THE FA FAMILY NEWSLETTER

Newsletter Number 4
March, 1988

c/o Frohnmayer, 2875 Baker Blvd., Eugene, Oregon 97403 - (503) 686-0434

CONFERENCE ON APLASTIC ANEMIA

The Aplastic Anemia Foundation of America sponsored a significant meeting on December 4, 1987 in Washington D.C. Many of the world's foremost experts in aplastic anemia and FA attended. Proceedings were tape recorded and, eventually will be published. The Worthy family of our group attended, as did Dave Frohnmayer. Highlights relating to FA follow. Please share this part of the newsletter with your treating physician for any further medical advice!

I. Overview: Dr. N.T. Shahidi, University of Wisconsin, Madison.

The incidence of aplastic anemia (all forms) is 5 to 10 persons per million population. In Europe, the incidence is estimated at 13 per million population.

The condition is very important for medical/scientific study. The prognosis of AA generally is very serious: 40% still succumb [FA is far more lethal ultimately.ed.]. Scientists must learn more about the physiological mechanisms of the disease (cell-to-cell reactions, relationship to immune system, etc.). There is a need (echoed by many) for concentrated study by many medical centers together. [This last theme may lead to an important outcome of the conference.ed.]

II. Constitutional Aplastic Anemia: Dr. Blanche Alter, Mt. Sinai School of Medicine, N.Y., N.Y.

"Constitutional Aplastic Anemia" refers to anemias which develop because of genetic conditions, present at birth, that result in bone marrow and thus blood system failure. Fanconi's Anemia claims the largest number of victims in this "Constitutional Aplastic Anemia" grouping. Major points:

- About 20% of all aplastic anemia cases in an early (1958-77) study were FA. [These years predate DEB testing for FA. ed.] At least a third of cases of aplastic anemia are due to some genetic disorder. This probably underestimates FA due to underdiagnosis or misdiagnosis.

- Dr. Alter's review shows approximately 600 cases of FA in reported medical literature worldwide. This is not total disease incidence; it is only the number of medically significant case reports.

- Males are victims slightly more often than females (1.3 to 1).

- Average age of diagnosis is age 8. The oldest age of reported diagnosis was 35. Ten percent were not diagnosed until age 16 or older. FA is therefore not an exclusively pediatric disease.

- FA is an exception to the usual conclusion of low response by aplastic anemia victims to androgens. Perhaps 75% of FA victims respond to androgen therapy.

- Approximately 95% of the FA victims in literature reports studied by Alter develop aplastic anemia; 9% developed leukemia, 3% other cancers and 4% develop liver disease. Dr. Alter does not think androgen therapy causes the reported leukemia. Ten of the 50 patient reports of FA leukemic development had not used androgens. [The relationship between leukemia and androgen therapy was the subject of many conflicting opinions and theories throughout the conference presentations. ed.]

- Other forms of constitutional aplastic anemia (Diamond-Blackfan; TAR; Schwachman Syndrome, etc.) can be distinguished from FA by chromosome breakage tests. (See Auerbach report, below)

Dr. Shahidi requested Dr. Alter's response to two case reports of families where chromosome breakage appears, but where the blood system is normal. Alter believes the explanation must lie with (1) heterogeneity [variety] at the genetic level; (2) heterogeneity at the interactive gene level; and/or

Dr. Gluckman's hopeful early results in bone marrow transplantation (BMT) for FA have been noted in earlier editions of this newsletter. The most current report on the Paris BMT group will be published soon, entitled "Bone Marrow Transplantation for Fanconi Anemia," by Dr. E. Gluckman, in Clinics in Hematology , March, 1988. [Your treating or consulting physician should look for this work.]

Dr. Gluckman's experience with matched sibling donors for FA victims continues to be positive. She expressed pessimism about any near-term hopeful results for FA mismatched transplants. Finally, in a personal conversation with this editor, Dr. Gluckman indicated her hope to relate results of unrelated donor matched transplants in the relatively near future.

* * *

FUND RAISING EFFORTS CONTINUE!

Brad and Lea Ann Curry wrote a fund-raising letter to friends and acquaintances in an effort to raise additional funds to promote Dr. Arlene Auerbach's research efforts. In January, 1988, they reported that their letter brought in over $11,000. This is the Curry's second major effort to raise money for genetic research.

Parents in our support group have now raised over $90,000 to assist Dr. Auerbach in her effort to locate the FA gene. Let's keep up the good work!

* * *

RESEARCHER APPRECIATES EFFORTS

Dr. Arlene Auerbach, in a letter to the Frohnmayers, writes that "The contributions we received have enabled us to purchase equipment and supplies necessary for starting a project to map and clone the FA gene. We have also been able to pay the salary of an additional research assistant to work on this project."

"Your continuing efforts on behalf of our FA research are much appreciated."

* * *

CANADIAN DONOR REGISTRY EFFORTS

Barbara Lawrence of Chilliwack, British Columbia, is the mother of 15 year old Cindy, who suffers from Fanconi's anemia. Barbara has become active in an extrememly successful effort to increase the number of bone marrow donors in the Canadian Registry.

The Canadian Red Cross established a donor program in February, 1987. The Red Cross in British Columbia held a series of recruitment seminars but was not prepared to extend the program beyond the Vancouver area. However, extensive media coverage concerning the need for bone marrow donors produced a flood of letters and telephone calls from citizens wanting to be bone marrow donors.

Barbara was asked to coordinate the Community Bone Marrow Donor seminars. Her first seminar was in Chilliwack on February 10, 1988. Barbara reports:

"The response was overwhelming and the additional feedback and support have filled us with encouragement and enthusiasm."

"One hundred and sixty-one individuals signed donor forms. Tissue typing will be carried out right away and these individuals will be placed on the computer to add to the existing number in the Red Cross Bone Marrow Registry. I think that is pretty impressive when the registry has only had 400 listed for the entire province. Chilliwack is certainly doing its share."

"The second bit of good news. The Red Cross was so impressed at the support of our community that they have requested that I coordinate a sec-

THE ROCKEFELLER UNIVERSITY
1230 YORK AVENUE • NEW YORK, NEW YORK 10021-6399

February 16, 1988

Dear Parents:

The exciting news in genetics these days is that genes for human diseases can be localized to particular chromosomal regions by applying an old technique called linkage analysis to the study of distinctive DNA markers which detect genetic variation known as RFLPs (for restriction-fragment length polymorphisms). A good article by Ray White and Jean-Marc Lalouel describing this method has recently appeared in Scientific American (February, 1988, pp 40-48). Using this method, a number of genetic diseases, including cystic fibrosis, neurofibromatosis, familial colon cancer, and familial Alzheimer's disease, have recently been mapped. The exciting new development is that hundreds of RFLP markers with know chromosomal locations are now available. These markers span all of the chromosomes, so that by studying the inheritance of 100 carefully chosen markers in particular families with a disease, it is highly likely that a linked marker will be found.

We are now actively pursuing studies that will attempt to use these DNA markers to locate the gene for Fanconi anemia. Success in finding a linked marker will benefit families by providing a better method for diagnosis and carrier detection for FA, and should eventually lead to the isolation and cloning of the gene for this disorder. Recessive diseases like FA are more difficult to study by this method than are dominant diseases like Huntington's disease or X-linked diseases like Duchenne muscular dystrophy. These were the first two genetic diseases to be mapped with the help of RFLP linkage studies. Families which are especially important for the success of linkage studies in recessive disorders are those with two or more affected children, or those in which the parents of an affected child are related to each other. We have presently identified 25 such families and have collected blood samples for these studies from many of the family members. Two of the major centers for DNA linkage studies in the United States have recently become interested in this project to map FA, and are willing to collaborate with us. Their participation in these studies will contribute greatly to the potential success of this project.

We would appreciate hearing from any FA families who are willing to participate in this study. Please contact me directly, so that I can answer any questions you have regarding this project. Arrangements can be made to have the necessary blood samples sent to us by your physician.

Best regards.

Sincerely

Arleen D. Auerbach

Arleen D. Auerbach, PhD
(212) 570-7533

* * *

Florida: Civitan Regional Blood Center, Gainesville; Broward Community Blood Center, Lauderhill; South Florida Regional Blood Service, Miami; Community Blood Bank, St. Petersburg.

Georgia: American Red Cross, Atlanta.

Illinois: American Red Cross, Peoria.

Indiana: American Red Cross, Fort Wayne; Central Indiana Regional Blood Center, Indianapolis.

Kansas: American Red Cross, Wichita.

Louisiana: Blood Center for Southeastern Louisiana, New Orleans.

Maryland: Johns Hopkins Hemapheresis Treatment Center and American Red Cross, Baltimore; National Institutes of Health Platelet Pheresis Center, Bethesda.

Massachusetts: Dana-Farber Cancer Institute, Boston; American Red Cross, Dedham.

Michigan: American Red Cross, Detroit and Lansing; Michigan Community Blood Center, Grand Rapids.

Minnesota: American Red Cross, St. Paul.

Nebraska: American Blood Services, Omaha.

New York: American Red Cross, Albany, Rochester and Syracuse; Bone Marrow Transplant Service at Memorial Sloan-Kettering Cancer Center, New York.

North Carolina: American Red Cross, Charlotte.

Ohio: Hoxworth Blood Center, University of Cincinnati; American Red Cross, Cleveland, Columbus and Toledo.

Oklahoma: American Red Cross, Tulsa.

Oregon: American Red Cross, Portland.

Pennsylvania: American Red Cross, Johnstown and Philadelphia; Central Blood Bank of Pittsburgh.

Tennessee: American Red Cross, Nashville.

Texas: The Cancer Center at Wadley Institute, Dallas.

Vermont: American Red Cross, Burlington.

Virginia: American Red Cross, Norfolk.

Washington: Puget Sound Blood Center, Seattle; Spokane and Inland Empire Blood Bank, Spokane.

Washington, D.C.: American Red Cross.

Wisconsin: American Red Cross, Madison; Blood Center of Southeast Wisconsin, Milwaukee.

WHO CAN JOIN REGISTRY

Donors must be healthy adults under 55 years of age. They should have no history of serum hepatitis, malaria, acquired immune deficiency syndrome or intravenous drug abuse.

Currently most of the 50 participating blood centers are accepting only those who are willing to be regular apheresis blood donors, since they are typed for HLA A and B, which costs about $50. The typing is done using a few tablespoons of blood, the amount usually removed during routine medical tests. Some blood centers will accept bone marrow donors who are not also apheresis donors if the donor pays the $50 for the initial typing. Regional registries, like the one in New Jersey, ask but do not insist that donors contribute the $50 for typing.

* * *

Alice Nicholson, mother of five children, has a daughter and a son with Fanconi's anemia. She shares her experiences with us.

Nancy, now 31 years old, and Bobby, now 27, are our two middle children. The other three children are in good health and have no symptoms of Fanconi's anemia, although they have not yet been tested.

Nancy was born after a full term perfectly normal pregnancy, and was 5 lbs., 1 oz. and 17" long. She was born with a small head size and double thumbs which were surgically corrected by age 2. Although her health as a young child was somewhat fragile and she was susceptible to upper respiratory infections, she had a reasonably healthy childhood. However, her small size was a concern and she was seen at Massachusetts General Hospital in Boston when she was about 2 years old. Thyroid therapy and growth hormones were administered without success. Today, at 31, Nancy is 4'7".

Bobby also followed a full term, normal pregnancy, weighed 5 lbs., 2 1/2 oz. and was 17" long. He was born with a small head size but no other obvious abnormalities at birth. He developed a urinary infection when he was 10 days old and spent a month in an incubator. Following that, except for his small size, Bobby was a very sunny, active child and had very good health. It was found that he had undescended, underdeveloped testicles and these were corrected in two separate operations when he was 8 and 10. Bobby also was seen at MGH for his growth problems - neither growth hormones nor thyroid made any difference. Today, at 27 years of age, Bobby is 4'10".

In 1973 and 1974 Bobby's health made a dramatic change. He had pneumonia three times in one year. Blood and bone marrow studies revealed aplastic anemia, and he was started on a course of prednisone which was gradually reduced to a small maintenance dose until it was discontinued in 1980. His blood counts did not change following discontinuance - in fact, they did not significantly change while he was on prednisone but I felt it perhaps had a stabilizing effect. In his late teens Bobby was seen at Johns Hopkins Hospital in Baltimore where extensive blood tests led to the diagnosis of Fanconi's Anemia. He was put on testosterone therapy for hormonal deficiencies.

Today, Bobby is living in Australia, married one year and, with the help of a fertility clinic because of low sperm count, is the father of a healthy baby boy, born December 1, 1987. Bobby's health has been quite good and he seems to have good stamina in spite of sub-normal blood counts. This is now some 13 years following diagnosis of aplastic anemia. Praise the Lord for that!

Nancy was first diagnosed as having aplastic anemia in 1975, after a prolonged period of minor illness and exhaustion. She received prednisone therapy which was discontinued in 1980. Nancy, true to form however, did suffer many more upper respiratory infections, sinus problems, earaches, allergies and fatigue than Bobby. However, she was not hospitalized until October, 1987, following a prolonged illness. Blood levels had fallen considerably (red count dropped to 4.4; platelets to 11,000). A few days after her hospitalization she suffered a subarachmoid hemorrhage and had to have immediate brain surgery. For several days following surgery there was some partial paralysis on the right side and she was unable to speak. Now, just 3 months after surgery, she speaks clearly. Her recovery from the hemorrhage has been remarkable.

Unfortunately, Nancy's blood levels continue to be quite low and she is weak and exhausted. She is about to start on a course of oxymethalone and we are about to begin tissue typing in the event that a bone marrow transplant is deemed necessary. We pray that it won't be, but will trust God to lead us to the right treatment that will lead Nancy to a fuller, healthier life.

The Nicholson's address is listed on page 10. ed.

* * *

Dr. Auerbach asked us to author a few words about reactions of FA families for her forthcoming book on FA. Here's some of what we wrote. Eds.

Fanconi's Anemia: Reactions of Families on the Receiving End

This disease doesn't happen very often, but it happens to real people. They have names, families, hopes and plans. Fanconi's Anemia will affect them profoundly and forever. The experience can be devastating.

1. Denial occurs first. It isn't happening; it can't happen. A lethal, childhood illness isn't in our plans. If it is not simply a bad dream or a false diagnosis, there is a quick fix. Medicine...prayer...flight (physical or psychological)...in some combination all might cause the disease to go away.

2. You feel shock . Relief to hear a physician say "It's not leukemia!" is replaced by slowly growing knowledge that this diagnosis could be worse. We are persons accustomed routinely to news reports of medical miracles. Diagnosis of childhood illness is nearly equivalent to promise of cure. Then, painfully, you learn that this life-threatening illness is not yet fully understood, and that no risk-free therapy promises an easy cure.

3. Helplessness accompanies this news. Your fate is in the hands of medical professionals; experts who themselves do not have answers and sometimes do not agree with one another. Your child is alive, but threatened. Where do you turn?

4. You probably experience deep, profound anger. You are outraged by the visitation of an undeserved and unanticipated lethal condition. There was no warning, and...really...no possibility of one. You had other plans for your life. You still do. How can you be expected to cope?

5. Guilt feelings may be profound, though not always near the surface. You, together with your spouse, unknowingly passed this disease, poisonously hidden deeply within your genes, to a blessed innocent child. No matter that it's no one's "fault," and that it cannot routinely be detected by the unsuspecting. The knowledge of genetic responsibility lies deeply in the subconscious, but it can weigh heavily on the soul.

6. Isolation overwhelmes almost all FA families. No one you know, usually even experts, has routinely treated (or sometimes even heard of) this orphan disease. No one else exists to share the anguish, the occasional hopes and the peaks and valleys of crisis after crisis.

   Isolation has two other aspects. First, your problems are different in quality and dimension from those of other parents. A friend worries understandably about behavior problems, or frets that her child's grades will not be competitive for entrance to a top college. Your concerns are whether the last platelet count is telling you that the downward spiral has continued; that your child may not live long enough to experience a single year of college. Will there be another birthday, another Christmas? Will health insurance...if there is any...enable you to secure every possible lifeline of hope?

   The second aspect is your own potential victimization. You are apart, and people sense it. The wisest of them ask and help, but sometimes even the most sensitive of friends is at a loss for words. You both know it, and without meaning for it to happen, it can wrench you from your community roots and family support.

7. Grief and sadness are a continuing part of your life from the start. We would happily trade places with our children because we've had our chance. There is some completeness in our lives, joys, tragedies and experiences of life-fulfillment.

   How cruel that a child bright with talent and promise might not possess the genetic constitution to know and learn of this vast and wonderful world; to make the choices that shape life; and to have at least the fleeting moments of mature reflection we have known. Any parent wants to be his child's companion, and share the experiences of a child's maturity. It wrenches. "You cry for them, and you cry for yourself," one FA parent remarked.

best: Families communicating with each other give us all strength. At Vicki's request, we are reprinting her letter:

The Frohnmayers

I want to thank Dave and Lynn Frohnmayer for all they have done for Fanconi anemia patients and their families. When my son Shawn was diagnosed with FA almost 12 years ago, we were alone, in the dark and had nobody to share our emotions with. Shawn is doing very well and thanks to Dave and Lynn's hard work (and grief) more people are now aware that this disease exists and how devastating it is. Most of all, I am thankful for the network of support they started with other families through the FA newsle

Vicki Phillips
Albany, N.Y.

* * *

CONGRATULATIONS TO BRAD AND LEA ANN CURRY!

On January 14, 1988, Lea Ann Curry gave birth to a healthy baby daughter, Emily Elizabeth. Emily's arrival brought an additional measure of joy and optimism to the Curry family.

During the first trimester of her pregnancy, Lea Ann underwent prenatal testing. The Chorionic Villus Biopsy revealed that the new baby was not affected by FA, and also that she was an HLA match for Natalie Curry, age 3, who suffers from Fanconi's anemia. These results were later confirmed by an amniocentesis. Following Emily's birth, a cord blood test also concluded that Emily will be a suitable bone marrow donor for her sister.

We share in the special delight that this new addition brings to the Currys, and offer them our heartfelt, warmest congratulations!

* * *

From British Columbia Barbara and Leslie Lawrence write of their daughter, Cindy Rene, and her battle with FA. Now almost 15 years of age Cindy was diagnosed just before her sixth birthday. Adopted by the Lawrences when she was only weeks old, Cindy exhibited the following symptoms: low birth weight, small head size, second thumb on the right hand (surgically removed) and skin pigmentation problems.

Prior to her diagnosis, Cindy was subjected to a variety of different infections that resulted in high fevers, severe bowel problems, rashes and orthopedic problems that made walking extremely painful. At age four, Cindy was frail, of small stature and easily prone to bruising. Throughout these years her pediatrician and a variety of hospital staff personnel were unable to put a name to Cindy's condition. It was only through sheer chance that a physician recognized the symptoms and was able to make the diagnosis while Cindy was at Vancouver's Children's Hospital in 1979.

To treat the low platelet and hemoglobin counts so characteristic of FA, Cindy was placed on oxymethalone and prednisone. The doctors involved offered little comfort and absolutely no hope. From the local pediatrician and family doctor to the physicians at Children's Hospital, the consensus was that Cindy's life span would be very short and they counseled acceptance of and resignation to the situation.

This attitude on the part of so many medical professionals who have little or no experience in dealing with FA is all too common. Additionally, the syndrome can compound and complicate even a simple childhood disease such as chicken pox. In 1985, Cindy contracted chicken pox and the physician covering for the vacationing family doctor could not be convinced of the seriousness of the situation until it became life-threatening.

To help her contend with some of her many medical problems, Cindy has sought and received the assistance of a hypnotherapist. Under the guidance of Dr. Marlene Hunter, Cindy has learned concentration techniques that appear to have disposed of a particularly bad case of warts.