ribosomopathy which has helped direct research efforts on many aspects of this disease. Approximately 50% of DBA patients have mutations in one of the 11 known genes. In the remaining patients, the defective genes have evaded detection by conventional DNA sequencing. Dr. Gazda now plans to use sophisticated whole genome approaches to identify these remaining genes. The aim of this study is (1) to perform comparative genomic hybridization to search for deletions and duplications in ribosomal protein genes that could not have been picked up by DNA sequencing; (2) to perform whole exome sequencing ("next generation" sequencing) to potentially identify non-ribosomal protein genes that may be mutated in DBA. This latter approach is daunting in that tens of thousands of genes will need to be sequenced and analyzed for sequence changes that may be linked to patients with DBA. This project will result in a more complete picture of the genetic causes of DBA and the pathogenic mechanisms that result.

Emanuela Tolosano, Ph.D., Professor at the University of Torino School of Medicine, was awarded $25,000 from the DBAF to fund a project aimed at defining the role of the Feline Leukemia Virus, subgroup C, Receptor (FLVCR) in the pathogenesis of Diamond-Blackfan anemia (DBA). FLVCR encodes a protein that exports excess heme from cells. It has been suggested that defects in globin synthesis, perhaps as a result of ribosomal protein mutations, could result in excess heme in erythroid progenitors that would need to be exported from cells to reduce heme toxicity. Thus, FLVCR could play an important role in DBA pathogenesis. Recently, it has been reported that mice lacking FLVCR show a phenotype very close to that of DBA patients, including erythroid failure and malformations. However, no mutations in FLVCR have been found in a small subset of DBA patients. One of the goals of this study is to test additional DBA patients for mutations in FLVCR. It is possible however, that FLVCR could have a role in DBA pathogenesis without being mutated in DBA patients. Studies have shown that FLVCR is a complex gene giving rise to a number of related proteins that have different functions. Moreover, different tissues may express different forms of FLVCR protein. Given the complexity of the FLVCR gene it is possible that mutations in ribosomal protein genes could alter FLVCR expression. Therefore, this study will also focus on possible changes in FLVCR expression in cells with mutant forms of RPS19. Finally, the Tolosano laboratory will continue to study the role of different forms of the FLVCR protein in erythropoiesis.

DBA Foundation Research Overview

By Steve Ellis, DBAF Research Director

I have been asked to provide an overview of research supported by the Diamond Blackfan Anemia Foundation for this edition of the newsletter. To coin a term used in business, I would say that the DBAF has a diverse research portfolio. As I see it, this portfolio has two major subdivisions: grant support and dissemination. The diverse nature of the portfolio is evident in both of these major subdivisions. I will focus initially on grant support and then tackle dissemination.

Grant support

The DBAF provides grant support for investigator-initiated research ultimately aimed at understanding the pathophysiology of DBA with an eye toward improving the lives of individuals and families living with DBA. Here, I use the term pathophysiology as a catch all to describe the molecular basis for the disease and how these changes at the molecular level give rise to the clinical features of the DBA, including response to therapy. Some of the grants funded over the years could fall under the heading of applied research or research directed toward a highly specialized goal. These could include grants to Drs. Lipton and Vlachos to help set up the North American DBA Registry, or grants to Dr. Hanna Gazda, to identify genes responsible for DBA. Other grants tend to be more broadly based and tend to be directed toward understanding molecular mechanisms underlying DBA. These mechanisms can, in turn, give rise to new and unanticipated therapies. I used the term "broadly-based" as an approach to research funding, because time and time again major scientific discoveries have come from unexpected quarters. An example from the DBAF files would be Dr. Kathleen Sakamoto's grant to study a zebrafish model of DBA. One might reasonably ask what zebrafish could tell us about this human disorder, but Dr. Sakamoto's model system provided a vital link between the loss of Rps19 and p53 activation, ultimately signaling to cell death pathways. This finding has guided the field for the past few years and dissecting components of this pathway could lead to new therapeutic targets. More recently, DBAF support has gone to drug discovery efforts and the improvements of animal models for DBA where the drugs could be tested.

A list of investigators and grants supported over the years is given below. Space limitations prevent me from discussing each name and proposal separately, but consider this list a veritable "Who's Who" of DBA research!

Dr. Jeffrey Lipton – 1995, 1996, 2000 – DBA Registry, Molecular basis of DBA
Dr. Niklas Dahl – 1998, 1999, 2000, 2001 – Gene Discovery, Rps19 function
Dr. Douglas Templeton – 1998 – Iron overload
Dr. Colin Sieff – 1998, 2007, 2008 – Molecular basis of DBA
Dr. Monhandas Narla – 1999 – Red cells/DBA
Dr. Stefan Karlsson – 2000, 2001, 2004, 2006 – Mouse and Cellular DBA models, Gene therapy
Dr. Gil Tchernia – 2001, 2003, 2004 – DBA pathophysiology, Metoclopramide efficacy and toxicity
Dr. Adrianna Vlachos – 2002, 2004 – DBA Registry, Molecular basis of DBA
Dr. Kathleen Sakamoto – 2002, 2005 – AML in DBA, Zebrafish models of DBA
Dr. Sarah Ball – 2004, 2005 – Understanding and enhancing the steroid response in DBA
Dr. Hanna Gazda – 2004, 2005, 2007, 2010 – Gene Discovery
Dr. Steven Ellis – 2004-present – Research director, Ribosomes and DBA
Dr. Irma Dianzani – 2006 – The Rps19 interactome
Dr. Fabrizio Loreni – 2007 – Rps19 function
Dr. Johan Flygare – 2007, 2009 – Mechanism of steroid action, drug discovery
Dr. Lydie DeCosta – 2009 – Cellular models of DBA
Dr. Shuo Lin – 2009 – Zebrafish DBA model
Dr. David Bodine – 2009 – Mouse DBA model
Dr. Paul de Figueiredo – 2010 – Drug discovery
Dr. Emanuela Tolosano – 2010 – Pathogenesis of DBA

Research Grants, review and funding decisions

Proposal review

Proposals received by the DBAF are sent out for review by Foundation's Research Director (currently me). In general, three reviewers are solicited for each grant. The reviewers are typically in the DBA field with expertise in the basic science or clinical arenas. Frequently reviewers are members of the DBAF Scientific Advisory Board but other reviewers are also used. It should be pointed out that reviewers give of their time and expertise without financial compensation. Once the reviews have been received I write up a summary of the reviews, and the reviews plus my summary are forwarded to members of the DBAF Board.

Funding decision

The Board of Directors of the DBAF ultimately makes funding decisions. A number of criteria are employed in making these funding decisions. These criteria include:

- Relevance to DBA, either from a clinical or basic science perspective
- Scientific rigor, are the experiments or clinical trials well planned and based on sound principles?
- Productivity of investigator, does the investigator have a solid record of scientific accomplishments?
- Does the investigator has a strong commitment to the DBA field?
- Does this proposal represent an opportunity to bring a new investigator into the DBA field?
- Is this a young investigator (with fewer accomplishments to date) but has the long term potential to contribute to the DBA field?

The Board's discussion may not only include whether or not to fund the proposal but also whether the proposal should be funded in full or if cuts in the budget should be considered.

Scope of funding – from pilot projects to NIH support

In general support from the DBAF is for pilot projects to test new ideas and obtain preliminary data for much larger proposals to government agencies like the NIH. Many of the researchers funded above have maintained their research programs through support from other sources after having received support from the DBAF. Of particular note in this regard, is that several investigators listed above received grant funding through an NIH program on "Molecular Mechanisms of Diamond Blackfan Anemia and Other Bone Marrow Failure Syndrome" stimulated by lobbying efforts of the Daniella Maria Arturi Foundation.

Dissemination

An important part of the research enterprise is dissemination of information. Communication between interested parties whether they be physicians, scientists, politicians, or patients and families is integral. The DBAF supports a number of venues that support the dissemination of information relevant to DBA. The DBAF is a regular sponsor of scientific meetings in specialized areas relevant to DBA. These meetings include the biannual meeting of the BioIron Society and the triennial Ribosome Synthesis meeting. Clearly complications of iron overload are a major factor in DBA patients being treated by transfusions. While the discovery of a number of ribosomal protein genes as the cause of DBA has clearly established DBA as a ribosomopathy affecting ribosome synthesis. Sponsorship of these meetings heightens awareness of DBA among these investigators and helps recruit new investigators into the field.

The DBAF has also been a long time supporter of the premier showcase of DBA research, the DBA International Consensus Conference hosted by the Daniella Maria Arturi Foundation. This meeting brings together leading investigators in DBA and related fields for the free exchange of information and ideas and has fostered many collaborations that have contributed substantially to our understanding of DBA pathophysiology.

Finally, the DBAF organizes and sponsors the scientific sessions at Camp Sunshine where attending families regularly hear the latest in DBA research from both basic scientists and clinicians.

I hope you will find this brief overview of research sponsored by the Diamond Blackfan Anemia Foundation informative. I hope that I have conveyed to you the excitement that has been building in this research area for the past few years and how we now stand poised to translate some of these basic science discoveries to clinical application. It has been an honor to serve as the Research Director for the DBA Foundation these past 7 years.

Your Help is Needed

The DBA Foundation is proud of the accomplishments that our families and friends have made possible through their fundraisers, personal contributions, and monthly donations. Currently, we have an unprecedented number of research proposals awaiting review. Our hope is to be able to fund all of the approved projects. We cannot do this without your help!

We appreciate everyone's involvement and hope that you will join us in our efforts to understand DBA and find better treatment options for our patients. We recognize that while there are many worthy causes, the rarity of DBA places an extra burden on our families. We rely on your commitment to DBA patients to further our mission of providing support for DBA patients… families… research.

To get involved, please contact **Dawn Baumgardner** at **716.674.2818. THANK YOU!**

Word From the Board

By Anita Shier Bruton

Happy Spring! My name is Anita Shier Bruton. I am a DBAF Board Member and the DBAF Webmaster. My son, Gabriel, who turned six the day before Halloween, has DBA. He is transfusion dependent, steroid non-responsive, and takes Exjade. My daughter Grace is four and doesn't have DBA- as far as we know. Like 50% of DBA patients, we don't know what mutation my son Gabriel has but are eager to find out.

Fortunately, we are at an exciting time in scientific research. Since our last newsletter, we had our priceless DBA week at Camp Sunshine and have funded more research. At camp, the DBAF presented Dr. Gazda with a check for $51,512 to further her studies in finding the unknown genes. Dr. Gazda's research was paramount in finding most of the 11 mutations in ribosomal protein genes, accounting for 50% of DBA patients. The focus of her research, at this point, is expanding out from those 80 ribosomal protein genes to other areas of the human genome. For a more detailed description of her work and other projects recently funded, please go to www.dbafoundation.org and click on DBA News. Some of the research that the DBAF is able to fund is looking for these unknown genes, while some is approaching it from other angles such as discovering therapeutics for the DBA.

Being a biology teacher living in the realm of DBA really has its perks. Not only do I get to immerse myself in the new research and discoveries, but I also get to educate my students about DBA and the amazing progress that has taken place in just the last ten years. There have been ground-breaking studies in developmental evolution (evo devo), the human genome project, RNA, ribosomes, and the list goes on. The fields of science that have been studying DBA come from many different angles and, although they seem to be quite different, it is because of those different approaches that important connections are being made. Discovering that DBA is a ribosome-based disorder is just one example. One of the newest avenues is looking at what scientists have been calling junk DNA which makes up about 98% of our genome. Some is viral, some areas are called pseudogenes (sections of our DNA that originate from our ancestors but no longer code for proteins), some are switches, and some are still unknown as to their function. The intricate design of who we are is slowly getting clearer and, as it does, by continuing to fund research through your contributions to the DBAF, DBA is right there to reap the rewards.

As a DBA mom and a scientist, I am really excited about what may be found in those unknown areas. As I watch my son play and wonder what his future may hold, all I can feel is hope. I am constantly inspired and grateful by the science that is happening around the world to actively be working toward unraveling this mystery. Fundraising is so very vital to our common search for a cure. It doesn't matter if it is a small event or effort; every little bit counts. If you are newly interested in fundraising, here are some ideas in which you could start small: bake sale, garage sale, car wash, GoodSearch/GoodShop, DBAF bracelets, letter writing to friends and family, birthday wish, or holiday wish. I am also able to upload your loved one's picture on the DBAF brochure so you can print a more personal brochure to have available at your event.

If you would like to have your DBA patient's picture, CaringBridge/ CarePage link, fundraiser, or have a family DBA article or news link on the website, you can email them to me at asbruton@dbafoundation.org. If you haven't already registered or if you've moved, please sign up on the website under "For Families" on the navigation bar so we can send you the DBAF newsletter and other educational materials.

Sometimes the journey we are traveling isn't easy, but I am so grateful for our DBA community. Armed with your support, I can honestly say that I am incredibly hopeful about the future of DBA. Together we can do this, and we will continue to fight for the cause and a cure for DBA. In closing, the DBAF looks forward to being a resource and support to you and your family on this DBA journey.

Many blessings,
Anita Shier Bruton
asbruton@dbafoundation.org
DBA Foundation Board Member and Webmaster
www.dbafoundation.org

IVF/PGD in the News

Many of us are familiar with this technology thanks to the Trebing Family who made pre-implantation genetic diagnosis (PGD) a household name within the DBA community when a book about their journey, The Match by Beth Whitehouse, was published about a year ago. Dr. James Stelling is the reproductive specialist responsible for orchestrating the miracle on miracle that allowed a baby boy, free of DBA and a perfect sibling match, to provide the life-saving marrow that gave little Katie Trebing a chance to be the big sister that Christopher needed.

Dr. Stelling visited Camp Sunshine to share information on the advances in science and medicine that enable dreams to come true for families stricken with genetic disorders like DBA. Although PGD/IVF is not an option for everyone, many families found themselves inspired by his detailed description of "how babies are made" in his laboratory. For more information on pre-implantation diagnosis with in vitro fertilization, please visit rsofny.com or genesisgenetics .org. Dr. Stelling can also be reached at (516) 739-2100.

Flygare on Steroids

It has been maintained by physicians and researchers that although we realize that Prednisone works to eliminate the need for blood transfusions in many diagnosed with DBA, we still do not fully understand why this drug works to stimulate red cell production. At Camp Sunshine this past July, Johan Flygare, MD PhD took some time to speak about what he is doing on this front to improve the lives of those with DBA who struggle with the side-effects of chronic steroid use.

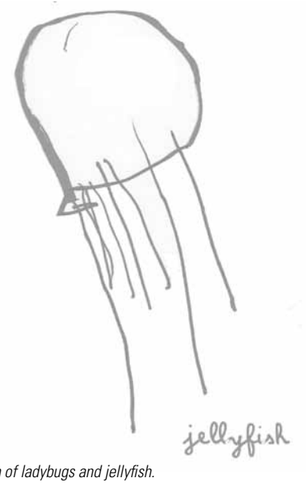
We know that Prednisone activates the glucocorticoid receptor which then goes into the cell nucleus. In the nucleus the glucocorticoid receptor will turn some genes on and others off, but we have no idea of which genes it turns on or off in order to improve red cell production in DBA. Work is being done to understand this process in hopes of finding other drugs that activate the glucocorticoid receptor as Prednisone does but have a more specific effect on the genes important for DBA and less effect on genes that cause side effects. It may also be possible to identify other drugs that regulate the Prednisone-regulated genes that improve red cell production in DBA but do so independently of the glucocorticoid receptor. Such compounds could boost the effect of or even replace Prednisone.

The Refrigerator Door

Do you have a beautiful picture hanging in your home that you would like to share? The DBA Newsletter is requesting submissions of your or your children's artwork, photography, poems, short stories, etc. to include in this publication. Please send a copy of your work to Jacy Downey at 1200 W. Euclid Indianola, IA 50125 or electronically to jdowney@dbafoundation.org.

Peyton Green shares her interpretation of a red blood cell.

Finn Gunderson's rendition of ladybugs and jellyfish.



Meet the Scientific Advisory Board

In each issue of the DBA Newsletter we will spotlight a member of the DBAF Scientific Advisory Board. The Foundation is very lucky to have an esteemed group of medical professionals who are dedicated to working with the Board to achieve our mission. Dr. Johnson M. Liu, M.D. is an Adult Hematologist at Cohen Children's Medical Center of New York (formerly Schneider's) and has taken a special interest in transitioning DBA patients from pediatric to adult care. Dr. Liu has offered his advice in the form of a Q & A session.

Taking Charge of Your DBA: A Message for the Young Adult

Q: What is the most important thing you can do as a young adult DBA patient?

A: From my perspective as an Adult Hematologist, my most important message is to take charge of your DBA. Try to learn as much as you can about what you need to do to care for yourself and be aware of some of the complications of DBA. Start looking for an Adult Hematologist who is interested in blood diseases like DBA as a teenager so to ease the transition from your Pediatrician to that Adult Specialist.

Q: What do we know about adult DBA patients? Are there any concerns that are specific to adults?

A: With advances in supportive care, transfusion and steroid therapy, and stem cell transplantation, DBA is evolving from an exclusively childhood disorder to a disorder also affecting adults. There are known DBA patients who survive late into adulthood, as well as patients newly diagnosed as adults. Due to a lack of information, however, there are many unanswered questions about how the disease progresses and what factors lead to long-term survival. It is also unclear whether DBA worsens over time. Cancer is also part of the natural history, but the true risk of cancer is not known at the present time.

There are some concerns that may be specific to adult patients, namely post-adolescence and hormonal changes; aging; concomitant chronic diseases (heart disease); sexually transmitted diseases; lifestyle diseases (alcohol abuse, smoking, illicit drugs); fertility and pregnancy; psychosocial and financial concerns. Thus, the lifetime management of DBA patients by a multidisciplinary team may include pediatric and adult hematologists, internists and subspecialists. The challenge is to find a group of physicians that is committed to this approach.

Q: Can you give a few pointers about iron overload management?

A: First, we need to be aware that iron overload from blood transfusions is an extremely important cause of problems and death in DBA patients. Specifically, patients can suffer from dilated cardiomyopathy (heart failure), liver fibrosis and cirrhosis, and numerous endocrine complications such as growth retardation, failure of sexual maturation, diabetes mellitus, and insufficiency of parathyroid, thyroid, pituitary, and adrenal glands.

One unit of blood contains about 200-250 mg of iron. Therefore, a patient receiving 15-30 units of blood/year receives between 3-6 gm of iron (which is 3-6 times the annual requirement). There is a wide range of variability in the degree of organ toxicity among persons with the same amount of tissue iron. Consequently, both organ function (heart, endocrine system) and tissue iron concentration must be monitored. Heart involvement is the most life-threatening iron-related complication. MRI (magnetic resonance imaging) is an accurate and noninvasive means of measuring the amount of iron in the heart and liver.

In the USA, both Desferal (DEFEROXAMINE) and Exjade (DEFERASIROX) are approved for chelating iron. They each can cause side effects and need to be monitored carefully. Another drug that can be effective but is available in the USA only on research studies is L1 / DEFERIPRONE.

Q: How about steroid therapy complications and osteoporosis?

A: Steroids are associated with weight gain, diabetes mellitus, adrenal suppression, hypertension, psychiatric and cognitive changes, osteoporosis, and avascular necrosis (usually of the femoral head).

I particularly want to talk about steroid-induced osteoporosis, which is under-recognized and under-treated. Steroids can cause rapid bone loss and increased fracture risk early in the course of therapy. At this time, drugs called biphosphonates are the main treatment option for preventing broken bones due to steroid-induced osteoporosis.

Q: Can you talk about the management of pregnancy in women with DBA?

A: First off, I should say that improvements in the management of pregnant women with DBA have resulted in an increase in survival, quality of life and reproductive potential. Consequently, DBA women who have reached childbearing age in good condition are now willing and able to experience pregnancy. Of course, since DBA is a genetic disorder, there is a 50% recurrence risk in offspring from a DBA parent.

No prospective study on pregnancy in women with DBA is available. However, there have been many case reports in the medical literature. Complications of pregnancy can occur in the mother, the child, or both. Some of these potential hazards include fetal loss, pre-eclampsia, preterm delivery, intra-uterine death, infants with intra-uterine growth retardation and children with birth defects.

One important thing to keep in mind is that iron chelation therapy cannot be continued during pregnancy as deferoxamine may cause birth defects. Therefore, chelation should stop when the patient is planning to become pregnant, or as soon as a pregnancy is recognized. To the extent possible pregnancy should be planned, and when necessary, an intensification of iron chelation should be performed before contraception. Any woman with DBA contemplating pregnancy should undergo a thorough evaluation of any feature that may interfere with pregnancy outcome, including the presence of blood-borne infections, iron overload and related diabetes mellitus, hypothyroidism or cardiomyopathy. Care should be administered in a high-risk obstetrical practice in collaboration with hematologists and other specialists. In cases where the father of the child is the DBA-affected individual, the pregnancy should also be considered high risk and be closely monitored for signs of fetal distress, hydrops fetalis and other complications of the fetus.

Steroid responsive women often experience an increased steroid requirement or become transfusion-dependent during pregnancy. In most cases, increasing the pre-pregnancy steroid dose fails to maintain a satisfactory hemoglobin level. Steroid toxicity must be considered in both the mother and the fetus. Many times, transfusion therapy becomes necessary during pregnancy.

Scientific Advisory Board

Eat much?

Would you like a few new recipes to shake up your family's meal routine? How about more than a few?

Betty Lightner, DBA mom, took on the challenge of organizing The DBA Cookbook Project and has turned a thrice-daily dilemma into a tasty supper solver with a dash of dollars for DBA mixed in for good measure!

The DBAF would like to thank Betty and the other moms that have worked tirelessly to input over 400 recipes in preparation for printing. Betty is still taking orders, so please contact her at betty.lightner@gmail.com.

In order to ensure that the largest portion possible goes to further research for our beloved DBA Family, the DBAF urges you to not only buy one for your own kitchen but also to consider ordering ten or more cookbooks and committing to sell them all so that they can be shipped to you in bulk, saving in postage. No order is too small, but imagine how much money we could raise if every family made a minimum order of ten…or twenty. Now that's what you call bringing home the bacon!

Available NOW...
RECIPES FOR RESEARCH

A collection of recipes from individuals with DBA and their families and friends

Checks can be made out to:
DBA Cookbook Fundraiser
c/o Betty Lightner
104 Greenridge Road
Lutherville, MD 21093

Shipping Costs:
1 book-$5 total shipping ($5 per book)
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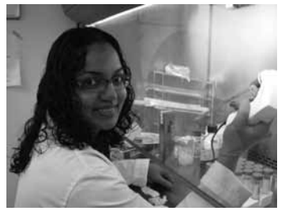
From the Office of…

Sharon Singh, MD
Attending, Pediatric Hematology Oncology
St. Baldrick's Foundation Scholar
Steven & Alexandra Cohen Children's Medical Center of NY



Hello! Thank you for the opportunity to share this news with the DBA community. My grant is entitled Diamond Blackfan Anemia: A childhood cancer predisposition syndrome. I will be investigating the role of p53 in DBA and the mechanisms that lead to cancer predisposition in DBA. Over-expression of the p53 protein, which protects against tumor formation, may actually lead to DBA. One of p53's functions is to cause cell death in damaged or stressed cells. Chronic over- expression of p53 may lead to an environment that leads to cancer transformation and survival. Understanding the conditions that promote the formation and survival of cancer cells is vital to improve early diagnosis and treatment of childhood cancer. I will be working with a mouse embryonic stem cell model of DBA as well as patient samples provided to the DBA Registry.

Dr. Lipton, who is very involved in the St. Baldrick's Foundation, is one of my mentors on this project. I am proud to say that I was actually the first St. Baldrick's fellow in 2005-2008 and was awarded the career development award from St. Baldrick's in July of this year. This award provides funding to research this topic and is for 3 years. The St. Baldrick's Foundation, which raises money to support childhood cancer through their head-shaving events, funds more in childhood cancer research grants than any organization except the U.S. government- exceeding $12 million in 2009 alone.

The DBA Foundation is proud to announce that Dr. Sharon Singh was awarded a total of $330,000 to go towards her DBA-related research. Thank you to the St. Baldrick's Foundation and to Dr. Singh!

ATTENTION!

We all know that since many doctors are not familiar with DBA it is very important for you to take an active role in managing your own or your child's care. As a parent who is functioning as a health advocate, it is important not only to know about DBA and understand the available treatment options in order to make the best possible choices for the health of your child, but, in time, it will become necessary to begin relinquishing this responsibility to your teenager or young adult with DBA so that they can become trained to properly manage their own care. With this step in mind, it is necessary to be able to provide your child with adequate records of his or her health history. In order to support your efforts, a Care Notebook designed specifically for DBA patients is available! These materials were created by the Centers for Disease Control and Prevention (CDC) in collaboration with doctors, nurses, other professionals, and DBA families. The DBAF has purchased enough patient care binders so that each DBA family may benefit from this valuable resource. If you did not attend Camp or haven't picked up these binders from a DBA Resource Center, please contact Dawn for one to be sent to you. Please limit one per patient. Note that additional worksheets may be downloaded from the dbafoundation.org website under "Downloadable Materials".

DBA National Resource Centers

Steven and Alexandra Cohen Children's Medical Center of New York
Adrianna Vlachos, MD
Head, Bone Marrow Failure Program
Hematology/Oncology and Stem Cell Transplantation
Director, Diamond Blackfan Anemia Registry
Surveillance and Awareness Program
Steven and Alexandra Cohen Children's Medical Center of New York
269-01 76th Avenue, Room 255
New Hyde Park, NY 11040
Main number: 516-562-1506
Ellen Muir, RN, MSN
Clinical Nurse Specialist
Phone: 516-562-1505
DBA Nurse Hotline: 1-877-DBA-NURSE (322-6877)

University of Texas Southwestern Medical Center
Zora R. Rogers, MD
Professor and Clinical Director
Pediatric Bone Marrow Failure Program
UT Southwestern Medical Center
Children's Medical Center Dallas
5323 Harry Hines Boulevard
Dallas, TX 75390-9063
Main number: 214-456-6102
Deborah J. Boger, MSN, RN, CPNP
Nurse Coordinator
Phone: 214-456-6102

Stanford University Medical Center
Bertil Glader, MD, PhD
Stanford University School of Medicine
Lucile Packard Children's Hospital
Professor of Pediatrics and Pathology
Division of Hematology/Oncology
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Palo Alto, CA 94304
Main number: 650-723-5535
Kirsten Mouradian, RN, MSN, FNP-C
Nurse Practitioner
Phone: 650-724-2448

Children's Hospital Boston
Colin A. Sieff. MB.BCh, FRCPath
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300 Longwood Avenue
Karp 80006
Boston, MA 02115
Main number: 617-355-8246
Jessica Teates, RN-BC
Hematology Nurse Coordinator
Phone: 617-355-8778

RECENT EVENTS

Peyton Greeen shows us a big smile as she enjoys her Make A Wish Trip!

The Mancuso Family held the 4th Annual Friends of DBA Golf Outing this past September. They are shown here with the Gunderson's who traveled to support them on their big day!

The Paye and Marchese Families of Colorado teamed up to raise money for the DBAF after meeting this summer at Camp Sunshine.

The Soto Family held a blood drive and bake sale to profit the DBA Foundation! Lily Soto shows off some of the goods while proudly wearing her fundraiser shirt!

Ty Wilkins had his face painted at a Dreams Come True Party. He proudly sported the DBAF emblem, sparking questions concerning DBA and the DBA Foundation that he was happy to answer. Thanks for raising awareness Ty!

Tammy and John Luddy ran the Richmond Half and Full Marathons this fall! All of the money they raised went to the DBAF.

Way to Go, Joe!

Sixteen hours, 2 minutes and 30 seconds after he dove into the water on June 27, 2010, DBA Ironman Joe Crelier of Albuquerque, NM, crossed the finish line! Exhaustion didn't stop him from proudly showing off his race shirt, stamped with the DBAF logo on the front and the names of DBA fighters on his back. The DBA Foundation is honored to have been Joe's charity of choice and is indebted to Joe and his family for all their hard work. Joe's heroic effort, sponsored by Janus Charity Challenge, raised over $20,000.00 for the DBAF. The DBAF and all our DBA families sincerely thank Joe for his will of iron and heart of gold. Way to go, Joe! Way to go TEAM DBA!

Stay updated by connecting with the Diamond Blackfan Anemia Foundation

For comprehensive information related to DBA, please visit our website frequently. On Facebook, become a Fan of our Page and a Member of our Cause. Sign up to follow our tweets on Twitter. Join an email support group on Yahoo.

www.dbafoundation.org

www.facebook.com/dbafoundation

www.twitter.com/DBAFoundation

blackfan@yahoogroups.com **dba21@yahoogroups**

Diamond Blackfan Anemia Foundation, Inc.