

Pathogen - CONTINUED FROM P.1

have been used successfully to inactivate pathogens in red blood cell products. FRALE's are reported to decompose after pathogen inactivation. Inactivation products and the remaining compound can be removed from the blood product. These compounds have proven very effective when tested against common viral and bacterial pathogens.

Currently the company making this inactivation system is testing it in a national transfusion study. At Children's Hospital & Research Center at Oakland some patients are receiving this product as well, as part of a clinical research study. In small doses, FRALE's can also be used to paralyze the white blood cells. Research with these compounds is ongoing at Children's Hospital Oakland Research Institute.

• **Ethylene imine**

Ethylene imine (PEN 110, Inactine System) is a unique low-molecular-weight water-soluble compound that also chemically inactivates DNA and RNA. The active compound is known as PEN110 and the process of pathogen inactivation is known as the Inactine process. This compound does not require light for activation and is effective in low concentrations. The process of inactivation

requires that the blood be washed 12 times with an instrument (Hemonetics) designed specifically for this process to remove the compound and the products of inactivation. The finished product is a unit of washed, leukoreduced, pathogen-free product in a standard preservation solution (AS-3).

• **Riboflavin**

Riboflavin (Vitamin B2) is a water-soluble coenzyme that participates in chemical reactions. This vitamin is normally ingested in the diet and is rapidly taken up by cells to participate in metabolic processes. The vitamin B2/pathogen inactivator has only been used in platelets because, like the psoralens, it is activated by visible light and chemically inactivates DNA and RNA.

Pathogen inactivation holds great promise for the future of transfusion medicine and blood banking. Like all new medical procedures and pharmaceuticals, the actual risk and benefits of these components and procedures will take years to determine. The cost of these procedures could be significant but the end result would be a blood product that would not transmit infection. Hopefully these systems would be made available in countries where blood products are much less safe than here. ■

P E R S P E C T I V E S

Northern California Thalassemia Center
Children's Hospital & Research Center at Oakland
747 53rd Street, Oakland, CA 94609

Address change requested

Perspectives

Newsletter of the Northern California Thalassemia Center - April 2003 - Issue XXV

*

Pathogen Inactivation of Blood Products

By Keith Quirolo, MD

Hemoglobinopathy, Children's Hospital & Research Center at Oakland

Pathogen inactivation has been a goal of blood banking since the 1940's when the pasteurization of albumin was used to prevent jaundice following transfusion. In those early days health-care providers and scientists knew that some people who received transfusions became jaundiced following the transfusion, but the reasons for the jaundice remained unknown. Over the next decades, researchers found that viral infections were responsible for these findings and identified some of the viruses. As a result, blood collectors used questionnaires and liver function testing to screen donors and to determine whether they would pose a risk to recipients. Blood bank directors decided whether to establish a blood testing policy for their own blood bank. It was not until the HIV epidemic of the 1980's that people became fully aware of how transfusion of blood and blood products could lead to serious and deadly consequences for recipients.

In the wake of this devastating time for recipients and for blood bankers, researchers in transfusion medicine began thinking of a way to make blood free from infectious complications. Their experiments in pathogen inactivation have used many compounds: porphyrins, phenothiazines (methylene blue), cyanines, psoralens, as well as other riboflavin, ethylene imines (PEN110), and FRALEs (frangible anchor-linked effector compounds: S303 and others) to inactivate viruses, bacteria, and leukocytes. Currently, the most promising methods of pathogen inactivation are psoralens, FRALEs (Helinx: Intercept System), ethylene imines (Inactine), and riboflavin.

• Psoralens

Psoralens are naturally occurring compounds used in the 1970's to treat psoriasis by oral ingestion followed by ultraviolet light exposure of the skin. At that time, scientists investigated the chemistry and toxicity of these compounds. Psoralens

combine chemically with nucleic acids exposed to ultraviolet light. The compounds formed are stable and halt the transcription of DNA or RNA making it impossible for viruses or bacteria to replicate. These compounds can be added to blood products in a dose that will overwhelm the DNA repair mechanisms of bacteria, viruses, and white blood cells, making the product safe. Neither red cells nor platelets require replication to function. They are not affected by psoralens. Because activation of these compounds requires light, they can only be used with platelets and plasma.

• FRALE (frangible anchor-linked effector compounds)

FRALE's (S-303, Helinx, Intercept System) are unique compounds that irreversibly cross-link DNA and RNA without the use of light. They

CONTINUED ON P. 6

Update on Innovations in Iron Chelation

By Jaqueline Madden, PNP
Children's Hospital & Research Center at Oakland

Twenty years ago, the availability of desferal therapy marked a monumental change in the lives of people with thalassemia and iron overload. The standard of care has remained very much the same since then. Clinical research over the years has provided a greater understanding of thalassemia and iron overload. In the coming years we may start to see the benefits from this basic research in the form of more options for chelation therapy. This new era begins with clinical trials and ends, we hope, with better care.

Last year, trials began on a long-acting IV chelator called 40SD02. This compound combines

CONTINUED ON P. 5

Blood Safety Study

By Laurice Compagno

In September 2002, I agreed to become a pilot of the Cerus-Baxter Blood Transfusion Study; I was the first patient (who receives regular blood transfusions) to experiment with a treatment. The goal of the study is to reduce pathogens in packed red blood cells used for transfusions.

All blood banks test donated blood for infectious agents such as Hepatitis C and HIV. Although the technology for testing blood has significantly improved blood safety, some infected units still remain undetected. Baxter Healthcare Corporation and Cerus Corporation have developed a process that uses a chemical known as S-303 to kill certain bacteria and viruses that can go undetected by testing procedures and cause disease following a blood transfusion. Before the United States Food and Drug Administration (FDA) can approve S-303, Baxter and Cerus need to determine how red blood cells treated with S-303 compare to red blood cells not treated with the same chemical. The study must determine whether treated blood cells last as long as regular blood cells; whether treated blood cells function as



LAURICE COMPAGNO RECENTLY SPOKE AT ICF BRANCH 184 IN LOS GATOS. CHILDREN'S HOSPITAL OAKLAND WAS THE FORTUNATE RECIPIENT OF \$1, 213. MANY THANKS TO THE MEMBERS OF BR. 184 FOR THEIR CONTINUED SUPPORT AND GENEROSITY.

effectively and are tolerated as well as untreated blood cells. The study must also assess the safety of the treated red blood cell transfusions and compare it to untreated red blood cell transfusions.

As a research participant, I have agreed to receive at least eight transfusions using blood treated with S-303 and eight transfusions using untreated blood. The course of the study is 12 to 20 months. This is a blind

study which means that only the researchers know what blood I am receiving at the time. During my type and cross match and then immediately before receiving a blood transfusion, extra lab tests are performed to determine how the cells compare. This amounts to approximately five to seven extra vials of blood before each transfusion.

This study will involve 50 patients with either thalassemia or sickle cell anemia and will take place at the centers of specialty for thalassemia across the US. If this treatment program is successful, it would aid reducing the risk of disease transmission for all people requiring blood transfusions. ■

* * * * *



4TH ANNUAL BLOOD DRIVE
IN HONOR OF
INTERNATIONAL THALASSEMIA DAY
MAY 5, 2003

FOR MORE INFORMATION, PLEASE CONTACT LAURICE COMPAGNO AT (510) 528-8617.

Iron Chelation - CONTINUED FROM P.1

desferal with a starch that keeps the desferal in the blood so it can work longer. The goal is to have a once-a-week, one-hour intravenous infusion of 40SD02 replace a week's worth of subcutaneous desferal therapy.

Of 17 people who agreed to be screened for participation in the study at sites in Oakland and New York, 12 received one dose of the study drug. Single doses of up to 600 mg/kg of 40SD02 were found to be safe and well tolerated and clinically significant iron excretion was demonstrated. Based on these results, the study has been expanded to include one higher dose level of 1200 mg/kg, which should achieve a consistent therapeutic level of iron excretion.

Many, many thanks go to all the people who agreed to be screened and participate in the study so far. It takes a great deal of courage to be willing to be among the first people to receive a new drug, especially when the direct benefit is very small. Without these pioneers, treatment could not advance.

Another long awaited drug is just beginning clinical trials. This is the oral chelator called ICL670 made by Novartis. Two studies have begun enrolling subjects in Europe and are about to start in North America. Both studies are open to people at least 2 years old with transfusion-related iron overload. The studies involve a year of treatment with visits every four weeks and require, with few exceptions, liver biopsies at the beginning and at the end of the treatment period. In one study, people with beta-thalassemia are randomized to receive either standard desferal therapy or the oral chelator for one year. Although almost everyone would prefer to receive the oral drug (which is not a pill but a tablet that is dissolved in water that you drink), this study design is the most reliable way of showing that the new drug works as well as—or better than—the standard therapy on similar groups of people.

Another study is open to people with many kinds of anemias (except sickle cell) treated with regular transfusions that result in iron overload, including people with beta-thalassemia who cannot be treated with desferal. Everyone in this study will be given ICL670. Trials for people with sickle cell disease are scheduled to begin in the summer.

When the studies are completed, everyone who participated will have the opportunity to

receive the oral chelator until the drug is approved by the FDA and becomes available by prescription. North American sites in Atlanta, Boston, New York, Oakland, Philadelphia, Stanford, and Toronto will be enrolling people in the studies this spring.

The decision to participate in clinical trials is not an easy one. It requires a commitment of time and energy that can be difficult to maintain over a week, or a month, or a year, or sometimes even longer than that. But without these studies, change is impossible. Advances in the standard of care for all are based on the results of well-designed studies done with close adherence to the protocol by the few who participate. Clinical trials and better care begin and end with you. ■



DESFERAL CAMP FOLLOW-UP ACTIVITY:
VALENTINE'S PARTY, FEB. 13, 2003.



MAE FERRARO FROM ICF BR. 4 AND
TOUTU YONGPHRACHANH, THALASSEMIA
OUTREACH COORDINATOR WITH
DONATIONS FROM PAK 'N' SAVE IN SAN
JOSE, CALIF. THANK YOU PAK'N' SAVE!

* * OUTREACH * *

★ **SPRING FLING FUNDRAISER**

On April 3, 2003, the Hematology/Oncology department held its annual "Spring Fling" fundraiser benefiting patients and families who are afflicted with thalassemia, sickle cell anemia, cancer, and other blood disorders. The event was a great success, raising approximately \$5,000. During the event staff volunteered to sell craft items, tote bags, baby gifts and accessories, children's clothes, delicious homemade baked goods, and Asian delicacies such as lumpia, pancit, fresh spring rolls, fried rice, chow mein, Thai chicken curry, baked pork buns, and potstickers.

There was a raffle with a grand prize of two free Southwest Airlines tickets. Teresa Lopez from Care Access Center at Children's was this year's grand prize winner. A heartfelt thank you goes out to all of the donors and volunteers whose generosity and time made this fundraiser possible:

- Southwest Airlines
- Signature Theatres
- Albany Bowl
- Penzoil Speed Oil Change Center
- Starbucks
- Crate & Barrel
- Gentle Hair Cuts
- Claremont Hotel
- Todai Restaurant
- Lucky House
- Japanese Snacks
- Nora Wu
- Dora Goto
- Nancy Noonan
- Sherrie Shiota
- Cora Lindayen
- Brenda Wells
- Mary Jane Prieto

- Vicki Vannalath
- Excel Club
- Mae & Nick Ferraro (ICF Br. 4)
- Rose & Don Arnaudo (ICF Br. 184)
- Kay & Lisa Liu
- 5 South Nursing Staff
- Day Hospital Staff
- Mohini Singh
- Lieng Vongphrachanh

A special thank you goes out to the Children's Hospital staff for all their support and to Mrs. Sperrazzo, a recent donor.

* * * * *

★ **CALIFORNIA OUTREACH UPDATE**

- Jan. 24:** Disco Bingo fundraiser hosted by ICF Br. 285 benefiting Children's Hospital & Research Center at Oakland's Thalassemia Program, Livermore
- Jan. 5-6:** Flower Market Fair, San Francisco
- Feb. 1-2:** TET Festival, Vietnamese New Year, Santa Clara
- Feb. 13:** Desferal Camp follow-up activity: Valentines Party
- Feb. 15-16:** Community Street Fair, San Francisco
- Feb. 22:** ICF Br. 184, Los Gatos - Laurice Compagno
- April 3:** Spring Fling fundraiser, Oakland
- April -6:** TAG Conference, Anaheim
- April 12:** Ch. 47 Health Fair, Fresno
- April 14:** Cambodian Health Fair, Lodi

* * * * *

★ **UPCOMING OUTREACH EVENTS IN CALIFORNIA**

- May 5:** 4th Annual Blood Drive, Oakland
- May 10:** 5th Annual Children's Health & Safety Fair, Tracy
- June 22:** Oakland Chinatown Health Fair, Oakland
- June 28:** California Chapter Conference, San Diego
- July 12-13:** Lotus Festival, Los Angeles

* * * * *

★ **ARE YOU AT RISK FOR HAVING A CHILD WITH THALASSEMIA?**

The thalassemia trait is the most common single gene disorder in the world. It is found in many regions, especially those where malaria is prevalent. Some areas include:

- Southeast Asia** • Vietnam
- Cambodia • Laos • Thailand
- Malaysia • Singapore • Indonesia
- Southern China** • Hong Kong •
- Pacific Islands** • Philippines • Samoa • Papua New Guinea • Melanesia • **Middle East/**
- North Africa** • Iraq • Iran • Kuwait • Lebanon • Saudi Arabia
- Syria • Algeria • Tunisia • Morocco • Libya • Egypt • **India** • Bangladesh • Afghanistan • Pakistan • Sri Lanka • Burma • **Mediterranea** • Italy • Greece • Cyprus • Turkey • **Tropical Africa sub-Saharan Africa**

Thalassemia is not bound by borders or nationality. It is found everywhere people from these regions migrate, including the United States, Canada, France, and the United Kingdom. Ask your doctor about getting tested for the trait!

* * OUTREACH * *

* * * * *

★ ARE YOU INTERESTED IN ATTENDING A WORKSHOP OR LEARNING MORE ABOUT THALASSEMIA?

Contact:
Thalassemia Outreach
510-428-3885 ext. 4398

Thalassemia Nursing/Medical
510-428-3347

* * * * *

★ DO YOU WANT TO GET TESTED FOR THE THALASSEMIA TRAIT?

Ask your doctor for the following tests:

- Hemoglobin electrophoresis (with quantitative A2 and hemoglobin F)
- Complete Blood Count (CBC) - Free erythrocyte protoporphyrin (FEP, or ferritin, or other iron status test)

* * * * *

★ THALASSEMIA COMPREHENSIVE EVALUATION CHECKLIST

The following tests are recommended in addition to monthly CBC's, quarterly chemistry panel, and ferritin:

- **Cardiac Evaluation:**
 - Cardiac Echo
 - EKG
 - 24 hour holter monitor
 - Cardiac stress test (for patients 18 years and over)
- **Liver Function Evaluation:**
 - Annual Hepatitis C surface antibodies. (if Hep C Ab (+) draw Hep C PCR)
 - Liver function enzyme screening

(SGOT, SGPT) every three months.

- Hepatitis B panel (Hep B Sab, Hep B Sag, Hep B Cor)
- Annual Hepatitis A panel (if negative in the past)
- Liver biopsy to evaluate liver iron (should be considered every two years)

• **Endocrine Function Evaluation**

- Annual TSH, free T4, parathyroid hormone level, CA
- Annual fasting AM cortisol
- Annual oral glucose tolerance test (for patients 10 years or older)
- Annual bone density (for patients 15 years or older)
- Annual test for zinc, copper, selenium, and vitamin C & E
- Annual HIV
- Annual LH, FSH for girls 12 years or older and boys 14 years or older
- If delayed puberty suspected, GnRH testing and bone age

• **Ophthalmology Evaluation:**

- Annual evaluation by ophthalmologist (if patient is on Desferal and also for those who have diabetes)

• **Audiological Evaluation:**

- Annual hearing screening (every six months if on Desferal)

• **Dental Examination:**

- Annual dental exam (if splenectomized, dental prophylaxis)

* These tests should be performed at least once a year. Since each patient's case is unique, your physician may recommend certain tests be given more or less frequently.

Checklist courtesy of:
Thalassemia Action Group
129-09 26th Avenue
Flushing, NY 11354
1-800-935-0024

Sponsored by the Cooley's Anemia Foundation

Special thanks to Elliott Vichinsky, MD and Dru Foote, PNP, Northern California Thalassemia Center, Children's Hospital & Research Center at Oakland

* * * * *

★ THALASSEMIA RESOURCE LIST Children's Hospital & Research Center at Oakland

- Main website: www.childrenshospitaloakland.org
- Thalassemia: www.thalassemia.com
- Sibling Donor Cord Blood: www.siblingcordblood.org

Cooley's Anemia Foundation and the Thalassemia Action Group (TAG)

1-800-522-7222
www.cooleysanemia.org

Thalassemia International Federation

thalassemia@cytanet.com.cy

United Kingdom Thalassemia Society

www.ukts.org

Thalassemia Association of Hong Kong

www.thalassemia.org.hk

National Marrow Donor Program

1-800-MARROW-2
www.marrows.org

Blood Centers of the Pacific

1-888-393-GIVE
www.bloodcenters.org