FANCONI ANEMIA RESEARCH FUND, INC.

FAMILY NEWSLETTER

#26 A Semi-annual Newsletter on Fanconi Anemia for Families, Physicians and Research Scientists Fall, 1999

Kids by the lake at the Family Meeting

Families Enthusiastic About Family Meeting

Thirty-eight families from the United States, Canada, Germany, and Chile met at Aurora University at Lake Geneva, Wisconsin, for our 9th annual FA Family Meeting. Attendees expressed great enthusiasm about this year's meeting. Families had ample opportunity to share experiences with one another, learn from an outstanding group of presenters, and participate in small group discussions. Volunteers provided children with a wide range of indoor and outdoor activities, from swimming in Lake Geneva to games and arts and crafts. Youngsters participated in small group discussions and formed meaningful ties to others sharing the same experiences. It was rumored that late-night campfires sometimes continued until the wee hours of the morning.

Most of the medical and scientific presentations occurred over the weekend, for families unable to extend their stay into a work week. Nonetheless, many families stayed the full four days and reported that the last night's talent show was the best ever. We learned a lot, we talked and relaxed, and all felt enriched by the experience.

Readers are encouraged to review the *Science Letter* for detailed information on all medical and scientific

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Will Fludarabine Improve Bone Marrow Transplant Survival Rates?

In August 1998, at our Family Meeting in Wisconsin, John Wagner, MD, reported that overall survival for alternative donor transplants (donors other than matched siblings) was a discouraging 31% to 34%. The major obstacle to successful transplant in this population was graft failure (approximately 39% failed to engraft). In addition, transplanters have always been concerned about the toxicity of conditioning regimens for all FA patients, given the susceptibility in this population for later malignancies.

Several transplant centers have

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HIGHLIGHTS

MEDICAL NEWS

FA Gene Therapy Symposium

On May 15, 1999, twenty-two geneticists, hematologists, and gene therapy researchers from the US, Canada, France, and Germany attended a gene therapy symposium in Chicago, Illinois.

Presentations focused on recent advances in the field of gene therapy and their specific applicability to FA. Researchers discussed different viral vectors and their potential for reaching dividing and non-dividing hematopoietic stem cells. Adenoviral, lentiviral, and retroviral vectors have been tested or are currently being tested in vitro, in mouse models, and in primates. Several patient trials are in preparation. Researchers discussed issues of safety, toxicity, patient recruitment, and the regulatory status of gene therapy.

The symposium was well received by the participants, and new collaborations were initiated. Researchers discovered that they are encountering similar problems and compared strategies to overcome those. The central issues for stem cell-targeted gene therapy are the questions of how to reach the elusive stem cells and how to achieve "stable expression," meaning the successful repopulation of the bone marrow from stem cells carrying the corrected gene(s). Lively discussions centered on the merits of different approaches. Researchers agreed that the field is advancing rapidly and expressed confidence that gene therapy for FA and other conditions will become a reality. They also agreed that significant hurdles remain to be overcome. ◆

NIH Conducting Trial on Patients with Oral Leukoplakia

The August 1999 issue of the *NIH (National Institutes of Health) Record* states that "NCI (National Cancer Institute), NIDCR (National Institute of Dental and Craniofacial Research), and NIDCD (National Institute of Deafness and Communication Disorders) are recruiting patients with oral leukoplakia for a study testing a nonsurgical treatment for this condition. A leukoplakia lesion is white to gray in color and develops on the tongue or in the mouth in response to chronic irritation such as cigarette smoking or other tobacco use...."

Leukoplakia and its evolution to squamous cell carcinoma of the mouth is a serious health concern of the older FA patient. In our last newsletter, we described 21 FA patients who reported solid tumor malignancies to FARF or to the German support group in the past two years. The most common kind of cancer was squamous cell carcinoma of the mouth, head and throat (8 cases). Most of these malignancies developed in patients in their mid-20s, 30s, and 40s. These numbers represent only those patients known to our support groups and, therefore, greatly underestimate the extent of the problem.

In Fanconi anemia, patients can develop leukoplakia independent of smoking cigarettes. Leukoplakia in the general population can represent a benign or premalignant condition. In our FA population, several patients have reported a period of leukoplakia followed by the diagnosis of squamous cell carcinoma of the mouth.

The NIH study is presently being conducted at the National Cancer Institute in Bethesda, Maryland. It will expand to include a center at the University of Colorado in Denver and at MD Anderson Hospital in Houston, Texas. Fifty-seven patients will be enrolled in the trial. There are openings for additional patients.

NIH researchers are using the liquid form of Ketorolac, which researchers hope can both prevent and arrest the development of premalignant cells in the mouth. It is administered as a mouthwash and, therefore, bypasses the gastrointestinal tract. Only a very small amount enters the bloodstream. Early results suggest that this drug is well-tolerated.

This is a double-blinded study. Two-thirds of all patients will receive the active drug; one third will receive a placebo. The patient takes the active drug or placebo for 90 days. At the end of the study (which could be 12 to 18 months from now), all patients receiving the placebo will be offered the active drug, if it is found to be effective.

This study involves five trips to the study location. At the NIH site the first trip will be at the expense of the patient, but subsequent visits will be paid for by NIH. Study-related medications and care at the NIH site are free of charge. At the other two sites, patients are responsible for their travel costs and other medical costs.

Some FA patients have mo

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Fanconi Anemia Sample Repository at the Dana-Farber Cancer Institute, Children's Hospital, Boston

Tissue samples from patients with Fanconi anemia or from their family members have proven again and again to be critical for productive scientific research. For example, the judicious use of FA patient-derived cell lines has led to the identification of discrete complementation groups (subtypes) of Fanconi anemia, to the cloning of several FA genes, and to the molecular characterization of the Fanconi anemia proteins (encoded by the FA genes). Our laboratory in Boston, in collaboration with the laboratory of Dr. Markus Grompe at Oregon Health Sciences University, has generated an FA cell repository and patient database. The procedure outlined below will allow for the efficient establishment and transport of more of these critical materials for our research programs.

More recently, we have become interested in collecting tumor samples (fresh surgical biopsies of cancers or leukemia) from FA patients or family members who develop cancer. These tumor and leukemia samples will be critical to our understanding of the process by which normal human cells transform into tumor cells. Understanding these processes may lead to more rational diagnostic procedures and drug treatments of FA patients with cancer.

Skin Sample Collection

A skin sample can be obtained by your local physician. The skin is numbed with a local anesthetic and a tiny (1/10 inch) circle of skin is removed. Skin samples are sent at room temperature in a special fibroblast tissue culture medium (Dulbecco's Minimal Essential Medium with 10% fetal calf serum and antibiotics or equivalent). This medium can be obtained from us if your physician or laboratory does not have it available. The samples are sent via overnight Federal Express to our address (see below). The cost of shipping will be paid by our office.

Blood Sample Collection

Your physician should collect two 10cc tubes of blood drawn in sodium heparin (not lithium heparin!!); this can be done while you are undergoing other blood work for diagnostic or treatment reasons. The samples need to be sent at room temperature (not refrigerated!!) via overnight Federal Express to our address (see below). The cost of shipping will be paid by our office.

Tumor and Leukemia Collection

We are extremely interested in obtaining fresh samples of tumors or fresh leukemic bone marrows from FA patients who develop cancer. Because of the special care required for preparing and transporting these samples, please contact Alan D'Andrea directly as indicated below. We would be happy to discuss appropriate procedures directly with your physician or surgeon. ◆

For additional information please contact:
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Fludarabine

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added fludarabine to their preparatory regimens in an effort to suppress the host bone marrow and facilitate engraftment. An additional hope in some centers is that the toxicity of the conditioning protocol can be reduced by adding fludarabine.

In 1997, Dr. Shimon Slavin of The Hadassah University Hospital, Israel, pioneered the use of fludarabine, no radiation, and a reduced conditioning approach, in an FA patient. We report on early results of fourteen FA patients transplanted with fludarabine as part of the conditioning protocol. Two had matched sibling donors; twelve had alternate donors. Transplants occurred at five different centers. The conditioning protocol varied considerably from one center to another. The number of patients transplanted is small and the follow-up time post-transplant is short. Nonetheless, preliminary results are encouraging.

See pages 4 and 5 for more articles on Fludarabine. ◆

New Resource for Complementation Studies and Mutation Analysis

Alan D'Andrea, MD, has announced that a large grant from the Hood Foundation has enabled him to expand his laboratory at the Dana-Farber Cancer Institute and Children's Hospital in Boston, MA. His laboratory is now able to perform mutation analysis, complementation studies, and DEB testing. Dr. D'Andrea is an internationally recognized scientist in the field of FA research.

For contact information see box to left. ◆

Israel Achieves Early Success Using Fludarabine, No Radiation

Transplanters at the Department of Bone Marrow Transplantation, Hadassah University Hospital, Jerusalem, report on two successful Fanconi anemia transplants using fludarabine. The first transplant is documented in *Bone Marrow Transplant*, 1997 Dec; 20(12): 1109-10. A 12-year-old girl with FA transforming to AML was given non-manipulated bone marrow from her HLA matched cousin. She was conditioned with fludarabine (30mg/m2 x 5d), ATG (10 mg/kg x 4d), and cyclophosphamide (5mg/kg x 5d). She was given no radiation. Low dose Cyclosporine A was administered as graft-versus-host disease prophylaxis. Engraftment was rapid. Toxicity was mild with grade II mucositis, diarrhea, and abdominal pain. This child did not develop severe GVHD. She is alive and well, more than two years post-transplant.

These transplanters report on a second FA transplant using fludarabine, no irradiation, and matched sibling cord blood. This is described in the *Journal of Pediatric Hematology Oncology*, (21[3]:237-9, 1999, May-June). This 12-year-old girl received pretransplant conditioning consisting of fludarabine (30 mg/m2/d) from day -10 to day -5, cyclophosphamide (10 mg/kg/d) on day -7 and -6, and ATG (10 mg/ky/d) from day -4 to day -1. Cyclosporin A (3 mg/kg/d) was administered from day -1 as graft-versus-host disease prophylaxis. After the transplant, the patient was given granulocyte colony stimulating factor (GCSF), in combination with erythropoietin.

Engraftment was normal and sustained. The regimen was well tolerated with very mild toxicity and no major transplant-related complications or >grade II graft-versus-host disease. Chimerism was 100% donor origin. Patient is alive and well.

The authors conclude that it is possible to achieve sustained engraftment and only mild toxicity in FA after human umbilical cord blood

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Cincinnati Uses Fludarabine in New Alternate Donor Protocol

Richard Harris, MD, Cincinnati, announced a new protocol for patients who lack matched sibling donors. He utilizes cytoxan 5 mg/kg/day for 4 days, fludarabine 10 mg/m2/day for 6 days, and total body irradiation 450 cGy along with ATG, cyclosporine, and T-cell depletion of the donor marrow. So far, one patient with a 6/6 unrelated donor has received this new regimen. She experienced rapid full engraftment and no evidence of GVHD. She is now out about 5 months from transplant with normal blood counts and no significant complications.

Editors' note: Date post-transplant accurate as of 10/99. ◆

Memorial Sloan-Kettering Reports on Two Successful Mismatched Transplants, Using Fludarabine

Farid Boulad, MD, Memorial Sloan-Kettering, reported at our Family Meeting on the successful transplants of two FA children with 4/6 matched related donors. His first patient was Jack, a five-year-old who developed aplastic anemia refractory to treatment with steroids, androgens, and hematopoietic growth factors. He had received multiple transfusions. He first received a 4/6 cord blood transplant and he did not engraft. He received a second transplant from his 4/6 matched father, day +46 after the first transplant. This time he was given fludarabine (30 mg/m2 each day for five days), cyclophosphamide, ATG/steroids and FK506 and G-CSF post-transplant. He engrafted by day 11 post transplant with minimal toxicity and no GVHD. He is now 15 months post transplant with no chronic GVHD. He developed a complete immune recovery by 8 months post transplant. He has returned to school.

Boulad's second patient, Justin, age 10, developed aplastic anemia and then myelodysplastic syndrome. He also had received multiple transfusions. He had no closely matched donors (family or unrelated). He received cytoreduction with TBI 450 cGy, ATG/steroids, fludarabine (same dosage as above), and cyclophosphamide and received FK 506 and G-CSF post transplant. He received G-CSF mobilized T-cell depleted peripheral blood stem cells from his HLA 4/6 matched sister. Toxicity included minor mucositis, minor hemorrhagic cystitis, and steroid-dependent diabetes. These have all resolved. Justin engrafted on day +10 post transplant. He is now 5 months post transplant. He is on a taper of his FK 506; he is off steroids, off G-CSF, and is transfusion independent.

Editors' note: Dates "post-transplant" are as of 10/10/99. ◆

Alternative Donor Transplants Using Fludarabine

Wolfram Ebell, MD, Charity Hospital, Berlin

Fludarabine belongs to a group of drugs which are not crosslinking agents and probably do not increase chromosomal breaks in FA. We thought it would be an ideal candidate for conditioning of FA patients. We wanted to know if we could: (1) decrease early toxicity and secondary tumors by omitting cyclophosphamide (a cross-linking agent) and radiation by using instead fludarabine +/-ATG; (2) limit the risk of GVHD, especially in unrelated and mismatched transplants by T-cell depletion; (3) ensure engraftment by giving a megadose of peripheral stem cells; and (4) cryopreserve (freeze) autologous stem cells in an early phase of the disease for reinfusion in case of rejection and/or poor condition.

We have transplanted three FA patients using fludarabine. They are described below. (Note: fludarabine and ATG were administered intravenously).

1) Our first patient had a matched sibling donor. We used undepleted bone marrow and conditioned with fludarabine (4 x 40 mg/m2) and ATG (4 x 5 mg/kg). This patient achieved a stable engraftment and normal blood counts. There was no toxicity and no GVHD. Patient is alive and well six months post-transplant.

2) Our second patient's donor was a one antigen mismatched father. We used T-cell depleted peripheral blood stem cells (CD34 cells > 10 x 10E6/kg, T-cells < 1 x 10E5/kg). Conditioning consisted of fludarabine (4 x 40 mg/m2) and ATG (4 x 5 mg/kg). This patient achieved a transitory engraftment with no toxicity.

A second transplant was performed, again using the one antigen mismatched father. We used undepleted bone marrow. Conditioning consisted of fludarabine (6 x 30 mg/m2); busulfan (2 x 0.5 mg/kg, p.o.) and ATG, (4 x 5 mg/kg). The patient achieved a stable engraftment, normal blood counts, and had no toxicity. The patient is alive and well two months after the second transplant.

3) Our third patient had a 6/6 matched unrelated donor. We transplanted using T-cell depleted peripheral blood stem cells (CD 34 cells > 10 x 10E6/kg, T-cells < 1 x 10E5/kg). Conditioning consisted of fludarabine (4 x 40 mg/m2) and ATG (4 x 5 mg/kg). We achieved a transitory engraftment with no toxicity.

A second transplant was performed using a 6/6 matched unrelated donor. We used undepleted peripheral blood stem cells. Conditioning consisted of fludarabine (6 x 30 mg/m2), busulfan (2 x 0.5 mg/kg. p.o.), and ATG (4 x 5 mg/kg). We achieved a stable engraftment with no toxicity. The patient is alive and well two months after the second transplant.

In summary, both combinations used (fludarabine plus ATG and fludarabine plus busulfan and ATG), even in the retransplant situation, are more or less non-toxic. There was no hair loss, no mucositis, etc. Fludarabine (around 160 mg/m2) plus ATG does not allow stable engraftment when T-cell depletion is being employed. We plan to prove systematically whether one should use undepleted cells or rather add other agents like low-dose busulfan. These "low risk" protocols clearly require a stringent follow-up because early after transplant there is usually a mixed situation, and it might require several weeks to months to get a complete donor engraftment. The patient numbers are still so small that it is difficult to draw final conclusions.

Editors' note: This protocol aimed to decrease toxicity by eliminating cyclophosphamide and radiation. Other centers have achieved engraftment using T-cell depletion in combination with varying dosages of fludarabine, ATG, cyclophosphamide, and radiation. Dates of post-transplant condition are as of October 5, 1999. ◆

Minnesota Reports on Six Alternate Donor Transplants Using Fludarabine

John Wagner, MD, Minnesota, has enrolled six FA patients in a trial using fludarabine. Patient age ranged from six to twenty-six years. Five patients received unrelated donor bone marrow (matched or mismatched at one locus), and one received a two antigen mismatched umbilical cord blood graft. Preparatory therapy included total body irradiation (450 cGy); cytoxan (10mg/kg/day for 4 days); fludarabine (35 mg/m2/day for four days); methylprednisolone, and ATG. Bone marrow was T-cell depleted.

All patients tolerated the therapy, and all engrafted. No one developed graft-versus-host disease. All are alive. The follow-up, however, is short (maximum is seven months post-transplant as of October 1999). ◆

IL-11, Platelet Growth Factor, in Trial

Preliminary Results

Dr. James Croop, MD, James Whitcomb Riley Hospital for Children, Indiana, released very early results concerning his center's IL-11 trial. This drug is a colony stimulating factor which researchers hope will increase platelet production. Croop expressed concern about the small sample size, noting that a "a few more patients one way or the other could change the results dramatically."

Croop has enrolled four FA patients in this trial. Three did not have an improvement in their platelet count after receiving IL-11 for four weeks. One patient had an increase in the platelet count of about 9,000, but wished to stop the IL-11 because of muscle aches after about two weeks of treatment. The criterion for a successful increase in the platelet count is 20,000. Croop would like to see a response rate of 40% of the enrolled patients to consider this agent worth pursuing for additional study. He is investigating the probability of reaching this goal, given the current results.

The most common side effect is fluid accumulation. This is manifested in a number of ways. There can be mild swelling, most notably in the ankles and wrists, and this may cause muscle aches in some patients. Some may have a temporary cough or conjunctival injection (the blood vessels over the white part of the eyes are more prominent). The increased fluid can temporarily decrease the relative hemoglobin level (the same number of RBCs in a larger fluid volume). If the hemoglobin is already low, this could mean the possibility of needing a RBC transfusion. There has also been swelling of the optic nerve in a small number of patients receiving IL-11.This has not caused vision problems, but is closely monitored by an opthamologist. ◆

Israel Achieves Early Success

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transplant with a conditioning regimen of fludarabine, ATG, and low dose cyclophosphamide with no irradiation.

Dr. Shimon Slavin of The Hadassah University Hospital is convinced that the "mini-transplant" or non-myeloablative conditioning, with reduced procedure related toxicity, represents the beginning of a new era, replacing stronger chemical warfare with more effective biologic warfare against the basic disease. Slavin has developed a new protocol for mismatched donor transplants using T cell depletion, fludarabine, and a reduced conditioning approach. This can now be offered to patients in need with no matched donors. ◆

Oral Leukoplakia Trial

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ulcers in addition to leukoplakia. Physicians do not know if this mouthwash would worsen or lessen the ulcerative condition.

Most FA patients with leukoplakia are eligible for this study. If the leukoplakia is caused by injury (e.g., dentures) a patient would not be eligible. An FA patient who has had surgery to remove cancerous lesions and has no present evidence of mouth cancer, but has leukoplakia, would be eligible.

If you are interested in this study, discuss these issues with your treating physician. Your physician can enroll you in this trial by calling: Dr. Jane Atkinson (dentist) at (301) 496-2069 or Dr. James Mulshine (oncologist) at (301) 402-3721. ◆

The Effect of Bone Marrow Transplant on Ultimate Height

Ten European transplant centers collaborated on an article concerning the relationship between bone marrow transplantation and the ultimate height reached by patients (the study did not focus on Fanconi anemia patients). Results were published in *Blood*, Vol. 93, No. 12 (June 15), 1999: pp. 4109-4115. We quote from that article:

"Few data are available on the long-term effect of bone marrow transplantation (BMT) on growth. This study examines those factors that play a role in the final height outcome of patients who underwent BMT during childhood. Data on 181 of 230 patients with aplastic anemia, leukemias, and lymphomas who had BMT before puberty (mean age, 9.8 ± 2.6 years) and who had reached their final height were analyzed. An overall decrease in final height standard deviation score (SDS) value was found compared with the height at BMT ($P < 107$) and with the genetic height ($P < 107$). Girls did better than boys, and the younger in age the person was at the time of BMT, the greater the loss in height. Previous cranial irradiation + single-dose total body irradiation (TBI) caused the greatest negative effect on final height achievement ($P < 104$). Fractionation of TBI reduces this effect significantly and conditioning with busulfan and cyclophosphamide seems to eliminate it. The type of transplantation, graft-versus-host disease, growth hormone, or steroid treatment did not influence final height. Irradiation, male gender, and young age at BMT were found to be major factors for long-term height loss. Nevertheless, the majority of patients (140/181) have reached adult height within the normal range of the general population." ◆

New Fanconi Anemia Center at Dana-Farber Cancer Institute and Children's Hospital

Dana-Farber Cancer Institute and Children's Hospital in Boston have established a comprehensive Fanconi anemia program. This program will support a broad range of activities and services and will ultimately lead to a better understanding of the molecular and cellular bases of Fanconi anemia, as well as improved methods for its diagnosis and treatment.

As an important part of the establishment of the Center, Alan D'Andrea, MD, and Eric Nisbet-Brown, MD, are conducting a survey of Fanconi anemia patients and their families. The data gathered in this survey (which has been approved by Human Subjects Review Boards at both Institutions) will provide the basis for a Fanconi anemia patient registry and database. This initiative has been made possible in part through the generous support of the Charles H. Hood Foundation of Boston.

The following are some of the activities that will go on in the Center:

- A basic research program in the molecular biology of Fanconi anemia, conducted in D'Andrea's laboratory.
- The creation of a Fanconi anemia patient cell repository including lymphoblastoid cell lines, skin fibroblast cell lines, and tumor cell lines from patients and family members. These samples will be used to further research into the different complementation groups of FA and their significance.
- A Registry of FA patients from across the United States and Canada. Based on a brief initial questionnaire, we will establish a database of basic demographic information. A second questionnaire will collect treatment information, and further questionnaires will be used to gather information about family history, susceptibility to different cancers, and other areas of concern. These data will also be used to try to identify correlations between complementation groups and different clinical forms of the disease, so they can be studied further. Note that all questionnaires will be approved by the Human Subjects Review Boards at both Dana-Farber Cancer Institute and Children's Hospital, and that complete confidentiality is assured.
- The development of a Cytogenetics Core Laboratory (headed by Lisa Moreau) for diagnosis, DEB testing, complementation group analysis, and carrier detection.
- A Diagnostic and Evaluation Center for new and known patients with Fanconi anemia, which will be directed by Nisbet-Brown. This program will provide both consultative services and comprehensive care for patients with FA. A broad spectrum of treatment options will be supported, including androgens, transfusion therapy, hematopoietic growth factor therapy, and bone marrow transplantation.
- The development of a gene therapy protocol for treatment of selected patients with FA.

A number of patients and family members have already participated in the first stage of this program by completing questionnaires and providing skin and blood samples at the Lake Geneva Family Conference this past August. Other persons who wish to participate or who would like to obtain further information about the Center should contact:

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Patients and family members may participate in any or all of the above activities of the Center. We hope that collection of these data will allow us to gain a better understanding of the mechanisms of this disease, its course, and treatment.

Materials and information gained from these studies will be made available to other FA researchers on request, provided appropriate ethical protections are met. ◆

Joenje Corrects Newsletter Error

Hans Joenje, PhD, corrected an error in our last newsletter on the use of new nomenclature for gene symbols. Hans writes: *FANCA* (in italics) is the symbol for the group A gene. FANCA (upright) is the symbol for the group A protein and messenger RNA. FA-A is the indication of the complementation group and the phenotype. You can say "This patient must be FA-A since a mutation has been found in the *FANCA* (italics) gene." You can't say, however: "This patient is FANCA."

Thanks, Hans, for your clarification! ◆

FAMILY NEWS

A Sister's Remembrance and Gratitude

by Lynnette Lowrimore

My brother Mark Lamer was diagnosed with FA when he was 5, while a patient at Boston Floating Hospital. This was in 1964, and my parents were told he was the 101st in recorded medical history to be diagnosed with FA. As you might imagine, there was little the doctors could offer my parents. He was put on experimental steroid medications. Despite a valiant struggle, he died at Walter Reed Army Medical Hospital four years later, just days after his 9th birthday. That was almost 31 years ago.

As I was reading the latest Family Newsletter, I started tearing up as I read the first and second person accounts from parents and patients. The descriptions of symptoms and characteristics reminded me so much of Mark: he was short, had a congenital hip defect, and was very pale. But he had a wonderful spirit and lived his short life to the fullest. I will go to Arlington National Cemetery on his birthday in May to visit his grave.

I am fortunate that neither of my daughters has FA (Jennifer is 21 and Katie is almost 16) but I know that the gene is there somewhere. I contribute monthly to the FA Research Fund because I consider it a prudent line of defense for protecting my grandchildren and their grandchildren. I appreciate what your organization is doing and want you to understand I consider my contributions as a monthly "bill." And I wanted to thank YOU, Leslie, for the commitment of time and caring. I'm sure it makes a difference to the patients and families of those now afflicted and those of us fortunate enough not to be facing the struggle right now. I just felt compelled to e-mail you and let you know of my thoughts.

Thanks again! ◆

The Gift of Caleb

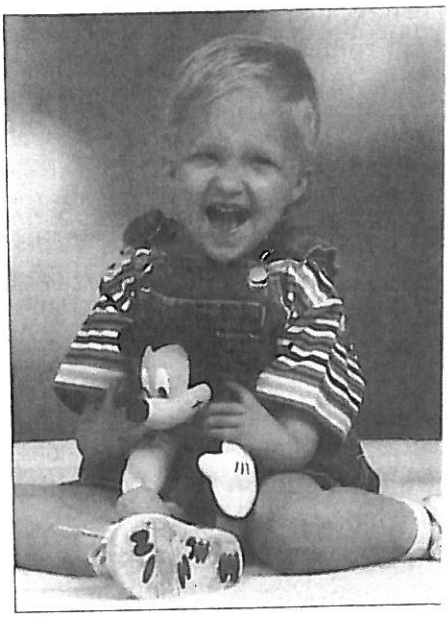
by Amy Glover

Whenever I stand back and think about life since our precious Caleb was born, I really find myself unable to describe it. How do you find words to paint pictures for the deepest of emotions and for what already feels like a lifetime of experiences?

Caleb's Biblical name means "courageous" or "bold one." He was only a few inches long when he was named, but we knew he would possess those qualities if he also were given the gift of life. Early in my pregnancy I was small and had an ultrasound to verify the due date. There, my husband, Steve, and I discovered that Caleb was hydrocephalic (he had fluid on the brain). At an appointment with a perinatologist we were told that he also had severe arm abnormalities. Repeatedly, we were told of the poor prospects for his quality of life, if he survived at all.

That's when we named him. Though we were wracked with pain, we vowed to celebrate his life for the miracle that it was and for whatever time God gave him to us. Steve and I share a faith in God, and we literally clung to His promises found in the Bible. He promises to never leave us or forsake us, to hold us in His everlasting arms, to give us strength, peace, hope and even joy, if we trust in Him. We threw ourselves and our often frail faith into those arms time after time, and He was faithful.

At 32 weeks after close monitoring, we were told that Caleb had to be taken by C-section. The fluid had grossly accumulated and, if he did not have a shunt installed quickly, he would be in a total vegetative state! On September 9, 1996, we were pre-



pared for a tiny, limp baby with hands or forearms (the ultrasoun had shown no hands and very lit under the elbows). The waiting roo was packed with family and frier praying and holding their brea

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Living with Cancer

by Chris Hull

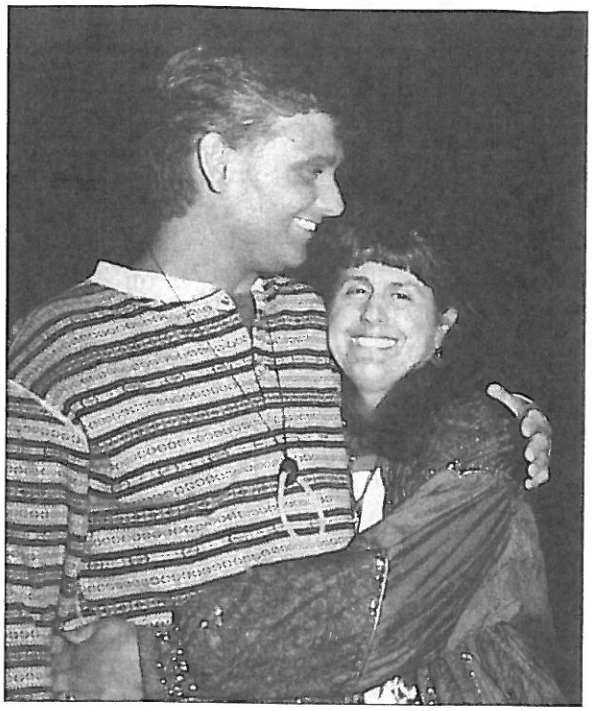
Living with cancer has been unpredictable. I have hepatocellular (liver) carcinoma, a cancer which seems to recur often and quickly. Thus the unpredictability. I never know if the cancer is going to return and, if so, when and where. To an extent, everyone's life is the same: we never know what tomorrow will bring us. Growing up with FA, I have always realized this uncertainty, and promised myself to enjoy every new day as much as the last. Now that I've been diagnosed with cancer, this uncertainty is even more evident. Fortunately for me, I have led a very normal life. I have great friends and family, who give me the strength and love needed to overcome these obstacles.

About three years ago, I needed this support more than ever. A large tumor was found on my liver. I experienced great pain in my side, daily fevers, and cold sweating spells. At first, my doctors treated me with antibiotics. The symptoms got worse instead of better, and finally they were unbearable. The tumor, along with a large portion of my liver, was removed in November of 1996.

It is assumed that the cancer was a result of 22 years of oxymetholone therapy. I started with high dosages, tapered to lower dosages over time, and for the last 11 years was on a small dosage (4mg/day). I have not taken oxymetholone since the summer of 1997. The oxymetholone allowed me to enjoy more years than my family anticipated. It managed my blood counts well. To some extent, I may have taken life for granted, even knowing the dangers of FA.

Now at the age of 33, a different type of uncertainty rests in the back of my mind. Without being able to block it, periodically, the questions "pop" into consciousness: "Will the cancer return?" "When will it return?" "How fast will it grow?" "What can we do to remove it or stop it from growing?" Unfortunately, there are few answers to these questions, so I must accept them. I try my best to ignore these questions, to think of something better. I think of all the good things about my life: my friends and family, my experiences, the promise for a future, and the beauty of today. Ironically, I urge my friends to try not to live in the past or the future, yet to enjoy the present. From time to time, when I cannot "shake off" those questions, even I look to the past to remind myself of the opportunities for a bright future.

In 2 1/2 years, I have had two tumors removed by surgical resection, and two more by a relatively new procedure called radio frequency ablation (RFA). The RFA is much less invasive to the body than surgery and has been successful for me thus far. (I had the RFA procedure in March and again in September 1999). However, both procedures have taken a toll on my blood counts. With each procedure, my counts have dropped. They are low now, but seem to be steady, and are manageable. My physical activity is limited. Mentally, I remain strong and continue to live in the beauty of today, and look forward to a bright and promising future. ◆



Chris Hull and Lynn Mendenhall

The Bridge Builder

by Will Allen Dromgoole

An old man, going a lone highway,
Came at the evening, cold and gray,
To a chasm, vast and deep and wide,
Through which was flowing a sullen tide.
The old man crossed in the twilight dim;
The sullen stream had no fears for him;
But he turned when safe on the other side
And built a bridge to span the tide.

"Old man," said a fellow pilgrim near,
"You are wasting strength with building here;
Your journey will end with the ending day;
You never again must pass this way;
You have crossed the chasm, deep and wide –
Why build you the bridge at the eventide?"

The builder lifted his old gray head:
"Good friend, in the path I have come," he said,
"There followeth after me today
A youth whose feet must pass this way.
This chasm that has been naught to me
To that fair-haired youth may a pitfall be.
He, too, must cross in the twilight dim;
Good friend, I am building the bridge for him."

Snake in the Grass

by Lynn Welfare Mendenhall

Cancer is a snake in the grass. A seething, conniving, slithering serpent. You know the snakes are there in the woods, but you can't see them until they show their ugly faces on your driveway. If you saw one on your driveway, you would probably want to run over it and kill the creature. I am told that unless you kill the snake by running over its poisonous, deadly head, you will find the snake still alive, and it is likely to strike again, and again, and again. Even if its tail is pinned down, the serpent will strike the tire over and over again in attempts to "kill" its prey.

Well, my friends, that pretty well sums up my last two years of dealing with dysplasia and squamous cell cancer of the mouth and tongue. The mouth cancers have come back to strike again and again. I have had six surgeries since January 1998. I present a chronology of my ordeal:

March 1997

I experienced redness/soreness in my mouth, then white sores. I knew that many FA patients had problems with mouth/oral cancers, cancer of the jawbone, larynx, and esophagus. I determined to take this seriously and not just be reassured when told "it's probably nothing."

April 1997

I went to the doctor for flu-like symptoms and persistent soreness and redness on the floor of my mouth and side of my tongue. Tried magic mouthwash.

May 1997

We changed antibiotics and the flu-like symptoms went away. Sores, soreness, and redness in the mouth continued. Magic mouthwash continued. My doctor did not know the cause of my mouth symptoms.

June 1997

No change in mouth. Reported this again to my doctor.

July 1997

I purchased cancer insurance with AFLAC so that if there were any problem and/or waiting period everything would be in place.

August 1997

Scheduled visit with dentist.

September 1997

I went to the dentist, thinking maybe the sore was the result of sleeping on my tongue and side of my mouth. My tongue had a thin line on it, like I had clenched my teeth on my tongue. I thought maybe the sore on the side of my tongue was due to my chipped back molar or my denture rubbing raw against my tongue. Nevertheless, the dentist, (whom I have kept informed about FA) said he wanted me to see my oral surgeon.

November 1997

I went to my oral surgeon, who stated "I do not like the look or feel of this." He referred me immediately to an ear, nose and throat (ENT) specialist. This specialist also did not like the look or feel of my sores. He immediately biopsied the area. The results were back in 1-2 weeks.

December 1997

The biopsy was positive for squamous cell carcinoma of the right side of the tongue. An MRI indicated that everything else was normal.

January 1998

I had surgery to remove tongue cancer. While in surgery, other suspicious areas were biopsied. A tracheotomy was put in, and I spent 5 days in intensive care. I had a right neck incision from my ear to the front of my neck and throat to surgically remove 10 or 11 lymph nodes in my neck to check for any malignancy not detected by the MRI. Grafts were taken from skin on my leg for tongue mobility.

June/July 1998

The soreness/redness returned, but in other areas of my mouth. Worrisome areas were found on the right inside and side of my mouth, the lower and upper inside of the right lips, and there was a white bump near or next to the original surgery site. We had biopsied this area previously, but it showed nothing. We planned to observe these areas for one month.

August 1998

Biopsy of July 1998 sites done. Gum irritation noted behind right tooth. Biopsy positive for squamous cell carcinoma on right inside of mouth.

September 1998

Surgery to remove carcinoma, and biopsy and remove other suspicious areas in the mouth/lip. White lump at the floor of my mouth near original surgery site removed. Removal o right lower lip for severe dysplasia White bump under my upper righ lip excised. Leg skin graft over th right inside of mouth.

December 1998

Soreness behind upper right bac molar. Area biopsied. White bum appeared in the center of the origina surgery site. Biopsy concluded squa mous cell carcinoma had returne again. Within days after the doctor

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Snake in the Grass

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visit, I noted a white sore again on the inside of my right upper lip and soreness/redness on lower inside lip again. The white lump was more painful as time went on, and it hurt even to drink water. Previously only swallowing food on that side hurt. Went for a pre-op visit two weeks later (neither the doctor nor I really wanted to believe that in a matter of a couple of days another malignant place had appeared so quickly, but we did not ignore it). It was biopsied and was squamous cell, not dysplasia. I had difficulty swallowing food and had numerous food choking episodes.

January 1999

A scope was put down my nose with a topical spray anesthesia (uncomfortable, but did not hurt). The barium swallow was fun to watch. A light was put down my throat to look at the esophagus/larynx. Results were good. They stretched my esophagus so that I could swallow food better and take medicine better. I did not realize until afterwards how good it felt to swallow normally again.

February 1999

CT scan for pre-op and labs done. Had an impression made of entire mouth day before surgery to make an upper roof mouth plate to protect area where tumor would be removed behind the right upper molar, and where the tooth would be removed from jawbone. They did not rule out the possibility that part of the jaw would need to be removed. They removed the tooth, the tumor, and removed the white spot on the inside of the upper right lip. They removed the white "peak" at the bottom of my right tongue and floor of the mouth. They did not remove the jawbone but bits of jawbone were taken to the lab, along with the tooth, to biopsy while in surgery. While in surgery they discovered that the "insignificant, little white spot on the inside of my upper lip" was cancerous and removed it. A plate was inserted to allow healing of the area where the tooth was pulled.

July 1999

The top left gum area next to the molar, plus four other sites were biopsied in July. Because of increased pain, one area was rebiopsied.

September 1999

The final biopsy showed moderate to severe dysplasia inside my upper lip. A biopsy under my neck was negative. Laser surgery was performed to remove the dysplastic areas.

October 5, 1999

I had surgery to extract a very painful tooth. At some point we will biopsy that area, too, but not right now.

Everything is now under control until the next time, if you know what I mean. I will try to answer some of the questions I am asked frequently:

1) How did you know you had cancer?

I did not know. I was concerned that I had a sore on the side of my mouth that eventually went to the floor of my mouth, and that it would never go away. I also know that FA patients are prone to cancers of the mouth, larynx, esophagus, reproductive organs, etc.

2) Now that you have had this surgery and the cancer has been removed, do you think this will take care of the problem?

I hate to tell the doctors, friends and family the answer to this question. I fear that my cancer will return because of the genetic problems and nature of Fanconi anemia. The surgeries have been successful, even life-saving! But one's guard must never, ever be let down. I check my mouth daily for ANY suspicious irritation or soreness. It does not matter whether you think it is "gum irritation," a white bump, or bump that goes away then comes back. Get a biopsy! Remember the snake. He is still hiding in the woods.

3) Can anything be done?

I personally believe that because the problem is on the genetic level, it needs to be treated on a genetic level. I am pursuing approval of an FDA gene therapy trial with every ounce of my being because I believe this is a first step. I have spoken with many doctors, and the consensus is that radiation and/or chemotherapy will not be of benefit to me. They would weaken my system as a whole. What we have been doing is the best option for now.

I advise all of you to stay on top of things! Put pressure on your treating physicians to find answers to unusual symptoms. Do not be fooled by reassurances when your gut instinct tells you something is very wrong. The best of luck to all of you! ◆

A Parent Writes...

by Lorne Shelson

The best thing you can do is to make as fully informed a decision as you can, based on the current state of medical science at the time. Read as much as you can, ask as many questions as you can. When you arrive at a decision, give it your full support. Then don't look back. Don't punish yourself with "what onlys?"—because you did the best you could at that time. And take every opportunity to enjoy the "todays" that you spend with your child. ◆

Kelly Turner: An Update Seven Years Post-Transplant

by Jan Turner, Mother

I want to contribute an update on how our daughter Kelly is doing 7 years post transplant. I wrote a book about Kelly's life called *We Just Want Our Daughter to Live* (published by Penguin - July 1996), and I know some of you have read it, but for those who haven't, I will give a brief overview of how we got to today.

Kelly received an unrelated transplant (French donor) on February 14, (Valentine's Day) 1992, at St. Louis Hospital, Paris. As you know, the decision to proceed with a transplant of this kind is not made lightly. We were fortunate that Kelly had a common tissue type, and Professor Gluckman found a donor on the French Registry very quickly. The next 18 months we spent fundraising to take Kelly to Paris for the transplant. It doesn't sound like a big deal when it's said in one sentence, but to us it was a nightmare. Being thrust into the public eye throughout New Zealand, as we were, was horrible. There's a saying that goes, "Life is fairly simple, it's people that complicate it! "How true this is. All of a sudden we seemed to be public property. It's a long story, but we did get through it and flew over to Paris early January 1992, somewhat already worn out. By the way, we were fortunate that when we decided to proceed with the transplant, Kelly was in very good health, her platelets were low but manageable, and she had not had any transfusions or androgen treatment. Her healthy condition allowed us time to fundraise.

In Paris the conditioning regimen of chemotherapy and radiation Kelly underwent caused no unexpected problems. We were very relieved when she came through it OK. The actual transplant also went well. Then it was the yucky time with infections and living for the daily blood counts. We were delighted when after 10 days there were signs of the new marrow working. Kelly then contracted a cytomegalovirus that threatened to destroy the new marrow. Luckily, there were some excellent drugs available to treat this particular virus, and gradually it was eradicated. It was a difficult time, calling for much patience and perseverance on everyone's part.

Three months after the transplant, Kelly developed mild GVHD in the form of a skin rash. This was managed by adjusting her drug dosages to control it. We remained in Paris for 10 months until Professor Gluckman was happy with Kelly's progress and she gave her blessing for us to take her home to New Zealand.

Kelly remained on many drugs (prednisone, cyclosporine, zovirax, etc.) for the best part of 2 years post-transplant. She had a nasty bout of shingles in 1994, but she received treatment and got through it OK.

Kelly has remained healthy with no further signs of GVHD. Her blood counts have now been in the normal range for the past 5 years. She has a yearly bone marrow aspiration performed to keep an eye on the bone marrow, and the results have confirmed that the marrow is all of donor origin and is healthy. Last year Kelly was found to have a slight hearing loss (missing background noises, such as rustling leaves), and it is thought the cytomegalovirus must have caused it. It is not serious and is not affecting Kelly's daily living to any noticeable degree.

The one problem Kelly does have

Kelly Turner

is with her size. Just as I have read stories from other families recently, Kelly's bone age is delayed by approximately 5 years and, although she is now 16 years old, her physical appearance is that of an 11-year-old. She is progressing through puberty though and has the mental age of her peers. She enjoys all of the same things as any other teenager (like hogging the phone/computer), and we wouldn't have it any other way. Kelly often hands out a copy of my book to someone whom she feels needs to be educated on FA. Education does seem to be the key word doesn't it? The comments that people make at times about her size can be hurtful. I'm just glad Kelly seems to have the right attitude in dealing with it. She has a boyfriend with whom she enjoys going to the cinema and life goes on. I'm just so grateful she is alive.

I remember after we made the decision to proceed with the transplant how at times I started doubting our decision, wishing someone could give me a guarantee that Kelly would survive. There were times when I felt really strong and firm in my resolution that "this transplant is going to work." Then in the next instance I would feel like crawling away into a hole with the thoughts of what Kelly was going to go through (losing her

continued on page .

Kelly Turner
continued from page 12

beautiful hair and swelling up with the steroid treatment) and then maybe dying. Remember, we had 18 months to think about it, and during that time we were constantly in the newspapers, so there was a constant reminder each day about where we were headed. But there is never a guarantee. Not for anything in life. What did keep me going was knowing that we had a chance for Kelly to live and we had to pursue it while she was still in good physical health.

I believe there is NEVER a right or wrong decision. We can only do our best with what we know. I think it is important to search for all the information that is available before making a decision. How wonderful to now have the Internet to do it on. I completely saturated myself with everything I could find out about FA and transplants. It was empowering, as I felt I could then make the best possible decisions available at the time and also work on an equal level with the health professionals involved. Some found this threatening; others were quite accommodating. I also believe that, as parents, no one knows our children better than we do. I have learned that when my instincts are telling me something is wrong with my child, there always is. Coming to these realizations over the years has helped me become a stronger person and to be able to support Kelly through the rough times.

We don't know what's ahead for any of our FA children, but I believe it is important to share our stories so we can give hope to each other.

Hope is what gives us the strength to carry on and seek answers to give our children the best possible chance available. ◆

Chrissy Cachero's Trials and Successes in Dealing with FA

by Patricia Cachero, Mother

My daughter Christina Cachero, age 15, was born with bifold thumbs. From that day, I knew that Christina was one of God's special children! In November 1997, she was diagnosed with Fanconi anemia. We had grown concerned because of her increased fatigue, frequent illnesses and noticeable pallor for a child who was half Caucasian and half Asian. I asked her doctor to perform a blood test. Her hemoglobin was below 8, and all the other counts were drastically below normal. Her doctor was amazed that she could walk! Further testing revealed that she had Fanconi anemia. We had to act fast, for time was running out.

Both of our sons proved to be a perfect match for Chrissy! We felt that God was watching over us. She was admitted to Johns Hopkins University Hospital on 1/10/98 and transplanted five days later. Her brother Jimmy was her donor. Chrissy developed severe mucositis but somehow her strength held up. Her treating physicians were wonderful.

After Chrissy's release from the hospital, she was readmitted many times. First she had a cytomegalovirus infection, which made her extremely ill. Then she developed an aspirgillus infection. She experienced shaking and a very high fever. Doctors put her on three different dosages of amphotericin and finally, after a month, the infection resolved.

But now we are faced with her heart problem. She has fluid in the sac that surrounds her heart, and doctors don't know where this is coming from. We will see a heart specialist November 4. Meanwhile, her counts are climbing regularly; her bone marrow is functioning well.

Chrissy has a great deal of anxiety, knowing that she has this orphan disease. She has been a true trooper, full of love and trust. She has been through a war that no child should have to endure! As her parents, Patricia and Rimundo Cachero, we pray that God will touch all of his special children and send an angel to soothe their pain! ◆

Saved by the Light

The True Story of a Man Who Died Twice and the Profound Revelations He Received

by Dannion Brinkley

Book review by Carol Siniawski

My 9-year-old son was asking a lot of questions about heaven and dying, and because my family believes in a life after death he was very curious. The priest at Children's Hospital recommended a book, *Saved by the Light* by Dannion Brinkley. Dannion has had a near death experience. He tells of how wonderful life is after death. He is no longer afraid of dying. The book is easy to read. The words and language used are simple and the chapters themselves are broken up into smaller sections. It really did bring me comfort. I feel better, honestly, about discussing death, since reading this book.

I'd recommend it to anyone struggling with this very difficult topic. Maybe it can help other parents or FA patients, as it has been helping us. ◆

We Welcome New Families Who Have Joined Our Support Group

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Lisa (32) and Christopher (24)

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fitzentp@vnet.net
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Robert - DOB 7/8/94

Charlene Fitzpatrick
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(619) 423-7042 H
Jake - DOB 4/12/87
James - DOB 12/8/84
Ariel Land - DOB 1/9/90
Mark Lepper - DOB 5/4/96

Mitchell & Tirzah Haik
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(707) 643-2459 H
Veronica - DOB 1/13/93

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Sam - DOB 2/18/98

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Sharlene Evans - DOB 11/9/85

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Salmaa - DOB 4/24/95

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INDIA
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011 91 22 5295649 Fax
Kajol - DOB 8/11/96, deceased 4/15/99

Paul and Martha Villarreal
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Daniel - DOB 10/20/94

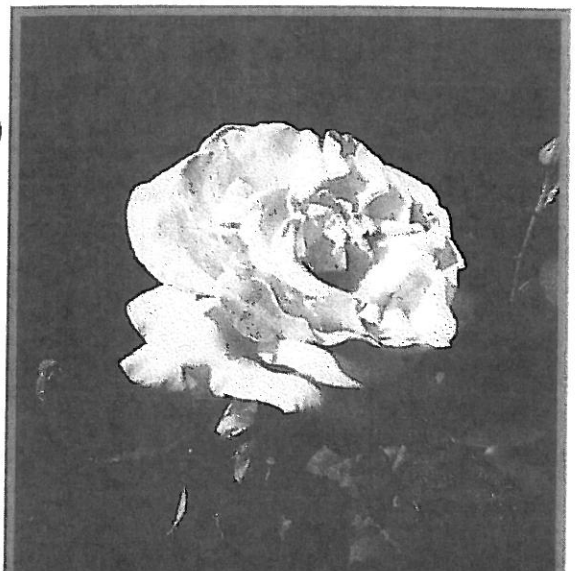
Names in bold print indicate person with Fanconi anemia. ◆

Editors' Note and Disclaimer

Statements and opinions expressed in this Newsletter are those of the authors and not necessarily those of the editors or the Fanconi Anemia Research Fund. Information provided in this Newsletter about medications, treatments or products should not be construed as medical instruction or scientific endorsement. Always consult your physician before taking any action based on this information.

Use of Logo

This is just a reminder to our FA families: please use our logo or letterhead only after you have consulted the staff of the FA Research Fund, and received their approval. This is necessary to be sure our messages are accurate and consistent. It also helps to avoid legal complications. We are happy to collaborate on fundraisers and mailings.



In Loving Memory

Danielle DiMarino
5/7/87 - 8/24/99

Carrie Janock
1/31/91 - 4/27/99

Alexandra Gallagher
11/27/91 - 5/7/99

Chelsea Napoles
6/8/87 - 10/9/99

Joseph Pray
5/18/87 - 4/23/99

Alexander Schweigardt
4/22/83 - 6/29/99

Kajol Shah
8/11/96 - 4/15/99

Morgan Woody
7/6/81 - 4/6/99

Although the world is full of suffering...
it is also full of overcoming it."
~ Helen Keller

We Remember Them

At the rising of the sun and at its going down
We remember them.

At the blowing of the wind and in the chill of winter
We remember them.

At the opening of the buds and in the rebirth of spring.
We remember them.

At the blueness of the skies and in the warmth of summer
We remember them.

At the rustling of the leaves and in the beauty of autumn.
We remember them.

At the beginning of the year and when it ends
We remember them.

As long as we live, they too will live, for they are now a part of us as
We remember them.

When we are weary and in need of strength
We remember them

When we are lost and sick at heart
We remember them

When we have joy we crave to share
We remember them.

When we have decisions that are difficult to make
We remember them.

When we have achievements that are based on theirs
We remember them.

As long as we live, they too will live, for they are now a part of us as
We remember them.

~Author unknown

The Gift of Caleb

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Awesome was the moment he came out kicking and screaming and flailing his little "wings" as my dad called them! He was 3.5 lbs, was breathing on his own and had hands! They weren't normal, but he had them! Evidently, his arms were curled up to his chest and they had been unable to see his hands from that position. He had no thumbs, no radius on either arm and his ulnas were bowed, but we were so grateful for those fingers!

Caleb's shunt was installed, and he was in the NICU for only two weeks. On the ninth day (the "mother - load" of all days, shall we say) we received the news that he had FA! I felt like I'd just been hit by a semi. The more I learned about FA, the worse it got, and I felt the future suffocating me. My sweet baby who had just overcome so much would spend how long battling for his life? I felt myself battling for mine. The ground was completely ripped out from under me. When I was at one of my darkest moments, I realized I had a choice. Psalm 61:2 says, "When my heart is overwhelmed, please lead me to the Rock that is higher than I" (that Rock being God). I could ignore this safe, high Rock and go on floundering or I could let the Lord lift me up and set my feet on the Rock, where I'm safe and can see things from His point of view. Not that I will ever completely understand why things are the way they are, but to ask for the courage to accept them. To realize Caleb is deeply loved by Him and that there is a beautiful plan for his life. To live life not allowing the fear of tomorrow to rob us of today's joy. We have enough to fill today. Life is filled with fun and things to be grateful for. Caleb loves life and lives it more fully than anyone I've ever known! There is something about him that awes people, including me. People watch him and love him, and you can just see the twinkle come into their eyes. Who better than little people like him to love, live life and show the world what life is really all about? Granted, nothing shields him nor us from the pain and many tears that result from this illness. Still, we have a hope and a peace that doesn't come from ourselves and remains in the midst of deep suffering.

Caleb has just turned three. Miraculously, he suffered no cognitive damage and is a little chatter box (despite a mild hearing loss). He had surgeries on his arms and hands and has adapted beautifully. He ends up in the hospital every few months, and his platelet count has been dropping. He loves singing, reading books (over and over), experiencing water in any form, and eating mint chip ice cream! I am now five months pregnant with twin girls. So far all the ultrasounds look good although we won't know for sure if they have FA (or if they are a match for Caleb) until they are born. We will continue to run this race called life with our eyes fixed on the Rock. ◆

Please

Parents who have lost children are sometimes the recipients of well meaning yet insensitive comments. This poem by Rita Moran, published in *The Compassionate Friends*, speaks to many who have lost children, and offers advice for those who do not know what to say.

PLEASE, don't ask me if I'm over it yet.
I'll never be over it.
PLEASE, don't tell me she's in a better place.
She isn't here with me.
PLEASE, don't say at least she isn't suffering.
I haven't come to terms with why she had to suffer at all.
PLEASE, don't tell me you know how I feel,
Unless you have lost a child.
PLEASE, don't ask me if I feel better.
Bereavement isn't a condition that clears up.
PLEASE, don't tell me at least you had her for so many years.
What year would you choose for your child to die?
PLEASE, don't tell me God never gives us more than we can bear.
PLEASE, just say you are sorry.
PLEASE, just say you remember my child, if you do.
PLEASE, just let me talk about my child.
PLEASE, mention my child's name.
PLEASE, just let me cry.

Impressions of the FA Family Meeting

The following is a letter sent by Ray Cronin to Gail King.

Dear Gail,

I promised to let you know how the FA family meeting went. Words cannot express how I feel but I will try.

I am downright in love with every person I met on this adventure, from the parents to the tiny children with Seckel to the volunteers who overwhelmed us with their enthusiasm and dedication to making wonderful memories for all the children—and us also.

I have never seen such a large group living together for five days with not a hostile word uttered. Friends met day one with a sincere loving hug, and newcomers were welcomed with enthusiasm I have never experienced. I am shy and introverted in person, yet I found myself not able to get a coffee without talking to someone new for 20 minutes at the coffee machine. I met and became friends with well over half of the people who attended. A large portion of the children I know by name, and they know me well enough to initiate contact or ask me questions—very rewarding.

Our children were cared for by volunteers with such dedication that many of them and the kids cried on parting. For the teenagers, there were chaperones and classes to discuss their issues. I believe all enjoyed being there.

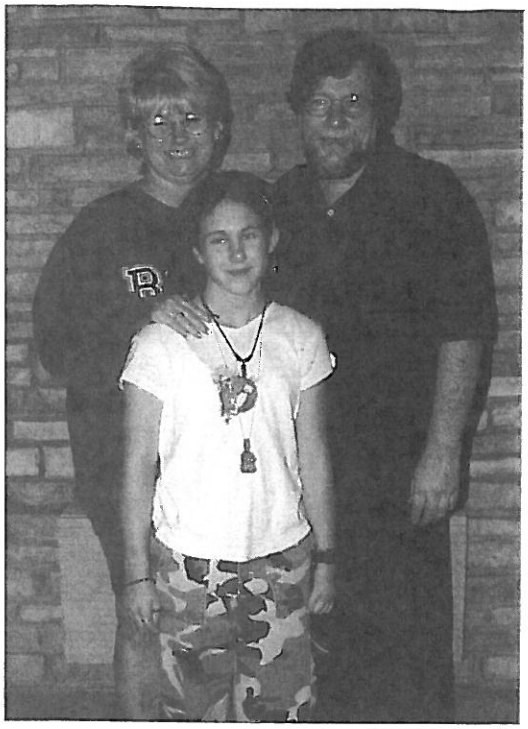
We had days full of classes overflowing with information and enthusiasm for advances being made in both transplants and gene therapy. These discussions overflowed our breaks and lunches because we couldn't pull ourselves away. Every spare moment of each day overflowed with personal interaction, exchanging histories, ideas, and just enjoying being with each other. The doctors would talk to anyone as long as you like without making you feel you were taking up too much of their time. Ralf Dietrich from Germany makes a career from interviewing every family in the world, I think, and getting their histories. He suggests when we can do better for a child and shares his "gut" knowledge so we will ask the right questions of our doctors to improve our children's chances.

Nights were filled with social activities that reminded me of being a pre-teen, you know, back before we forgot how to have fun. The highlight for me was Tuesday night, when the kids and volunteers put on a talent show. It's too bad some of the families had to leave and miss it.

There are many people I would like to mention personally, but I would likely leave someone out and hate myself. I would, however, like to suggest we give something to the volunteers for their extreme dedication. It would not detract from the fact that they gave themselves so completely with no thought of reward.

I could easily turn this into a book, but I'll keep it short so you'll read other peoples' experiences also.

Ray, Diane & Sandra (12) ◆



Diane, Ray and Sandra Cronin

Bone Marrow Samples Needed

Chris Walsh, MD, PhD, has created new vectors for FA-A and FA-C, which he would like to insert into patient bone marrow cells in the laboratory. He would greatly appreciate receiving a bone marrow sample from patients in either of these complementation groups who is undergoing a routine bone marrow aspirate.

Contact Chris directly for specific information on preparing and sending the appropriate sample:

Chris Walsh, MD, PhD
Gene Therapy Center
University of North Carolina
Thurston Building, Room 7101, CB 7352
Chapel Hill, NC 27599
(919) 966-9116
e-mail: cwalsh@med.unc.edu

FUNDRAISING

A Heartwarming Message from the Vangel Family

by Beth and Michael Vangel

I just wanted to share an experience we had. A friend of mine has asked several times what she can do to help. I know that all of you have had that asked of you several times. I know for me I never really have a good answer.

Well, this time I did. I loaned my friend the fundraising book to show her different ways to help. The next thing I knew she was in touch with the Research Fund and on her way to putting together a letter writing campaign (with our permission, of course). She will send these letters to her friends and family who actually live out in the New Jersey area and her neighbors here in Hingham, MA.

My friend made several comments about how much help Esther and Leslie gave her. They gave her suggestions, postage and even printed up the letters for her. She was so impressed with the help she received!!!! All that I had to do was get 70 prints made up of Amy and Dennis and hand them to her.

Maybe the next time somebody is interested in helping out, keep this idea in mind. I really can't think of an easier one. The Research Fund really, really does it all!!!

Thank you again to Leslie and Esther. ◆

Goddesses Run for FA

The "Eugene Road Goddesses" are a group of Eugene area women over 40 years old. They run the Hood to Coast annually and raise money for the charity of their choice. The Hood to Coast race is well-known in Oregon. It starts at Timberline Lodge near the top of Mt. Hood and ends 195 miles later at the Pacific Ocean at Seaside, Oregon. Each member of each 12-member team runs three legs of the race. This year, the Goddesses ran for Fanconi anemia research. Through their diligent fundraising efforts, they raised $6,670.40 for the fund. A very impressive feat! ◆

Canadian Research Fund Expands Outreach, Increases Effectiveness

The Canadian Fanconi Anemia Research Fund (CFARF) was founded in 1994 as a charitable association by Tami and Peter Dunstan-Adams of British Columbia. Approximately thirty Canadian families are served by CFARF, which publishes a bilingual newsletter to serve both English and French speaking families. CFARF also publishes a fundraising brochure.

Canadian FA families pursue a broad range of fundraising activities. CFARF's fundraising efforts have included the sale of enameled CFARF lapel pins, community barbecues, casinos, recycling drives, tribute cards, pancake breakfasts, and even trail rides. To date, families have raised approximately $50,000 for FA research. Because the organization has no paid staff, nearly every dollar raised is earmarked for research.

CFARF also raises awareness of FA across Canada. *Fanconi Anemia: A Handbook for Families & Their Physicians* has been distributed to every children's hospital and major obstetrical department in Canada and all prenatal screening clinics in the Province of Ontario. CFARF has obtained listings on numerous patient/parent resource websites. Earlier this summer, Ontario Region FA families attended a wonderful picnic.

Plans are underway to incorporate CFARF and shift its administration to Toronto where Canada's leading BMT and FA research facility, the Hospital for Sick Children, is located. Lorne Shelson and Annette Waxberg will manage CFARF on a day-to-day basis, but the Dunstan-Adams family will remain involved as CFARF's West Coast contact. Dr. Manuel Buchwald has agreed to serve as CFARF's medical advisor. A new CFARF brochure is in preparation. CFARF plans to hold a French language chat on the internet. Most significantly, CFARF hopes to commit to funding at least two Canadian research proposals within the next twelve months. ◆

Fundraising Concerns

by Leslie Roy

The FA Research Fund is coming to the close of its tenth year. During this time, our organization has raised over $6.5 million for research and family support. This is truly a wonderful accomplishment!

There are two troubling facts. The Frohnmayer family, in one way or another, has been responsible for raising approximately 85% of that amount. And more than 90% of all our funds over this ten-year period were raised by only 3% of the families in our support group!

Through the efforts of the Frohnmayers, we obtained the Meyer Memorial grant and many other community grants. Through their annual fundraising letter, we have received large and small individual donations. The worrisome truth is that, when an organization relies primarily on one or even a few families for a substantial portion of its money, that organization is at real risk.

We recognize that many families have played a significant role in raising funds. We also know that things change in families, affecting their ability to help. But we have to ask ourselves this question: could we survive as an organization if 85% of the funds presently being raised were to disappear? What would we give up? Our family meetings, our research support, our FARF staff, our scientific conferences, our publications? What would we do if the Frohnmayers were not able to continue? I know that Lynn worries about this constantly. She has told me that she is NOT proud of these troubling statistics and sees this as a terrible organizational weakness. We need to create an organization that will last until a cure is found for this awful illness, not an organization which will last until a few fundraising families become too exhausted to continue.

I recently stated at a regional meeting that the Fund is not the Frohnmayers, the Board of Directors, or the office staff. The Fund is every family in our support group. Efforts big and small all lead toward the end result, a CURE. Many of you have suffered the pain of a lifetime because of a genetic defect that you did not know you had. My heart is moved greatly by those of you who have lost everything to this disease, but remain connected and dedicated to seeing that we move forward toward our goal. We are in this together. What one can't accomplish alone, we can all do together.

Congratulations and a big thank you to all the families who made special efforts toward raising a total of $1,217,658 during the first six months of 1999. This total includes memorial donations of $14,734 and United Way/Combined Federal Campaign contributions of $14,993.

Funds raised from January 1 through June 30, 1999, were attributed to the following families:

$1,080,000 +
Lynn & David Frohnmayer*

$17,000 - $22,000 +
Susan & Chris Collins
Deane Marchbein & Stuart Cohen
Vicki & Andrew Athens

$10,000 +
Laurie Strongin & Allen Goldberg

$ 5,000 +
Debby & Jeff Slater

$ 4,000 +
Beth & Jeff Janock

$ 3,000 +
Ellis Family

$ 2,000 +
Connie & Bill Schenone
Lisa & Jack Nash
Beth & Mike Vangel
Linda & Mark Baumiller

$ 1,000 +
Gustavo Mulet
Susan & Mark Trager
Lynn & Rick Sablosky
Beth & Eric Losekamp

$ 500 +
Lisa & Boyd Bourgeois
Gary Gangwer
Pat & Mary DiMarino
Judy & Jeff Hoffman
Karilyn & John Kelson
Jennifer & Robert Kiesel
Fredi & Ron Norris
Karen & Bryan Siebenthal
Sandi & Marc Weiner

Up to $500:
Jeanne & Ken Atkinson
Kelly & Tyren Bennett
Gilbert Bodier
Kim & Kevin Frock
Maria Gamonal
Tirzah & Mitchell Haik
Chris Hull
Nancy & Lester Jansen
Peg LeRoux
Lynnette & Greg Lowrimore
Jackie & Bill Lucarell
Donna Barnes
Day Family
James Mathieson
Teddi Gray
Cecelia Meloling
Cecilia & Griff Morgan
Sheila Muhlen
Robin & Jessica Paulson

continued on next page

German Research and Support Group Continues Impressive Accomplishments

The German Fanconi Anemia Association, Inc., was founded in 1990 by Ralf and Cornelia Dietrich and five other German families. They maintain a central office and four regional offices, and have 250 members. Their executive director and four additional Board members are all Fanconi anemia parents. Twice a year they produce a newsletter in German. They are completing an updated German edition of the American FA Handbook.

The German FA Association holds an annual family meeting for FA families, doctors, and scientists from Germany and other European countries. They average 100 participants. They hold an international scientific workshop with FA doctors, researchers, and students in combination with their annual meeting.

Their support group includes 95 German families in addition to families in Northern Italy, Switzerland, The Netherlands, France, Great Britain, Greece, Syria, Bulgaria, and White Russia. They provide information to all FA families by phone, letters, e-mail, and personal visits if requested. Ralf Dietrich has also videotaped 120 interviews with patients and other family members, in an effort to compile extensive data about this illness. Ralf develops computerized graphs of patients' blood-counts, including information about responses to therapy. He maintains intensive contact with FA research labs in Germany, other European countries, and in the United States. He has transported many patient samples (blood, skin, and bone marrow) for research purposes.

Families in the support group have engaged in various fundraising activities. In 1998 they raised 100,000 German marks and gave research grants totaling 110,000 marks.

Our congratulations to the German Fanconi Anemia Association for all they have done to support families and promote scientific research. We are truly in awe of your many accomplishments which will benefit all of us! ◆

Fundraising Concerns
continued from previous page

Tom Plummer
Susan Sanchez
Shirley & Lynn Quilici
Marcia Reardon
Shirley & Ben Ricker
Therese & Terry Robertson
Rowland Family
Maureen & Glenn Russo
Lynn Mendenhall
Lori & Erik Salo
Andrea & Bob Sacks

*Note: In response to the Frohnmayer's annual letter, one donor, Phil Knight, CEO of Nike, gave our organization $1,000,000. In response to our telephone call of thanks, he stated that the Frohnmayer's letter convinced him that scientific progress was now advancing very rapidly, and this was the perfect time to push research ahead. ◆

A Child of Mine

Beth Janock read this beautiful poem at their daughter Carrie's funeral. She shares it with all of us.

"I'll lend you for a little time,
A child of Mine," He said.
"For you to Love the while she lives
And mourn when she is dead.

It may be six or seven years,
Or twenty-two or three,
But will you, till I call her back,
Take care of her for Me?

I cannot promise she will stay,
Since all from earth return.
But there are lessons taught down here
I want this child to learn.

I have looked the world-wide over
in search for teachers true.
And from the throngs that crowd life's lands,
I have selected you.

Now will you give her all your Love,
Nor think the labor vain,
Nor hate Me when I come to call
To take her back again?"

We fancied that we heard them say,
"Dear Lord, Thy will be done!
For all the joy Thy child will bring
The risk of grief we run.

We will shelter her with tenderness,
We will Love her while we may,
And for the happiness we have now,
Forever grateful stay.

But shall the angels call for her
Much sooner than we planned,
We shall brave the bitter grief that comes
And try to understand."

Regional FA Network Meetings

In our last newsletter we described the generous grant we received from the Meyer Memorial Trust to establish FA regional networks. We are happy to report that we have held a number of successful meetings over the past several months.

The Northeastern region met in Boston, Massachusetts, under the leadership of Deane Marchbein, MD. Families learned more about blood counts from Dr. Andy Eichenfeld, gained insights about complementation groups and gene therapy from Dr. Alan D'Andrea, and discussed coping skills with Nancy Cincotta.

The Central region met in Houston, Texas, at Baylor College. Blanche Alter, MD, presented helpful information about understanding blood counts and the basics of FA. Hagop Youssoufian, MD, talked about his research with the gene protein and what research hopes to accomplish. Adult FA patient Chris Hull shared experiences from his life, which the families deeply appreciated. Leslie Roy led a discussion on coping skills.

The Midwest region met at Silo's restaurant outside of Chicago, Illinois. This was a smaller gathering, where three families met to offer support and talk about fundraising options. Vicki Athens discussed her extensive fundraising experience. As a result of this meeting, all three of these families are undertaking fundraising events this fall.

The Western region met on October 2 at the VA Medical Hospital in San Francisco. Paula Guidara's sister, Carol Ceresa, who is the Clinical Nutrition Section Chief at this facility, obtained a conference room for our meeting. Twenty-two people representing ten families participated. Chris Hull shared his experiences as an adult with FA, and Carol Ceresa gave invaluable information about the importance of good nutrition and health. Dolores Ceresa, Paula's mother, provided a wonderful lunch and snacks. Families made the following comments:

"This meeting provided an opportunity to speak with other Fanconi parents and hear their experiences. The nutritional information was very useful."

"I appreciated learning more about issues that we need to prepare for."

"The fundraising talk was very helpful."

We will hold additional meetings over the next year. Please let us know if you have suggestions for topics or specific locations. ◆

Sacks Family Teaches Medical Students

On September 24, the Sacks Family (Bob, Andrea, Sean and Dani) taught first-year medical students at Johns Hopkins Medical School a class on Fanconi anemia. The family discussed basic facts about this illness and their own personal experiences. Bob Sacks writes "the students were amazed at our knowledge and our updating of the slides used by the professor." Blanche Alter, MD, attended the meeting and reminded the students how lucky they were to have a well-informed family. She advised them never to be threatened by a family's knowledge or to be so arrogant that they fail to listen to the life-threatening symptoms we all are living with. This is the sixth year the Sacks have given a class at Johns Hopkins on Fanconi anemia.

Congratulations to this wonderful family. The physicians they reach will undoubtedly be far more sensitive and better informed advocates for patients with our disease and many others! ◆

Grants Funded in 1999 (year to date)

Investigator: C. Anthony Blau, MD, Assistant Professor, Department of Medicine, Division of Hematology, University of Washington School of Medicine, Seattle, Washington

Title of Project: "In Vivo Selection for Fanconi Anemia"

Amount Funded: $73,537

Relevant to Research Initiative: Gene Therapy

Investigator: Madeleine Carreau, PhD, Department of Genetics, Hospital for Sick Children, Toronto, Ontario, Canada

Title of Project: "Hematopoietic Stem Cell Development in FANCC Mouse Model and Long-Term Curative Potential of Lentivirus-Targeted Gene Transfer"

Amount Funded: $47,026

Relevant to Research Initiative: Gene Therapy

Investigator: Eva Guinan, MD, Pediatric Oncology, Clinical Director, Bone Marrow and Stem Cell Transplantation, Children's Hospital, Dana-Farber Cancer Institute, Boston, Massachusetts

Title of Project: "Amifostine for the Treatment of Fanconi Anemia"

Amount Funded: $38,001

Relevant to Research Initiative: Treatment of Aplastic Anemia

Investigator: Maureen Hoatlin, PhD, Assistant Professor, Oregon Health Sciences University, Division of Hematology/Oncology, Portland, Oregon

Title of Project: "Production and Characterization of Polyclonal and Monoclonal Antibodies Specific for FAA and FAC"

Amount Conditionally Approved: $54,575

Relevant to Research Initiative: Causes of Bone Marrow Failure (BMF); Gene Therapy; Pathogenesis of Clonal Evolution, Myelodysplasia and AML

Investigator: Hans Joenje, PhD, Senior Scientist, Free University, Amsterdam, The Netherlands

Title of Project: "Complementation Analysis in Fanconi Anemia"

Amount Funded: $69,000

Relevant to Research Initiative: Causes of Bone Marrow Failure (BMF); Therapy for Acute Myelogenous Leukemia; Pathogenesis of Clonal Evolution, Myelodysplasia and AML

Investigator: Hans Joenje, PhD, Senior Scientist, Free University, Amsterdam, The Netherlands

Title of Project: "Cloning and Characterization of the Fanconi Anemia Genes FANCE and/or FANCF"

Amount Funded: $30,150

Relevant to Research Initiative: Causes of Bone Marrow Failure (BMF); Therapy for Acute Myelogenous Leukemia (AML); Gene Therapy.

Investigator: Chris Mathew, PhD, King's College, London, England

Title of Project: "Investigation of the Effect of Mutations in the Fanconi Anemia Genes on the Expression and Function of the FA Protein"

Amount Funded: $60,000

Relevant to Research Initiative: Causes of Bone Marrow Failure (BMF); Gene Therapy.

Investigator: Jordi Surrallés, PhD, Group of Mutogenesis, Department of Genetics and Microbiology, Universitat Autonoma de Barcelona, Barcelona, Spain

Title of Project: "Fanconi Anemia: Study on Telomere Shortening and Development of a Novel Molecular Cytogenetic Diagnosis"

Amount Funded: $41,750

Relevant to Research Initiative: Causes of Bone Marrow Failure (BMF); Prevention of Leukemia.

Investigator: G. Malcolm Taylor, MD, Immunogenetics Laboratory, Manchester, England

Title of Project: "Pilot Study to Assess the Risk of Early Onset Sporadic Childhood Leukemia Associated with Sequence Variations in the Fanconi Anemia Group G (FANCG) Gene"

Amount Approved: $35,000

Relevant to Research Initiative: Prevention of Leukemia; Therapy for Acute Myelogenous Leukemia (AML); Pathogenesis of Clonal Evolution, Myelodysplasia and AML

Investigator: John Wagner, MD, University of Minnesota, Minneapolis, Minnesota

Title of Project: "Treatment of Fanconi Anemia by Alternate Donor Hematopoietic Stem Cell Transplantation"

Amount Funded: $65,000

Relevant to Research Initiative: Bone Marrow Transplantation (BMT)

Investigator: Chris Walsh, MD, PhD, UNC Gene Therapy Center, University of North Carolina, Chapel Hill, North Carolina

Title of Project: "Genetic Correction of Fanconi Anemia Group C Patients"

Amount Funded: $57,199

Relevant to Research Initiative: Gene Therapy

1999 Year to Date

Total Approved and/or Funded: $665,420

Total Amount of Proposals Pending: $319,000

E-Mail Groups Formed

The FA Research Fund has established three e-mail groups, so that families can more readily give support to one another and share experiences and information. There is a group for teenagers and another for bereaved parents. A third group, now numbering over 100 families, shares information on a wide range of topics. A few physicians have given generously of their time and expertise to answer parents' and patients' medical questions. We quote from just a few exchanges:

Question: **Should FA patients be given flu shots?**

Answer: All FA patients should have flu shots unless they are profoundly immune suppressed. Therefore, for all intents and purposes, all patients should have flu shots unless they have undergone BMT or are about to undergo BMT. After BMT, their doctor will advise them as to when to start the flu shots again. However, it is helpful that all members in the immediate family get flu shots. Indirectly this may help reduce the exposure to the FA patient. (John Wagner, MD)

Question: **When is it appropriate to use neupogen?**

Answer: Neupogen is the same as G-CSF which is a growth factor to increase the white cell count. It is as yet unclear as to whether it will increase the risk of a cytogenetic abnormality.Your child should be followed closely for this complication should you start G-CSF. Use of G-CSF is a reasonable approach for the treatment of patients with isolated neutropenia (low white count). (John Wagner, MD)

Question: **Should FA patients be given the chickenpox vaccine?**

Answer: I would recommend the chickenpox vaccine. On the few patients who have had a titer done after a dose of the vaccine, the titers have been protective. So, a second dose is probably not necessary. (Richard Harris, MD) Note: Two parents wrote back to say that in the case of their children, the titer showed no antibodies, and a second shot was necessary. Judy and Jeff Hoffman wrote "Based on our personal experience and the severity of chicken pox with FA kids, it is our recommendation that all patients should have a titer done."

Question: **What is meant by a 10/10 match for a bone marrow transplant? So far I have only known of 6/6. What are the 4 additional factors?**

Answer: There are numerous antigens that we test for: HLA A, B, C, DR, DQ, DP. Hence, a lab may report up to 12. The significance of matching at 10 or 12 antigens is unknown for FA. Only A, B and DR matching are of importance to the best of our knowledge right now. (John Wagner, MD)

Question: **How many transfusions can my daughter have before a bone marrow transplant?**

Answer: The effect of RBC/platelet transfusions on transplant outcome is not clear in my mind. The concern is based on data in patients with severe aplastic anemia which indicates that patients transfused with >20 RBC and/or platelet units have a greater risk of graft rejection. This observation held up only in patients transplanted with sibling marrow after a preparative therapy consisting of cytoxan alone. The association disappeared in patients prepared with cytoxan and total body irradiation.

Data in FA patients is less convincing. Gluckman et al. found an association between pretransplant platelet count and survival. Those with the lowest platelet count had a significantly worse outcome after sibling donor BMT as compared to those with a higher platelet count. Why was this? One explanation is that those with the lowest platelet counts were likely to have received the highest number of transfusions, but this does not prove that there is any direct association. For example, it may simply mean that those transplanted with the lowest platelet counts may have had a longer duration of bone marrow failure which, in turn, increased the risk of infection.

In our own experience at Minnesota, we cannot yet detect a clear association between number of transfusions and any outcome after unrelated BMT. However, this is difficult to assess since most of my patients have had 20-100+ transfusions. Nonetheless, the fewer the transfusions, the better. The more red cell transfusions, the more iron in your body, and this is harmful. The more platelet transfusions, the more likely you will become unresponsive to platelet transfusions in the future.

Transfusions should be performed thoughtfully. If transfusions are absolutely needed, the products should be white cell depleted, CMV (cytomegalovirus) negative (if the patient is CMV negative), and irradiated. (John Wagner, MD)

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E-Mail Groups Formed

continued from page 24

Question: **When should one be given CMV negative blood products?**

Answer: We give CMV negative filtered blood products to FA patients who are CMV seronegative, but CMV unscreened filtered blood products to those who are CMV seropositive. Soon our center will be switching to "CMV-safe" blood products. These are blood products which have been filtered at the time of collection (not just prior to release from the blood bank, which is the current practice). Filtering at the time of collection from the donor effectively removes the white cells which carry the CMV virus.

Many centers are switching to this approach. This may even be safer than CMV-negative blood products which are filtered at the time of release from the blood bank. Why? Because donors can be seronegative but still carry the virus. Their infection may have been so recent that they have not yet developed antibodies to the virus (and thus are seronegative by the testing done). Platelets which are filtered at the time of use may have broken up white blood cell fragments, since the platelet packs may be kept at room temperature on a rocker for several days before use. These broken up white cell fragments may contain the CMV virus, and these fragments may make it through the filtering process and, thus, be in the final platelet product given to the patient. Filtering blood products at the time of collection removes the white cells before they have a chance to deteriorate and break up into little pieces of membrane. Thus, filtering done at the time of collection effectively removes the virus from the blood product. (Richard Harris, MD)

Question: **Should we use blood products from family members for our FA child?**

Answer: Use of blood products from family members should be avoided unless you know for sure that there are no related donors. Once you have determined that there is no related donor, then it is not an issue. (John Wagner, MD)

Question: **Is a 6/6 sibling cord blood transplant better or worse than a 6/6 sibling bone marrow transplant?**

We received two thoughtful answers to this question.

Answer: I would readily take the cord blood. However, if the choice is between an unrelated cord blood vs. a matched sibling donor, I would clearly take the matched sibling donor. (Richard Harris, MD)

Answer: Dr. Gluckman and I recently completed the first comparative study between HLA matched sibling umbilical cord blood (UCB) and HLA matched sibling bone marrow (BM) using the databases of the International Bone Marrow Transplant Registry and EuroCord Registry. The results tell us four things: 1) the risk of graft versus host disease is significantly lower with UCB; 2) the risk of graft failure is greater with UCB; 3) time to white cell recovery after transplantation is longer after UCB transplantation; and 4) survival is exactly the same between UCB and BM transplant recipients.

The above data came primarily from patients transplanted for leukemia, not specifically FA. Both kinds of transplants carry risks. However, if your child is young, has not been heavily transfused and has bone marrow failure without myelodysplasia or leukemia, then your child will likely do well with either the UCB or marrow. (John Wagner, MD) ◆

The Eleventh Annual International FA Scientific Symposium

DECEMBER 1-2, 1999

Marriott Hotel
New Orleans, Louisiana

Timed to precede the 41st Annual Meeting of the American Society of Hematology, December 3-7, 1999

Family Meeting

continued from page 1

presentations. We describe a few highlights.

Attendees agreed that the most exciting new information came from three presentations on new methods for transplanting patients with unrelated or mismatched bone marrow donors. In the past, failure to engraft has been the major obstacle to success. Very early results suggest that adding the drug, fludarabine, to the protocol might improve survival rates.

Farid Boulad, MD, from Memorial Sloan-Kettering Hospital, New York City, reported on two successful transplants using fludarabine. The first child initially failed to engraft a 4/6 cord blood transplant and was subsequently given peripheral blood stem cells from a 4/6 relative. Fludarabine was added to suppress the host marrow. This child is alive and well fifteen months post transplant. A second FA child was given a peripheral blood stem cell transplant from his 4/6 mismatched sister. Fludarabine was added to the protocol. This child engrafted and is alive and well five months post transplant.

John Wagner, MD, Minnesota reported on four FA patients with unrelated donors (two matched at 6/6 antigens; two at 5/6) who all engrafted using fludarabine. All four are alive and well. Since his presentation, Wagner has transplanted two additional patients with alternative donors, and both engrafted.

Richard Harris, MD, Cincinnati, recently performed an unrelated, 6/6 transplant using fludarabine and the protocol he uses for matched, sibling donors. This patient engrafted and is alive and well five months post-transplant. All three physicians reported on low or no toxicity with fludarabine. The specific protocols used (amount of cytoxan, radiation and fludarabine) varied considerably from one center to another (see articles on pages 4 and 5).

Harris discussed survival rates in matched sibling donor transplants. Results have improved steadily and are now 86% at the Cincinnati transplant center.

Margy MacMillan, MD, Minnesota, sent a questionnaire to FA patients who were at least one year post-transplant. Eighteen responded. All of the complications noted were experienced in 10 patients. Eight reported having no chronic medical problems. Most related that their school ability, athletic ability, and friendships were quite acceptable. Satisfaction with personal appearance rated somewhat lower. In general, patients who do well after transplant do very well. Patients with chronic graft vs. host disease reported somewhat restricted physical ability but ranked their quality of life as very good.

Hans Joenje, PhD, Amsterdam, reported that there may be more than 8 FA complementation groups, but much work remains to pin them down. He also stated that there is a strong candidate gene for FANCF. Confirmation of its status should come soon.

Jane Sande, MD, Children's Hospital Medical Center, Cincinnati, Ohio, reported on the use of immunochemotherapy to both prevent and treat leukemia. These drugs are directed against the proteins (antigens) on leukemia cells and can prevent AML in mice. Theoretically, patients in remission from AML or those with a very small disease burden could be treated with these new drugs in an effort to prevent relapse.

Christopher Walsh, MD, PhD, University of North Carolina, continues to demonstrate that he can "cure" Fanconi anemia in the bone marrow of mice. He is confident that he is able to isolate and correct a very early human progenitor cell. Walsh has experienced frustrations in obtaining final approval for a human gene therapy trial, but now anticipates that this trial will begin in late 1999 or early 2000.

Sarah Jane Schwarzenberg, MD, University of Minnesota, gave a comprehensive, informative presentation on analyzing and treating children with serious gastrointestinal problems. Her presentation was considered highly useful to the many parents whose children have serious eating and digestive disorders.

Blanche Alter, MD, and **Alan D'Andrea, MD, PhD**, Boston, gave very useful information to families new to this disease. These efforts to explain basic information to families overwhelmed with new medical terminology and concepts were extremely well-received by all in attendance.

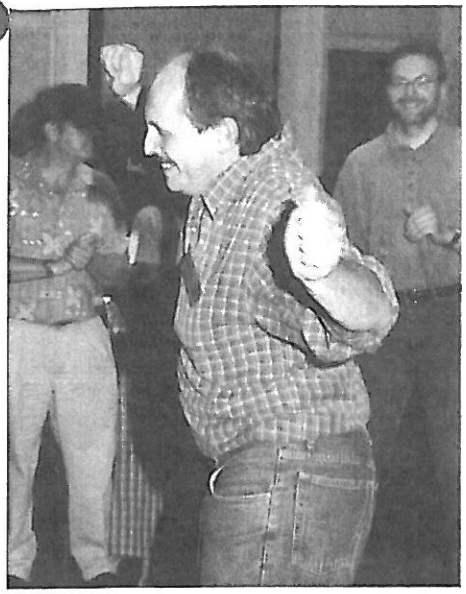
Debbie Justice provided useful guidelines on obtaining needed resources and support services for children with disabilities.

Carol Siniawski, FA parent, presented a flow chart she developed with Dr. Richard Harris, which gives guidance to parents concerning when to consider various treatment options. Carol will gladly share this chart with FA families and treating physicians.

The last two days of the Family

continued on page 2

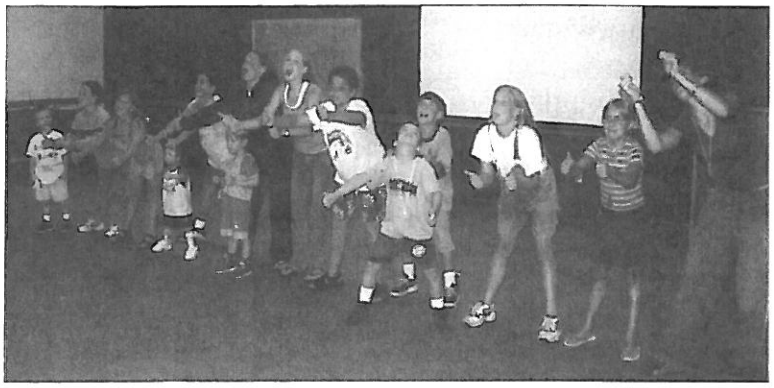
Fun Events at the Family Meeting



Ralf Dietrich

Karaoke night, L to R: Mary Heath, DeeDee Burzynski, Beth Vangel and Diana Fitch

Talent show, L to R: AJ Eichenfield, Kyle Burzynski, Pierre Lauzier, Sylvie Lauzier, Christian Collins and Colby Collins



Kids and volunteers having fun.

Karaoke, L to R: Tom Plummer, Mike Vangel and Pat Gleason

Volunteers and young adults at FA Family Meeting

Payroll Deductions for United Way and Combined Federal Campaign

Many friends and co-workers give to important causes each year by using United Way or the Combined Federal Campaign. Several FA families have found that asking co-workers to support our research fund through either of these campaigns has been a successful and an easy way to raise needed funds for research.

To give through United Way write "FA Research Fund" in the donor choice portion of the UW deduction form. Federal employees can choose to give to our research fund by writing in our CFC number 1363 on the CFC deduction form.

For some, it might be possible to speak briefly at a staff meeting. Consider handing out copies of the *BusinessWeek* July 12 article and/or showing our CBS film. This takes much courage to do, but the results could be most gratifying. ◆

Family Meeting

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Meeting focused primarily on issues of living with Fanconi anemia. Nancy Cincotta has endeared herself to all of us with her warmth, understanding, and caring support. She led sessions on day-to-day coping with FA, bereavement issues, and talking to children about this disease. She also led groups for older FA children and teens on living with this disorder. As always, feedback from Nancy's sessions was uniformly positive.

Many physicians gave generously of their time and expertise outside of their specific lectures. Some stayed for the entire Family Meeting to listen to concerns and answer questions on an individual basis. Consultation provided to families proved crucial to those faced with very difficult decisions. We are incredibly grateful to our wonderful, caring experts who give so generously of their time and knowledge. They make our decision-making burdens much easier to bear. ◆

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