

PERSPECTIVES

NEWSLETTER OF THE NORTHERN CALIFORNIA THALASSEMIA CENTER



Winter 2017

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Editor: Jin Mei, Thalassemia Outreach Coordinator.

Jin Mei graduated from UC Berkeley with a degree in public health. He plans to obtain a medical degree to become a general practitioner.

Iron Measurement and SQUIDS Across the Globe

Marcela Weyhmiller, PhD, Director of the Iron Overload Program

The sole purpose of the Iron Overload Program at UCSF Benioff Children's Hospital Oakland is to quantify iron in the body. The cornerstone of this program is the SQUID-Ferritometer® or SQUID. SQUID stands for Superconducting QUantum Interference Device and is a very sensitive magnetic detector. Using a small magnetic field, the device is able to directly measure iron concentration in the liver, the primary location of iron in the body, by detecting its response to a changing magnetic field or magnetic susceptibility.



Left to right: Silvana Audello, nurse and SQUID assistant (retired May 2016); Roland Fischer, PhD; Filomena Longo, MD, hematologist and director of the Iron Measurement Program at Torino and consultant pediatrician.

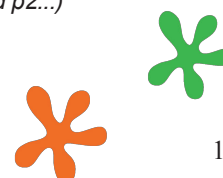
The procedure is pain-free, safe, and accurate. The special design of the machine allows for the measurement of iron in young children in as little as 10-15 minutes without the need for sedation. Since 2002, the SQUID has played a vital role in the management of a variety of diseases including hemochromatosis, myelodysplasia, sickle cell disease, thalassemia and other heavily transfused popu-

lations locally, nationally and internationally. Over 3000 measurements have been performed in Oakland alone with over ten-thousand performed globally. The SQUID is one of the original devices dedicated to non-invasive measurement of iron concentration, largely replacing the need to perform liver biopsies to measure liver iron concentration in our patients.

Over the years, the SQUID experience in Oakland has not changed much—the same familiar faces of the staff, having to wear blue paper shorts and cool ultrasound gel are still part of the measurement process. As Director of the Iron Overload Program, I have been busy working to develop a program with access to cutting edge techniques and helping develop the next generation in iron measurement technology. In recent years we have worked closely with our radiologists and cardiologist to support the cardiac T2* measurements. Under the guidance of Dr. Roland Fischer, physicist and pioneer of body iron measurements, we are developing tech-

niques to quantify iron in tissues such as the pancreas and bone marrow. With Dr. Ashutosh Lal, I have been working with 3 different groups to develop new susceptibility-based devices to measure iron which could be more affordable and accessible to patients across the globe.

I am always looking for ways in which we can improve our program here in Oakland. One of the challenges is that programs dedicated to measuring iron overload in the body are rare and SQUID-based programs are even rarer. There are three dedicated SQUID programs in the world. This program performs approximately 200 measurements per year—a similar number of patients each year to the program in Oakland. At the heart of their research program is a database which is similar to the one used in Oakland. This spring I had the privilege to visit our two sister programs in Hamburg, Germany and Torino, Italy where the other two SQUIDs are being used clinically. I was excited to meet the people who wrote classic papers on iron overload and with whom I communicated through email for several years. Above all I was excited to be surrounded by people who spoke my “language” and didn’t look at me curiously when I say that I “run the SQUID.” (Continued p2...)



...cont'd. from page 1:

My trip began in Hamburg to visit the University Medical Center Hamburg-Eppendorf (UKE) where I met up with Roland. Even though Roland is "retired" he coordinates a multidisciplinary Iron Group which consists of physicists, radiologist and pediatric hematologists who focus on quantification of body iron. Our first stop was to visit Prof. Peter Nielsen (PhD, MD), who along with Roland, runs the SQUID at the Institute for Biochemistry and Molecular Cell Biology. The Hamburg SQUID has been in operation since 1989 and has the same basic design as the Oakland version with some significant differences. We spent a typical day with



their program focusing on just one family scheduled to have a SQUID and an MRI. Our MRI programs were quite different. The MRI suite was busy with four different

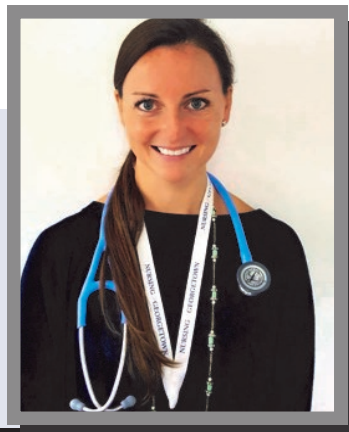
MRIs and workstations filled with radiologist busy analyzing data. T2*s were performed by the radiologist of the multidisciplinary Iron Group. (cont'd. p6...)

New Beginnings - Shannon Gaine, FNP

Interview by Jin Mei



Welcome Shannon Gaine. Shannon is a licensed Family Nurse Practitioner who joined the team in May 2016. She earned her Master's Degree as Family Nurse Practitioner at Georgetown University. After completing her Masters she worked at Columbia Presbyterian, New York City in the Pediatrics emergency room. Upon moving to California, Shannon worked in a small clinic in Mountain View before transferring over to UCSF Benioff Children's Hospital Oakland. She has an interest in working with the community in bringing more awareness and education about thalassemia in the future. When she is outside of the hospital, Shannon enjoys competing and training for Triathlons. She recently just competed in Ironman on October 1st in Maryland. Her favorite of all the races is swimming. Shannon is a very active and hardworking athlete.



JM: Why did you decide to go into nursing?

SG: Ever since I was little I always wanted to help people. I truly love what I do every day. My goal is to positively impact someone's day. I feel incredibly lucky and grateful that I have the ability to do that every day.

JM: What made you decide to come over to the West Coast?

SG: I had family here in California, but I also decided it was time for a change and so I moved to California. I worked at a small clinic in Mountain View before I came to UCSF Benioff Children's Hospital Oakland.

JM: What made you decide that you wanted to work here?

SG: I learned more about the Thalassemia Program and met the team and was drawn into their goals and vision. The staff here are also very friendly and it feels like family.

JM: What is it like caring for people with thalassemia?

SG: I am impressed by the patients every day. I am grateful to work with this population who are so welcoming and I learn every single day. Having worked in an emergency room, it is a nice change to be able to establish a relationship and build trust

and rapport with patients. I am truly thankful for this opportunity.

JM: Exactly how deep is your relation with the patients?

SG: I think nursing encompasses not just the medical side but also the whole life of the patient. I get to meet their family members, learn more about their life outside of the hospital and this enables me to help come up with a better plan of care that works for them.

JM: What are the differences between working in an emergency room compared to what you are doing now?

SG: I love the ability to connect and have time with patients and not feel constantly rushed. I get to have in-depth conversations and I establish more enduring relationships with my patients. I enjoy working day shift, although the 12 hour shifts were nice because there just never seems like enough time in the day!

JM: How does your day usually look?

SG: In the mornings I review labs, review the patients for the day and the majority of the time is seeing the patients all day. If I have time at the end, I check phone calls, return emails, collaborate with other providers and prepare for the next day.

JM: How many patients do you see and

how long do you usually spend with a patient?

SG: It really depends on a day-to-day basis, but it can be 3-6 in the day hospital. On clinic days, it can range from 2-5 patients. I spend about 30 minutes to an hour with each patient depending on the visit.

JM: Are there possible projects that you are planning to do in the future?

SG: Yes -- since I am relatively new, I want to make sure I learn as much as I can about thalassemia to truly understand the disease. Educating and inspiring is important to me so my goal is to try to find a way to apply what I know to reach out and educate as many people as I can.

JM: What do you do when you are not working?

SG: I spend time training and participating in triathlons. The Ironman consists of a 2.4 mile swim, 112 mile bicycle ride and a marathon, and it typically takes me 12 hours to complete. I also spend time participating in other small races to prepare for it. I have my third race coming up on October 1st in Maryland. I also enjoy spending time with friends and family, and traveling.

JM: Thank you so much for this interview!

SG: Thank you!

Talking Nutrition with Connie Schroepfer, MS, RD

These questions were directly from families who have a child with thalassemia. They were collected by Wendy Murphy and the interview was conducted by Jin Mei.



Perspectives: When do we have to focus on foods that are high in iron? Should we avoid them and at what age?

C: It depends on whether or not the child or adult is on routine transfusions. For those who are not receiving transfusions, a low iron diet is recommended. When a person is anemic, they will be much more efficient in absorbing iron. For transfusion dependent, there are just a few usual recommendations: avoid iron fortified foods, e.g. most ready to eat cereals, limit high vitamin C sources at meals. For both groups it is important to choose a multi-vitamin that doesn't contain iron, and to take it away from meals as it contains vitamin C which enhances the absorption of iron from food.

Q: What about homeopathic supplements for children with thalassemia? Any restrictions or recommendations?

C: My advice is to speak with the medical team about your interest in homeopathic supplements since they may contain unknown or harmful substances.

Q: How important is a specific diet for children with thalassemia?

C: Since every child is different, it is important to meet with a registered dietitian. Come with a three to four day food and beverage record as well as pictures and bottles of the supplements that the child takes. (From there the dietitian can assess the child's needs). Usual food intake along with growth records will be helpful for the dietitian in assessing the child's nutrition and providing individualized recommendations.

Q: Suggestions for "picky eaters" who generally like sweets and junk food such as pizza & French fries. How can I get my child to eat more healthy food?

C: Pizza and French fries are not everyday food but can be given on occasions. Pizza and French fries and some sweets may have a place in the child's diet, but not to the exclusion of other foods. Tell the child those are "not everyday foods, they are sometimes foods".

It is the parent's job to present the food. The child decides whether or not or how much of the food they will eat. Parents lead by example in eating a variety of food and presenting this variety to the child along with some of the food a child will usually accept. The mantra I use is, "make new usual". Parents should not force or pressure the child as it will create negative eating habits in the future. Meal time should be enjoyable which is why I think kids enjoy pizza and French fries since these foods are associated with having a good time.

One way to get kids to try new food is having them connect the idea of learning new things at school to trying new foods at home. Have the child participate in age appropriate meal preparation and grocery shopping. Another idea is doing a "science experiment" where the child is involved in tasting the different kinds of food. For example, buying three different brands of apples and have the child conduct an "experiment" to see which brand they like the best.

Finally, framing the question is also important. Rather than giving the child a multitude of options for lunch, simply ask if they want their sandwich in a square or a triangle. By limiting the choices to just a

variation of the desired food, the child will have a buy-in when they choose one of the options.

Q: Is there a caloric target for catch up growth?

C: Usually it depends on the age but to generalize, I would take the usual caloric intake of the child and add 200-300 more calories into their diet. (For a more detailed explanation of the math, see a registered dietitian). A registered dietitian may be helpful in advising ways to increase the child's caloric intake.

Q: Anything we should eat/avoid to help inhibit iron absorption? Such as milk, Vitamin C, etc.?

C: I think it is important for kids, especially children to consume milk because not only does the calcium in milk inhibit iron absorption, it also provides the calcium, fat and calories that the child may be lacking for growth. Another recommendation is to drink tea with meals since it reduces iron absorption. However, I would prefer the kids to drink the milk first before the tea with the benefits stated above.



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Interview with Huythong Nguyen by Jin Mei



JM: Let's start with an introduction, where are you from?

HN: I was born in Saigon, Vietnam.

JM: When were you diagnosed with thalassemia?

HN: Soon after I was born, I became very sick and jaundiced. When I was 2 years old, I was diagnosed with E Beta Thalassemia and needed a splenectomy. Shortly after, I began receiving blood transfusions.

JM: When did you come to America?

HN: My family and I immigrated to the U.S when I was six years old and lived in Virginia. I had my treatments at Fairfax County Children's Hospital. Later my family moved to Maryland and I was treated at the NIH (National Institute of Health) in Bethesda, MD.

JM: How did you end up in California and specifically, UCSF Benioff Children's Hospital Oakland?

HN: The job I had in Maryland was changing its medical insurance policy and that posed a serious financial burden -- which was why I moved to California to find a new job. I also wanted a change of scenery. Before I moved, I asked my doctor at NIH for a referral in the Bay Area. I heard good things about Dr. Vichinsky and his team. Around that time, my ferritin level was over 9,000. I also have diabetes due to being iron overloaded; it is well managed now with the use of an insulin pump.

JM: Wow that is intense! How was your treatment as a result of that fact?

HN: I have blood transfusions every three

weeks instead of four weeks. Before Exjade and Jadenu, Desferal was the only iron chelation treatment available. The medication was infused by a pump into you through a needle. The common area was your belly. It was definitely not fun.

and Thalassemia treatments. The financial aspect of thalassemia is also very costly. Without a good insurance coverage plan, my parents would have to pay thousands of dollars just on medication -- not to mention blood transfusions, lab tests, etc. Having Thalassemia adds an extra layer of responsibility. I feel being healthy is more important than having fun at times.

JM: Besides being a patient, what else have you been involved in with UCSF Benioff Children's Hospital Oakland?

HN: I was the Patient Travel Coordinator on the Tircon study. I assisted on other studies as a Study Coordinator. I'm helping you with the outreach projects. I volunteered for TAG (Thalassemia Action Group) years ago, which was an organization run by patients and focused on patient services. We would organize a

national annual conference for all thalassemia patients and their families to share the latest information regarding the treatment of thalassemia. I was the Treasurer and the Editor for the TAG Newsletter. Honestly, I enjoyed my experience with the TAG members. It was a great way for patients, siblings, and families to connect and to know that they are not alone with this disease. I am so thankful to the founding members of TAG for their dedication.

JM: Thank you for this interview!

HN: Thank you.



Photos

Left: Huythong Nguyen.

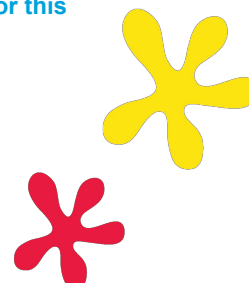
Right: With Jin Mei

JM: What were some of the obstacles you had to face with regards to the treatment?

HN: For Desferal, compliance was the biggest issue. No one wants to be poked with a needle and leave it in for 10-12 hours for the medication to infuse, 7 days a week. It was really uncomfortable. With Exjade, time is the issue. I feel it is inconvenient to wait an hour for medication to dissolve in water before I can drink it. Jadenu is now available as a blue pill... (not that blue pill). It's a few tablets to take every day, just like your other medications.

JM: How has thalassemia affected your personal life while growing up?

HN: I strongly believe living my life with thalassemia rather than having my life revolve around thalassemia. Having said that, it was definitely difficult balancing school, then work and going to college,



Genotyping to Determine Blood Type

Shannon Kelly, MD: pediatric hematologist & transfusion medicine specialist, UCSF Benioff Children's Hospital Oakland



Most people know their blood type as "O-positive" or "A-negative" or some combination of the ABO blood type (either A, B, O or AB) and the D blood type (positive or negative, meaning the D protein is either present or absent). While "blood type" commonly refers to only the ABO and D blood groups, there are actually 35 different blood group systems.

Among these blood groups, there are more than 300 different versions of proteins and carbohydrates that can be present on the surface of red blood cells. Some of these molecules have known functions. For example some serve as transporter molecules to move things in or out of

between the recipient and transfused blood, it is not typically a problem the first time the different blood is transfused. However, there is a chance that the recipient's immune system will recognize a different blood group as foreign and therefore make an antibody against this blood group. If that

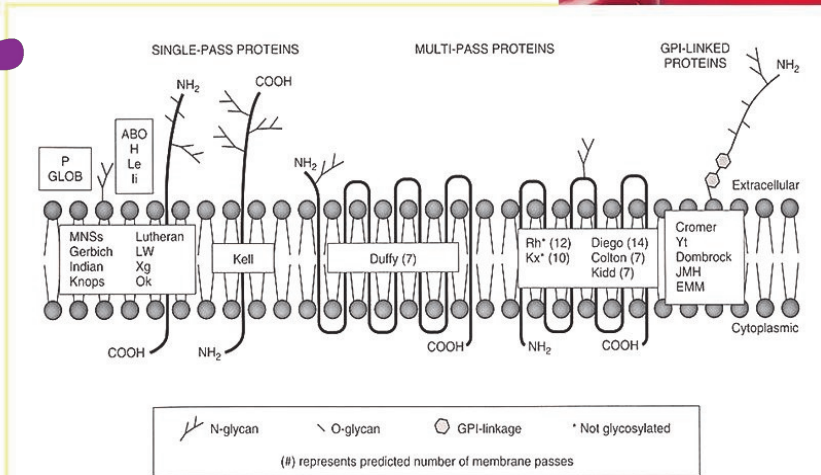
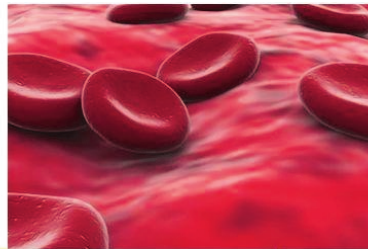
RBCs would be measured. Also, the testing is difficult in patients who have multiple RBC antibodies because the antibodies can interfere with the testing. Fortunately, the genetic basis of most of the blood groups is now understood. Most of the different blood proteins and carbohydrates found in the minor blood groups are determined by very simple changes in the DNA. Therefore, genotyping (testing for specific changes in the DNA) can be performed to easily determine the minor blood groups. ABO/D type similar to the minor blood groups.

Genotyping is becoming the standard testing method to determine the minor blood groups. Genotyping has several advantages over the serologic testing. The genetic testing is performed on the DNA extracted from inside white blood cells. Because most of the white blood cells are filtered out of the blood used for RBC transfusion, genotyping can determine the blood groups even if a patient has been recently transfused. Genotyping can also predict the blood groups in patients with antibodies that may prevent direct measurement of the blood groups antigens on the surface of red blood cells. Finally, the reagents needed to measure very rare blood groups on RBCs can be very expensive and only found in specialized laboratories in certain centers. Genotyping allows the identification of even rare blood groups in most large blood banks.

In addition to using genotyping to determine the minor blood groups of patients who need blood transfusion, genotyping is now increasingly being used to determine the minor blood group antigens of blood donors. As more blood donors are genotyped, a wider inventory of blood with rare blood types is created. People with these rare blood types may become critical to support patients with thalassemia or sickle cell disease who require this rare blood on a regular basis.

As further research is completed to develop the technology to perform blood group genotyping on a large scale in a cost efficient way, genetic matching of blood donors and patients who need RBC transfusion will be the future of transfusion medicine.

Red Blood Cell Membrane Components



red blood cells (RBCs). The function of other blood groups is not known.

The ABO blood group and Rh blood group (which contains D, C and E antigens) are determined by more complicated genetics, therefore traditional (serologic) testing is typically still used to determine the ABO and D type. However, there is significant research currently underway to understand the various genetic changes that result in the ABO/D types and therefore develop genetic tests that can quickly and easily predict These blood groups are important in transfusion medicine because blood groups on the transfused RBCs need to be compatible with the blood inside the transfusion recipient. For most people who receive blood transfusions, blood is only matched at the ABO and D blood groups and this is safe in the vast majority of people. If the minor blood groups are different

person were to be transfused with blood containing that blood group again in the future, the antibody could then react with the transfused blood and cause a transfusion reaction. People that receive many transfusions, such as people with thalassemia or sickle cell disease, are more likely to make antibodies and therefore transfused blood for these groups of patients are matched for some of the minor blood groups in addition to the ABO and D blood groups.

The various blood groups can usually be directly measured on the surface of RBCs. However, there are situations in which determining the blood groups using these older methods is quite challenging or impossible. For example, for patients who have recently been transfused, there will be a mixture of the patient's RBCs and the transfused RBCs and blood groups of both

Iron Measurement and SQUIDS Across the Globe —continued from page 2

From Germany we traveled to the Piemonte region in northern Italy. Roland and I spent the bulk of our trip with the group of Prof. Antonio Piga, one of Italy's premiere experts in Thalassemia and also the person who introduced the SQUID Program in Italy. Their measurement program is large, performing more than 1,000 measurements on about 600 patients per year. Torino's SQUID is two years older than the Oakland SQUID with a strikingly similar design. Dr. Piga's program recently moved to University Hospital San Luigi Gonzaga of Orbassano, where they were housed in a beautifully constructed custom built ferrous metal-free building. Their Iron Program is run by Dr. Filomena Longo, MD, consultant pediatrician, who is assisted by her nurse Silvana Audello (retired this past May). I was amazed at the efficiency of this program to perform such a large volume of measurements.

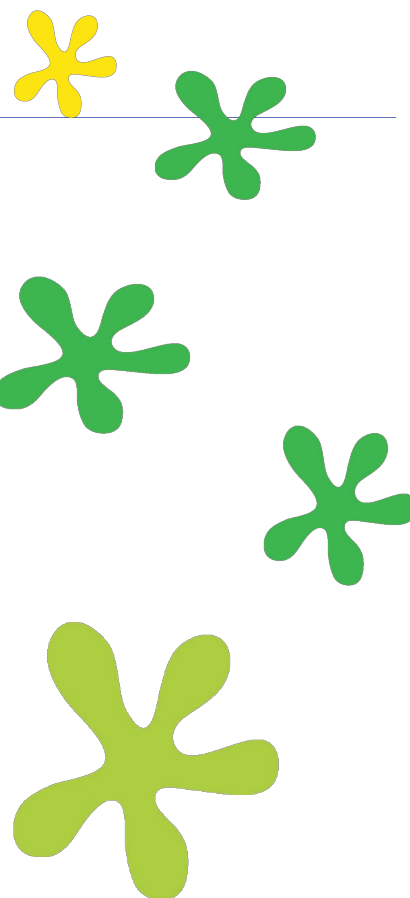
Around a half dozen patients pulled a number and waited for their turn. Silvana prepped patients, equipment and documents. She drew blood to measure ferritins and assisted Filomena with the SQUID. Filomena conducted the ultrasound, performed FibroScan (an ultrasound technique to assess liver fibrosis), SQUID and a chelation consult in about

20 minutes. In addition, she oversees the MRI measurements, analyzing the cardiac and liver MRIs. Due to the high throughput of patients, they no longer use their database and instead use a streamlined electronic medical record that they can use to do their research. Their MRI program is still growing, during my trip they were evaluating new software to help them analyze the liver and cardiac T2's. In addition they are developing new SQUID techniques such as measuring liver iron concentration in pregnant women and neonates. The majority of the patients in Torino have thalassemia hemochromatosis, hyperferritinemia and in some, sickle cell disease. However, with refugee migration the demographics of our European counterparts are changing with increases in number of patients with thalassemia syndromes and sickle cell anemia.

While the technology between all three sites is essentially the same the main differences between our programs are mainly logistical. The European SQUIDS have the European Union's version of FDA. We are incorporating MRI technology into our programs in order to track iron concentration in non-hepatic tissues. The longevity of the staff was strikingly similar. For all three SQUID programs, a

large percentage of the original staff is still working with retirement being the main reason people

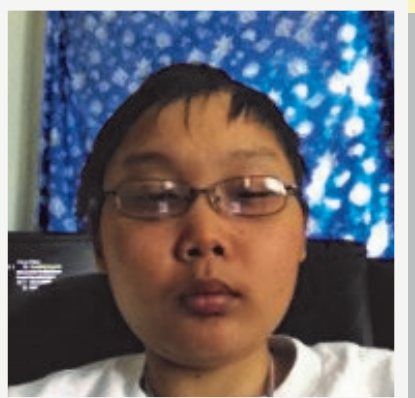
have moved on. I wonder what it is about this field that keeps the staff so dedicated. Is it that the more we understand the more questions there are to be answered? Is it the relationship we build with the patients and their families at yearly visits that feels familiar, like catching up with an old friend? Maybe it's the sense of pioneering and owning the future of this niche field? Whatever it is, I feel drawn to it as well. As one of the newcomers to the field, I feel a sense of urgency to learn from these pioneers. As an engineer with a background in magnetic measurements, I feel prepared to work towards the future. We have our work cut out for us to continue to evolve our iron measurement programs in order to better serve our patients and to work to increase access of body iron measurement to patients across the globe.



IN MEMORY OF STEVEN SRISAVAT

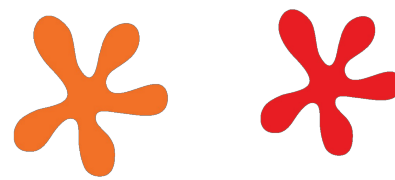
1986-2016

Patient, Colleague and Friend



4th Annual Thalassemia Adoption Clinic

Sponsored by the Northern California Comprehensive Thalassemia Center
at UCSF Benioff Children's Hospital Oakland on July 13th & 14th, 2016



Families who have adopted a child from other countries (China, India, and others) with Thalassemia came to our center for an annual comprehensive visit and consultation with our medical team. We saw families from five states, some traveling as far away as Oklahoma. This year, we had patients and families meet over two days in our clinic. They met several providers including thalassemia specialists, endocrinologists, nutritionists, and licensed clinical social workers.

That evening, families attended a dinner and talk. The children

participated in Dancin Power. (Dancin Power is a non-profit organization that teaches interactive dance classes to patients facing chronic and life-threatening illnesses).

Parents listened to several speakers discussing topics related to thalassemia such as fertility, nutrition and supplements, endocrine Issues and gene therapy. Afterwards, the speakers were part of a panel for an informal question-and-answer session. The speakers who presented at the Dinner Talk were Dr. Mark Walters, Dr. Titi Singer, Dr. Ash Lal, Dr. Elliott Vichinsky, Dr. Tariq Ahmad, and Ellen Fung.



Photos from the adoption clinic



Updated Research at Our Center

Results of the Gene Therapy Trial for Beta Thalassemia were presented at the 2016 annual meeting of the American Society of Hematology. Read the abstract here:

Lentiglobin Gene Therapy for Transfusion-Dependent β -Thalassemia:
Update from the Northstar Hgb-204
Phase 1/2 Clinical Study

<https://ash.confex.com/ash/2016/webprogram/Paper94600.html>

Information on the current open trial for gene therapy is available at this website:

<https://clinicaltrials.gov/ct2/show/NCT02906202>

To learn about options for stem cell transplant at UCSF Benioff Children's Hospital Oakland, please contact us at: 510.428.3885, extension 5396. If you are interested in learning about clinical trials in thalassemia, please contact: 510.428.3885, extension 2752.

Intrauterine Therapy for Alpha Thalassemia Major



Visit our web site to watch a video:

<http://thalassemia.com/services-intrauterine-therapy.aspx>

The UCSF Fetal Treatment Center and UCSF Benioff Children's Hospital Oakland Thalassemia Center have established a multidisciplinary center for Alpha Thalassemia Major.

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