Thomas Cheng of the Cooley's Anemia Foundation, California Chapter, and Toutu Vongphrachanh, Children's thalassemia outreach coordinator, at the Lotus Festival, Los Angeles, Sept. 9 to 10, 2005.

Special thanks to the following individuals for volunteering to help at the Lotus Festival: Thomas Cheng, Kiat Vongphrachanh and Gai Tran. We appreciate their time and hard work.

Announcements

★ **The Thalassemia Outreach Department just got bigger!**
Please welcome back Laurice Levine (formerly Laurice Compagno), who has returned to Children's Oakland to work with Toutu Vongphrachanh on thalassemia outreach.

★ **We need volunteers—for special events, health fairs and more!** If you would like to volunteer in the Thalassemia Outreach Program, please call: Laurice Levine at 510-428-3885, ext. 5427 or Toutu Vongphrachanh at 510-428-3885, ext. 4398.

★ **Cooley's Anemia Foundation Patient Incentive Awards**
- Awards are available to individuals diagnosed with thalassemia major or intermedia
- Awards of up to $1,500 annually are available to patients for college/university studies (both undergraduate and graduate) and to students enrolled in certificate programs
- An application can be found at www.cooleysanemia.org and is due by December 31, 2005.

★ **Children's Hospital in conjunction with Blood Centers of the Pacific will be putting on FIVE halloween blood drives in honor of Thalassemia on Oct. 29, 2005, 11 a.m. to 3 p.m.**
Please come donate blood at one of the five locations:
- The Village, Corte Madera
- The Mall at Northgate, Novato
- Broadway Plaza, Walnut Creek
- Somersville Towne Center, Antioch
- Bay Street, Emeryville

For more information, please contact Laurice Levine at 510-428-3885, ext. 5427

P E R S P E C T I V E S
Northern California Thalassemia Center
Children's Hospital & Research Center Oakland
747 52nd Street, Oakland, CA 94609

Address change requested

Perspectives Newsletter is produced by the thalassemia outreach coordinators, Toutu Vongphrachanh, Laurice Levine and the Marketing Communications department at Children's Hospital & Research Center Oakland. For questions regarding the newsletter or for more information on thalassemia, call 510-428-3885, ext. 4398, or visit www.thalassemia.com.

CHILDREN'S HOSPITAL
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ISSUE

PERSPECTIVES

NEWSLETTER OF THE NORTHERN CALIFORNIA THALASSEMIA CENTER - FALL 2005

PATIENT
PERSPECTIVE

My Experience with Desferal and L1

by Maria Hadjidemetriou

I am sure I speak for most thalassemia patients when I say how much we detest wearing our pumps. As much as I would love to say that I am the perfect patient who is always compliant with Desferal, that would be a lie.

I am two weeks shy of my 34th birthday, have thalassemia intermediate, and am someone who only recently accepted her disease and every aspect of it. Like many others, I don't like talking about my disease. Some people with thalassemia think of it as an anomaly, a no-no; I myself thought of it as a modern Pandora's box until I lived in Europe. I now speak about thalassemia as openly as I can and want to teach people about this genetic blood disorder.

Like many "intermediates," I was not always transfusion-dependant. I stopped being transfused at age 15 and terminated my chelation at age 16. I was thrilled at the thought that I would never have to wear the pump again. Throughout the years, I miraculously maintained a hemoglobin level of 8.5 to 9. I went to college, studied fashion design and marketing, worked for numerous fashion houses, and partied a lot, staying out until five in the morning while still being able to function the next day with a full load of classes and a part-time job. I thought this abundance of energy would last forever and felt a sense of being untouched by thalassemia. My body adapted and worked on this low hemoglobin until my mid-20s.

Around 25 years of age, my spine began hurting during my favorite routine exercise, bike riding, which I did for 90 minutes a day, four times a week. I stopped biking, but the pain continued while I was walking, sitting and sleeping. I went for an MRI—and if you are an intermediate, you already know what my diagnosis was—extramedullary hematopoiesis. As a result, my doctor started me on blood transfusions, bringing my very low hemoglobin level of 7 up to 10. After six months of hyper-transfusion, the mass of cells that was causing the pain in my spine decreased, so my blood transfusions were decreased to every 10 weeks.

During this time, my doctor advised me to start chelating with Desferal, but I did not listen. To all patients: please, please listen and just do it! I thought, "Why? I haven't been transfused for 15 years, I don't have time to chelate." As I reached my 30s, my blood requirement increased, and I began transfusing every seven weeks, but I was still not chelating.

Then a twist of fate came in early 2002 when I relocated to Cyprus, the warm and lovely island in the Mediterranean Sea. Though the Thalassemia Center in Nicosia, the capital of Cyprus, looks like a building from a third-world country, the treatment for thalassemia there is both pleasing and encouraging. I met many thalassemic women who either had children or were pregnant and all the patients were compliant with Desferal treatment. They could not believe my attitude and lack of compliance. One patient, an English/Cypriot, simply said to me, "Just get over it." But I couldn't. After not chelating for the past 15 years, and being transfused regularly for the past four years, my ferritin was around 1,800, which is pretty good. But I was having pain in my heart, which is a sign of iron overload. It was difficult to assess cardiac iron at that time, but currently MRI/T2 is being used to assess cardiac iron.

At times, I thought my heart was going to jump out of my body. Sometimes, as I lay in bed trying to sleep, I felt like I was taking my last breath. Yes, it was that bad! That is when I started an oral chelator called Ferriprox (also called L1 and deferiprone).

Many of you are a bit hesitant to try Ferriprox, and unfortunately it is not available in the United States. This medication is being used in 48 countries and has been around for 18 years. Doctors have found positive results with combination therapy (Desferal and Ferriprox), and I would urge everyone to go on Ferriprox. The side effects are not bad and may be different for everyone. During the first month on the med-

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EVENTS CALENDAR

First Annual East Coast Desferal Camp – Sept. 17–18, 2005
Holmdel, New Jersey
Sponsored by the Thalassemia Action Group (TAG)
For more information or to register for camp, call: Gargi Pahuja/TAG at 201-533-8454 or email TAG@cooleysanemia.org

National Anemia Conference 2005: Maximizing Health for Chronic Anemias – Sept. 24–25, 2005
Novotel, 45 The Esplanade, Toronto, Ontario
For more information, please call Margery Konan, Anemia Institute for Research and Education at 416-969-7457 or email margery@anemiainstitute.org

The California Chapter of the Cooley's Anemia Foundation and Children's Hospital Los Angeles Holiday Event – Nov. 12, 2005
11 a.m. to 3 p.m. The party is for patients and their families. There will be doctors speaking on the latest treatments, as well as food, entertainment and fun.
For more information please call: Christine Giannamore at 800-601-2821 or email ca_chapter@hotmail.com

Tenth International Conference on Thalassemia and Hemoglobinopathies
and
Twelfth International Thalassemia International Federation (TIF) Conference for Thalassemia Patients and Parents
Jan. 7-10, 2006
Dubai, United Arab Emirates
For more information, please email Gargi Pahuja, TAG President, at gargitag@mac.com

Combination Therapy

By Craig Butler
National Communications Director, Cooley's Anemia Foundation

For some time, people with thalassemia in the United States have heard a lot about "combination therapy." This treatment, involving both Desferal and deferiprone (also known as L1), is being used in other countries to significant benefit.

Deferiprone, for those who are not familiar with it, is an oral chelator—that is, a drug that is swallowed, rather than infused like Desferal (DFO). The dosage varies, but it usually involves taking two to three pills three times a day.

With combination therapy, a patient uses both DFO and deferiprone; the doctor and the patient decide exactly how many days each one is used. Renzo Galanello, MD, writing in *Hematology* in 2004, states that "combined chelation offers several potential advantages. Chelators with distinct chemical properties may have different iron carrying capacities and accessibility to different iron pools. Formal balance studies and clinical trials with DFO and deferiprone have shown that two chelators may have additive or synergistic effects, resulting in an increased efficacy."

Dr. Galanello also quotes from a study in the *British Journal of Haematology* that found that "giving deferiprone every day and DFO two days a week produced iron excretion comparable to that achieved with DFO administered five days a week. This regimen of chelation is more tolerable and may be attractive for patients who are unable to comply with regular daily use of DFO."

(Although the study cited here refers to a regimen involving deferiprone seven days a week and Desferal two days a week, we emphasize again that the exact regimen would be determined by a doctor and patient, based upon the patient's specific needs.)

Antonio Piga, MD, of Turin, Italy, presented information on deferiprone and combination therapy at the recent Eighth Cooley's Anemia Symposium in Orlando, Florida. The following is taken from his abstract:

Recent results from independent studies suggest that deferiprone may be more cardio protective than deferoxamine [Desferal]. Patients on long-term treatment with deferiprone have a better myocardial MRI pattern, and less chance to develop a new cardiac disease or to worsen an existing one. Most of these observations are retrospective and require a confirmation from randomized controlled trials. Other new observations regard the effects of combining the two chelators. Most results indicate an additional effect on iron excretion and a significant reduction of the time required to lower severe iron overload and to reverse clinical heart disease. Again these data require confirmation, as obtained at most on individual cases or small series of patients treated with a wide range of combinations of the two chelators, but the univocity of results is impressive.

Deferiprone has not been approved by the Food and Drug Administration (FDA) for general use in the United States. However, ApoPharma, the maker of Ferriprox (the brand name for deferiprone), is in the process of submitting data to the FDA. Once data submission is completed, the company hopes to obtain an expedited review from the FDA, meaning that the review process would be completed within six months of the data submission. At this point, we do not know when the data submission will be completed, but because Ferriprox is already available in 48 countries, ApoPharma should be able to begin marketing the drug relatively

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Combination Therapy [continued from page 2]

quickly upon receiving a positive decision from the FDA.

It should be noted that physicians can already obtain deferiprone for some patients in the United States through the FDA's Treatment Use Program, which allows patients to receive promising experimental drugs before they have been approved for sale in the United States. The FDA works to ensure that Treatment Use Programs provide high standards for the assurance of safety and protection of patients in these programs.

ApoPharma has established a Treatment Use Program to provide Ferriprox, free of charge, to physicians who have patients who are unable to take Desferal. To gain access to Ferriprox through this program, the physician and patient first must discuss the benefits and risks of Ferriprox. If both feel that Ferriprox may be of benefit, the physician must contact ApoPharma in writing to request treatment use of Ferriprox. ApoPharma will request information on patient medical history and current clinical status, after which ApoPharma will make a preliminary determination as to whether the patient meets the criteria for inclusion in the Treatment Use Program. If so, the physician must submit a single patient Investigational New Drug Application (IND) to the FDA. Such applications are generally answered within a month.

Obtaining optimum chelation is, of course, vitally important for people with thalassemia. If you and your physician feel that your current therapy is producing the best results for you, we urge you to continue with that therapy. But if you feel that an alternative is needed to ensure optimum chelation, you may want to discuss a treatment program involving deferiprone with your doctor.

The author may be emailed at c.butler@cooleysanemia.org

Tips on Mixing Desferal and Doing the Pump

1. When you get your delivery of Desferal for the week or month, sort everything out, and make individual bags for each night of the week. For example, put everything you need to mix Desferal (Desferal, sterile water, syringe, etc.) in a Ziploc bag, and then when you are ready to mix, you have everything ready to go.
2. Mix a few nights worth of Desferal all at once—it saves time! Note that once mixed with sterile water, Desferal lasts for up to seven days.
3. Wash your hands with warm water and antibacterial soap before mixing Desferal.
4. When you pop off the tops of the Desferal and sterile water vials, clean the vials with an alcohol wipe.
5. Always point the syringe and needle away from your body so you do not poke yourself by accident.
6. When mixing Desferal with sterile water, DO NOT shake the vials. To dissolve the Desferal, roll the vials in the palm of your hand, or place the vials in your sock or the waistband of your pants. Your body heat will dissolve the Desferal in a few minutes.
7. Put all needles in a sharps container.
8. Wash your hands and clean the site with alcohol before inserting the needle into your subcutaneous tissue.
9. Rotate the needle sites so that the tissue has time to heal before you use the same site a second time.
10. If inserting the needle is painful, take a few deep breaths and try to relax before trying again.
11. If you have a fever above 101°F, do not take Desferal.
12. Emla cream, a topical anesthetic, sometimes helps lessen the pain of the needle stick. Emla should be applied at least 30 minutes before needle insertion.
13. If you experience redness and itching at the infusion site, you may want to add hydrocortisone to your Desferal routine. Hydrocortisone cream, applied to the skin when the infusion is finished, may reduce itching, as well. Adding more sterile water to Desferal or running your pump for a longer period of time may also help reduce lumps and itching.
14. It is vital to use Desferal to prevent iron overload and to live a healthier life!

Thalassemia Outreach

AUG

August 20: Family Picnic, Aquatic Park, Berkeley

August 27–28: Eighth Annual Oakland Chinatown Streetfest

SEPT

September 2–5: Italian Catholic Federation 75th Annual Convention, Fresno

September 10: Friends, Neighbors and Resources Fair, Stockton

September 18: Eleventh Annual Arab Cultural Festival, San Francisco

September 23–25: Young Adult/Adult Retreat, Santa Cruz

OCT

October 7: Head Start Family Day and Resource Fair, Sacramento

October 15: YMCA Cheadle Family Health Fair, Stockton

October 15–16: Indian Festival, Fremont

NOV

November 11–13: Hmong New Year Festival, Stockton

DEC

December 17: Thalassemia Holiday Party, Children's Hospital Oakland

For more information about these events, please call Toutu Vongphrachanh at 510-428-3885, ext. 4398 or Laurice Levine at 510-428-3885, ext. 5427.

Iron Overload: Extremely Harmful, but Preventable!

by Titi Singer, MD
Hematologist, Children's Hospital & Research Center Oakland

Treating severe forms of thalassemia with regular blood transfusions has been an important element in the management of thalassemia for the past 30 years. Transfusions are given to correct anemia (low hemoglobin level) and minimize the other clinical manifestations of the disease, such as bone changes and enlarged liver and spleen. To reach these goals, most patients require blood transfusions every three to four weeks with a blood amount of 10–15cc/kg (approximately two to three units of blood).

The side effects of frequent blood transfusions

The primary function of red blood cells is to carry oxygen to all parts of the body. Since iron binds to oxygen, red blood cells are iron-rich. Therefore, transfused blood, called packed red blood cells, contains a large amount of iron. Unfortunately, the body does not have a mechanism to remove this excess amount of iron, which comes with each transfusion. As a result, a regular transfusion schedule will cause a rapid increase of the body's iron load. Each unit of blood contains approximately 200 milligrams of iron. It is estimated that by the age of 10, a transfused child will accumulate approximately 25 grams of iron, while an adult unaffected by thalassemia has a total of only about 5 grams of body iron. In addition, even more iron can accumulate from iron-rich foods and absorption in the gut, since the thalassemic body "thinks" it needs more iron to make more of its own blood.

Why is too much iron so bad?

In healthy people, iron is bound to storage proteins, but when there is excess iron coming from blood transfusions, it stays free (unbound) in the blood. This free iron generates extremely toxic elements called "free radicals" which cause tissue damage. If excess iron is not regularly removed with medication, it deposits in many body organs, where it causes gradual tissue damage. In some organs, the damage is more profound and can cause serious medical problems.

One of the places iron deposits is in the heart muscle. Over time, it makes the heart muscle stiffer and less elastic, so that it cannot pump blood as well. This results in cardiac failure. Iron can also cause serious problems with the rhythm of the heartbeat. Iron overload in the heart is still the most common cause of death for people with thalassemia.

Without regular chelation therapy to remove the iron, a regularly transfused child with thalassemia will die during the second decade of life, most likely from heart disease.

A lot of iron also accumulates in the liver, which acts like a sponge, absorbing high amounts of iron. The iron gradually damages the liver tissue, making it stiffer (fibrotic) and less healthy. Iron also tends to damage the sensitive endocrine glands; these are the organs that secrete hormones that regulate many bodily functions. Iron-loaded patients can therefore develop diabetes, since the pancreas gland, which produces insulin, is affected by excess iron. (Insulin is the hormone that regulates blood sugar; the pancreas does not make sufficient insulin in people with diabetes, so they require treatment with insulin shots to maintain safe blood sugar levels.)

Patients may suffer from a variety of other hormone deficiencies, including the following: thyroid hormone, which affects the level of metabolism and energy; parathyroid hormone, which controls bone calcium; growth hormone, which results in slow growth and short stature; and sex hormones, which causes delays in maturation and growth, making it extremely difficult for women to get pregnant.

Patients can have one or more of these hormone deficiencies, depending on the level and length of time of their iron overload. As a result, many patients need to get medications in the forms of tablets or regular shots to replace these hormones. It is thought that iron overload also causes direct damage to the bones and to the lungs, but these effects are less well studied.

Iron chelation therapy—a lifesaver

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Desferal, a chelation imaging a drug that can bind to metals like

Iron Overload

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iron—was introduced in the early 1970s, and is considered an extremely effective agent for the prevention of iron overload in thalassemia. Long-term studies have shown that its use allows patients to live much longer and have a better quality of life. When Desferal binds with iron, the iron becomes inactive, preventing the toxic effect of free radical formation. Unfortunately, Desferal is poorly absorbed by the gut and disappears rapidly from the blood. Therefore, only continuous, prolonged administration—infusion by pump (subcutaneous or intravenous)—is effective.

Although patients may have massive iron overload in their tissues, only very small amounts of iron are available for binding to Desferal. Administration of Desferal as an infusion over a prolonged time can remove more iron. The iron slowly comes out from the tissues into the bloodstream, where it is "captured" by Desferal. The Desferal-bound iron is then removed from the body, mostly by secretion in the urine, which gives the urine a reddish color.

Desferal is usually prescribed five to seven nights a week over an 8 to 12 hour period. Though undoubtedly not an easy medication to use, studies have shown remarkable results. First, it was shown that adequate therapy has led to survival curves approximating those of normal populations. Second, it was demonstrated that long-term use of Desferal resulted in long-term survival free of iron-induced cardiac complications. Third, studies showed that damage to the liver can be prevented; in fact, intensive Desferal therapy can sometimes reverse liver and cardiac dysfunction. The effect on the endocrine system is also beneficial, although it seems that some endocrine glands are very sensitive to iron overload, and even adequate chelation cannot always completely prevent or reverse complications. Adequate Desferal chelation, however, can reduce the likelihood of developing diabetes.

Intense research is still in progress to learn how to best use Desferal so it prevents iron overload damage while refraining from its overuse (because of Desferal's own side effects). In addition, studies seeking other chelators that can be given orally, combined with or without Desferal, are in progress.

Patient Perspective

[continued from page 1]

ication, my side effects were nausea, stomach cramps and tiredness. I have friends in Cyprus who did not experience tiredness, but instead had an excessive amount of energy. Another side effect experienced by some people I know is vomiting. Your body adapts to the drug after about a month, so some of the symptoms go away.

After about five months of using Ferripox, I began experiencing excruciating joint pain in the knees, which is synovitis. I blame myself and not Ferriprox for this, because I thought I could take the easy way out and just pop nine pills of Ferriprox a day, rather than doing a combination therapy of Ferriprox and Desferal.

I consulted a fine and talented doctor whom you may know, Dr. Fernando Tricta. He advised me to stop Ferriprox for about five months to alleviate the pain in my joints, and to do Desferal instead. I followed his instructions and chelated for five months, and then I began combination therapy of Desferal and Ferriprox. It worked, and my symptoms lessened. I do occasionally feel some joint pain, but it is nothing intolerable. Today, I am on six pills of Ferriprox a day and increasing it very slowly. I finally took the advice from my friend in Cyprus—I got over it and I feel FANTASTIC!

I am currently back in the beautiful Big Apple and am continuing with my combination therapy. My ferritin is getting lower and is now 1,400. Though I sometimes can't chelate four times a week, every week, I try. I know I've come a long way from my very sophomoric behavior, and I am now at a point in my life where I talk to people about my disease. We have a responsibility to educate others about thalassemia. There is no cure—but education is a form of cure.